HIV CURRICULUM
FOR THE HEALTH PROFESSIONAL

BAYLOR INTERNATIONAL PEDIATRIC AIDS INITIATIVE
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BIPAI
Baylor International Pediatric AIDS Initiative

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Baylor College of Medicine

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SECURE THE FUTURE INITIATIVE

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Introduction

"The global AIDS epidemic is one of the greatest challenges facing our generation. AIDS is a new type of global emergency – an unprecedented threat to human development requiring sustained action and commitment over the long term.” These are the words of Kofi Annan, Secretary-General of the United Nations. Statistics compiled by UNAIDS confirm this statement. Since the start of the pandemic, almost 60 million people have been infected with HIV/AIDS, more than half of them in southern Africa. HIV/AIDS is the leading cause of death in this region; worldwide it is the fourth-largest killer. It is estimated that 37.8 million people are currently living with HIV, indicating that the virus is not yet under control.

Nurses have been the front-line medical professionals responding to the pandemic, providing hands-on care to patients and comfort to families on a daily basis. In order to achieve the sustained action and long-term commitment that Kofi Annan has called for, it is critical that nurses be honored, respected, and valued for their professional and personal contributions to people living with HIV/AIDS. It is also critical that they be educated about the disease and empowered to serve as advocates for their patients and themselves. To this end, the first edition of this HIV training curriculum was written specifically for nurses. But health professionals of all kinds have sought out and benefited from the information it provided. The second edition of the curriculum was written with the intent of providing nurses, physicians, social workers, counselors, home-care workers, and students with the information they need to understand HIV and to offer the highest standard of compassionate care for HIV-infected patients. This revised, third edition of the HIV Curriculum for the Health Professional updates these tools with the latest research and practice insights presented for immediate, effective use in the field.

This HIV training curriculum was made possible by start-up funding from the Bristol-Myers Squibb Company’s SECURE THE FUTURE™ initiative. Working in partnership with the African nations of Botswana, Lesotho, Namibia, South Africa, and Swaziland, SECURE THE FUTURE™ is designed to find solutions for the management of HIV/AIDS in women and children and to provide resources to improve community education and patient support. The largest commitment of its kind ever made, the Bristol-Myers Squibb SECURE THE FUTURE™ program is intended to complement the broader efforts of governments to identify relevant and sustainable responses to the HIV/AIDS pandemic. Additional sponsorship for development, printing, and distribution of this edition of the HIV Curriculum for the Health Professional was provided by the Fogarty International Center of the National Institutes of Health and the U.S. Centers for Disease Control and Prevention Global AIDS Program.
The curriculum was developed, in collaboration with international partners, by the Baylor International Pediatric AIDS Initiative (BIPAI), a multidisciplinary team of health professionals based at the Baylor College of Medicine. Prior to launching this curriculum project in 1999, the BIPAI team had experience with health-professional education in developing-country settings such as Romania, Mexico, and Panama. The idea of creating a comprehensive curriculum on HIV/AIDS for nurses was a direct result of lessons learned from those early experiences. In order to develop a curriculum that would be appropriate for use in southern Africa, we conducted a needs assessment in the region and relied heavily on our African partners for content and feedback. The curriculum that follows is the product of years of close collaboration between BIPAI and our African colleagues.

After pilot-testing in Africa and substantial revision, the first edition became available in March 2001. The second edition followed in January 2003. Since then, nearly 6,000 copies of the curriculum have been distributed free of charge in 51 nations. During 2002 and 2003, BIPAI partnered with the Southern African Development Community AIDS Network of Nurses and Midwives (SANNAM) to conduct a series of train-the-trainer workshops for nurses in the 14 SADC countries. In addition, a series of train-the-trainer workshops for health professionals was offered in Uganda in 2004 and 2005 under sponsorship by the U.S. Centers for Disease Control and Prevention Global AIDS Program. Many of the changes and updates to the current edition of the HIV training curriculum are based on questions and feedback received during those training sessions. We are indebted to the workshop organizers and participants, who taught us how to organize and present the information in the most logical sequence and the clearest language.

This curriculum reflects our expertise and experience in pediatrics, but it is designed to improve the care of patients of all ages. It begins with a module on the global epidemiology of HIV, including information on the origin of HIV, the ways in which HIV is commonly transmitted, and the global spread of the disease. The next module describes the pathophysiology of HIV, including the normal immune system, the effects of HIV on the immune system, and the HIV life cycle. A module on

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The revised HIV curriculum is designed to improve the care of patients of all ages around the world.
the diagnosis of HIV infection explains the diagnostic
tests and clinical findings that identify the presence of
HIV. A series of modules on clinical manifestations of
HIV covers oral and cutaneous manifestations, HIV-
associated malignancies, neurologic and psychiatric
manifestations, pain as a manageable symptom of
HIV disease, gastrointestinal signs/symptoms, and
common illnesses associated with HIV. Other
modules describe the prevention and management of
common opportunistic infections and of tuberculosis.
The module on antiretroviral therapy has been
thoroughly updated and is complemented by a
discussion of metabolic changes related to ARV. The
curriculum includes in-depth reviews of child growth
and development, immunizations, and nutrition as
they relate to HIV. Modules on the prevention of
sexual transmission, prevention of perinatal
transmission, and standard precautions and post-
exposure prophylaxis are included. One module
explores complementary and alternative medical
approaches to HIV. Finally, the many ways in which
HIV affects people’s lives are explored in modules on
HIV counseling principles and skills, HIV pre- and
post-test counseling, psychosocial issues for adults and
children, and psychosocial interventions.

In writing, reviewing, piloting, repeatedly revising,
and implementing this curriculum in workshops in 15
African countries, we have followed a process of
collaborative curriculum development guided by a
number of principles. The first principle is
partnership. From the start, we sought to identify
collaborating organizations and institutions, and key
individuals within those organizations and institutions,
to partner with us in this endeavor. Our goal was to find
a way to mesh our strengths in health-professional
education and HIV care and treatment with our
collaborators’ expertise and firsthand knowledge of

the AIDS epidemic in resource-limited settings. We
have relied on our partners to co-author many of the
curriculum modules, and we have received their
feedback on all modules. This feedback has included
both formal, written feedback during the curriculum-
development phase and informal, oral feedback in the
form of questions and comments during the many
nursing workshops held throughout the region.

The second principle is flexibility. We have designed
the curriculum in a modular format so that it can be
adapted for use in different ways. One instructor
might choose a single module to supplement
information on HIV in a community nursing course.
Another might choose a group of modules to provide
a more complete review of, for example, HIV clinical
manifestations. All the modules can be used together
to form a comprehensive semester-long specialty
course on HIV.

The third principle is bi-directional enrichment. We
have learned at least as much from working with our
collaborators as they have learned from us. From the
pilot workshops in South Africa and Swaziland in
2000, which were designed to test draft curriculum
modules and to receive feedback on their
appropriateness for Africa, to the recent workshops in
Uganda, which allowed us to fine-tune the material,
we have learned something new about effective
presentation of information during every collaborative
experience. All workshops have been jointly taught by
U.S. and African faculty. Focus groups held in
conjunction with these workshops gave us the
opportunity to sit quietly and listen to the stories and
experiences of our health-professional colleagues in
Africa. Ideas and approaches to solving problems were
exchanged that have directly impacted our approach
to the management of children with HIV in our own
clinic in the United States.
Finally, the overall aim of this program is capacity building. Modules have been designed to be as complete and user-friendly as possible, providing objectives, key points, case studies, review questions, exam questions, and references. Our hope is that this comprehensive yet flexible resource will provide educators with new tools to improve the way HIV is taught and treated.

Acknowledgments

We are indebted to our international cadre of partners, who have shaped each module in this publication. We would not have undertaken the development of a full curriculum on HIV/AIDS without the support and encouragement of our nursing partners in Africa. The third edition, even more than the previous two, represents a global effort by talented authors and contributors from partner countries the world over.

Special thanks to graphic artist Mary McNeight, who designed this book; to editor Brian Howard, who reviewed and improved each module; and to photographer Smiley N. Pool, who provided many of the images, including the cover photo.

Over the past several years, the education team of the Baylor International Pediatric AIDS Initiative has worked intensely in the development and refinement of this material. Friendships have been forged and have deepened as we journeyed together, both literally and figuratively, in the development of this curriculum. We are grateful to all who have made this incredible experience possible.

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THE EPIDEMIOLOGY OF HIV

The purposes of this module are to:
1. Review the most recent data on the global impact of the HIV/AIDS pandemic.
2. Summarize theories about the origin of HIV.
3. Review the modes of HIV transmission.
4. Identify risk behaviors that facilitate HIV transmission.
5. Analyze societal factors that are contributing to the expanding pandemic.
6. Analyze the impact of HIV on the future of people living in regions with a high HIV disease burden.

Key Points
1. HIV is a preventable infection.
2. The global HIV epidemic is not under control.
3. Approximately 90 percent of all HIV-positive people in the world live in developing countries.
4. The life expectancy of people in southern Africa has decreased significantly because of HIV/AIDS.
5. Numerous societal factors are driving the spread of the epidemic, including people on the move, complex emergencies, cultural factors (such as the status of women), poverty, stigma, and denial.
6. HIV is most commonly transmitted during high-risk events such as unprotected sex with an infected person, blood-to-blood contact with an infected person, and pregnancy, childbirth, and breastfeeding by HIV-positive women.
7. About 15 million children under age 18 have lost at least one parent to AIDS.

Overview
Epidemiology is the study of the determinants and distribution of disease. In a world characterized by the rapid movement of people, goods, and information, HIV/AIDS has rapidly touched nearly every nation on this planet. This chapter considers the epidemiology of one of the most devastating and complex infectious diseases of the late 20th and early 21st centuries.

Global HIV/AIDS Statistics
According to UNAIDS, at the end of 2004, 39.4 million people worldwide were living with HIV or AIDS. Most of them reside in the developing world; about 66 percent live in sub-Saharan Africa. In 2004, nearly 5 million people were estimated to be newly infected with HIV, among them 640 000 children under age 15. This means that in 2004 there were nearly 13 700 new HIV infections globally per day, along with approximately 3.1 million AIDS-related deaths. It is believed that there have been approximately 20 million AIDS-related deaths since the disease was first recognized in the early 1980s. The numbers of incident (new) infections and deaths have remained stable over the past few years,
indicating a lack of progress in turning the tide against the pandemic. The following provides a snapshot of some of the more notable HIV epidemics around the world. Much of this information is excerpted from a 2004 report by UNAIDS.\(^1\)

**Sub-Saharan Africa**

HIV/AIDS is the leading cause of death in sub-Saharan Africa. AIDS killed 2.3 million Africans in 2004. The estimated 3.1 million new HIV infections in sub-Saharan Africa in 2004 mean that as many as 27 million Africans may now be living with the virus.\(^1\) Most are unaware that they are infected.

Life expectancy at birth in southern Africa – which rose from 44 years in the early 1950s to 59 in the early 1990s – is expected to drop to just 45 years between 2005 and 2010 because of AIDS. In contrast, South Asians, whose life expectancy had barely reached 40 in 1950, are living 22 years longer than their counterparts in southern Africa.

African epidemics are diverse, varying by country and region. A multitude of socioeconomic factors are believed to have contributed to the aggressive spread of HIV, including migratory labor, the status of women, poverty, high rates of other sexually transmitted infections (STIs), ineffective leadership, and political instability.

**Women and Children**

Among Africans ages 15-24, women are 2.5 times as likely to be HIV-infected as their male counterparts, according to six recent national surveys. Among all African adults, new information suggests that HIV infects between 12 and 13 women for every 10 men. There are a number of reasons why prevalence is higher among females than among males in this region, including the greater efficiency of male-to-female HIV transmission through sex and the younger age at initial infection for women.

UNAIDS estimates that only 1 percent of pregnant women in heavily affected countries have access to services aimed at preventing mother-to-child HIV transmission.\(^1\) This public health failure has daunting implications for children, maternal health, and future generations in these countries.

Worldwide, of the 640,000 children under age 15 who were newly infected with HIV in 2004, more than 90 percent were babies born to HIV-positive women. These infants acquired the virus in utero, at birth, or from their mothers’ breast milk.

Evidence shows that HIV also impairs women’s fertility. Once infected, a woman can be expected to bear 20 percent fewer children than she otherwise would have.

**Eastern Europe**

With an estimated 210,000 new infections in 2004, Eastern Europe is believed to have the fastest-growing epidemic in the world. UNAIDS estimated that 1.4 million people were living with HIV/AIDS in Eastern Europe and Central Asia in 2004.

Factors contributing to the epidemic’s growth in the region include trafficking in prostitutes, other heterosexual sex, and intravenous drug use.

**South and Southeast Asia**

This region contains the world’s two most populous countries, India and China. Both have escalating epidemics. In absolute terms, this region is believed to contain more than 7 million HIV-infected people – the second-largest number of people living with HIV/AIDS outside of sub-Saharan Africa.

In China, the epidemic is being spread through intravenous drug use, the selling of unscreened blood plasma for income, and heterosexual sex. In India, the epidemic is driven by heterosexual sex and to a smaller degree by men who have sex with men and intravenous drug use.

Knowledge about HIV/AIDS in the region is believed to be poor, a contributing factor to disease spread.

**Caribbean**

With regional prevalence estimated at 2 percent to
3 percent, the Caribbean is the most affected region in the world outside of southern Africa. More than 5 percent of the Haitian population is believed to be HIV-infected.

The Caribbean epidemic is driven largely by heterosexual sex and the commercial sex industry.

It is important to consider that every country in the world was, at some point, a low-prevalence country. HIV prevalence among pregnant women attending antenatal clinics in South Africa was less than 1 percent in 1990, and today it is around 20 percent. To understand this pandemic, we must examine the origins of the disease as well as the numerous biological and socioeconomic factors that foment its growth.

**Where Did HIV Come From?**

AIDS did not come to wide public attention until mid-1981, after clusters of deaths from *Pneumocystis carinii* pneumonia (PCP) and Kaposi’s sarcoma were reported among young, previously healthy homosexual men in New York City, Los Angeles, and San Francisco. Previously, PCP had been diagnosed only in people who were immunocompromised. The aggressive form of Kaposi’s sarcoma ravaging young men in the United States had previously been observed among older men of European or Mediterranean descent.

A summary of these early cases was published in 1982 in a journal called *Morbidity and Mortality Weekly Report (MMWR)*. This elicited similar reports from France, the Caribbean, and Central America. In the United States, the disease was first called “gay cancer” and then labeled “gay-related immune deficiency” because it was homosexual men who first exhibited characteristic symptoms. In some areas in Africa, the disease was called “slim” or “slim disease” because of the profound wasting and the association of death with progressive weight loss and diarrhea. About the same time, pediatric immunologists noted increased numbers of infants with unexplained immune problems.

It is widely believed that HIV is the result of an animal-to-human (zoonotic) transfer of a simian immunodeficiency virus. HIV-1, the retrovirus that to a simian immunodeficiency virus (SIV) that infects chimpanzees. HIV-2, which is prevalent in West Africa and has spread to Europe and India, is almost indistinguishable from an SIV that infects sooty mangabey monkeys. An animal source for a new human infection is not unique to HIV. The bubonic plague in Europe was transmitted from rodents. Influenza reached humans via pigs. Variant Creutzfeldt-Jakob disease in the United Kingdom was transmitted to humans through consumption of infected “mad cows.” Like these other infections, once HIV was established in humans, it began to follow human habits and movements.

**Modes of Transmission**

The following fluids from an infected person contain HIV:

- Blood
- Semen
- Vaginal fluid
- Breast milk

HIV is usually transmitted via:

- Sex with an infected person.
- Exposure to the blood of an infected person through contaminated needles and syringes, tainted transfusions, the sharing of unsterilized razors during cutting practices, or other mechanisms.
- Pregnancy, birth, or breastfeeding from infected mother to child.

While HIV antibodies may be present in saliva, tears, and urine, there is no epidemiologic evidence that contact with these fluids has resulted in HIV infection. HIV is not transmitted by the respiratory route or by casual contact in any setting, whether household, social, work, school, or prison. HIV is not transmitted by food, water, toilets, swimming pools, shared eating and drinking utensils, or other objects such as second-hand clothing or telephones.
Insects such as mosquitoes do not transmit HIV. When a mosquito bites, it sucks a small amount of blood from the person; the mosquito does not deposit any blood into the person.

It is important to emphasize that this disease is not transmitted through casual contact. All people need to be aware of how HIV is and is not transmitted, to reduce high-risk behaviors and to avoid unnecessary fears and stigmatization of HIV-infected people.

**Behavioral Risk and Vulnerable Groups**

Certain behaviors place people at greater risk of HIV infection. These include sex with an infected person, blood-to-blood contact with an infected person, and injection drug use. Groups of people who engage in these high-risk behaviors (or who are involved in high-risk events such as childbirth and breastfeeding) are considered vulnerable to infection. The following section provides more information about high-risk events and behaviors as well as vulnerable groups.

**Exposure Through Sexual Contact**

Sexual intercourse is the major route of transmission of HIV throughout the world.\(^4\) The precise risk of HIV transmission from a single act of sexual intercourse with an infected person is not known. While some people have had multiple sexual contacts with an infected person without acquiring HIV, others have become infected from a single sexual encounter. The probability that a person has acquired a sexually transmitted disease is, in general, proportional to the number of sexual partners that person has had in recent years. A study in Rwanda\(^6\) looked at behavioral risk factors for HIV infection and found that infection rates were higher among women who were single and reported having more than one lifetime sexual partner. Rates of infection were lower among married women and women in monogamous partnerships. However, even among “low-risk” women, HIV prevalence was about 20 percent. For some women, a steady male partner who has sexual contact outside of the primary relationship is the only source of HIV exposure. HIV is not just a disease of prostitutes and sexually “promiscuous” individuals.

Among men, several recent studies have shown that those who are circumcised are at lower risk of HIV infection than those who are not circumcised.\(^7,8\)

After controlling for behavioral differences between circumcised and uncircumcised men, researchers in India found that the removal of the foreskin resulted in...
in a nearly seven-fold reduction in the likelihood of infection. A similar difference in the incidence of other STIs between the two groups of men was not observed.

**Exposure Through Blood or Blood Products**

Direct exposure to HIV-infected blood, whether through a tainted blood transfusion, the use of non-sterile razor blades for ritual scarring or traditional healing, or “needle-stick” accidents suffered by health care workers, is an efficient way to transmit HIV.

Compared to industrialized nations, countries in sub-Saharan Africa experience a greater amount of transfusion-associated HIV transmission due to a higher prevalence of HIV infection in donor populations, a lack of HIV antibody screening in some areas, and a higher residual risk of contamination in blood supplies, despite antibody screening.

**Exposure Through Pregnancy, Birth, or Breastfeeding**

Transmission of HIV from mother to infant can occur at any point during pregnancy, labor, and delivery, or through breast milk after the baby is born. Without antiviral treatment, the rate of transmission of HIV from mothers to babies varies, depending on the region, from about 20 percent to 30 percent. Although it is known that HIV can be transmitted early in pregnancy, 50 percent to 80 percent of transmissions from mother to child are believed to occur at or around the time of delivery. Furthermore, epidemiologic data indicate that breastfeeding approximately doubles the risk of HIV transmission. Prevention of perinatal HIV infection is one of the most powerful methods available to reduce the global impact of the virus. Please see the chapter on prevention of mother-to-child transmission of HIV for more information on this topic.

**What Drives the Epidemic?**

Now that some basic information on the epidemiology, origins, and modes of transmission of HIV have been described, we will consider some of the numerous societal factors that make people vulnerable to HIV. Epidemics are the result of complex interactions between biology and the environment. The principal societal factors driving the spread of this disease are summarized below.

**People and Goods on the Move**

We are living in a global economy, with more people traveling than ever before. The most common reason for people to leave their homes and families is to seek work. HIV/AIDS has followed the routes of trade and commerce, the movement of labor, goods, and services. These are routes of legitimate commerce as well as illegal activities, such as trafficking in humans and illicit drugs. Migrant labor plays a particularly important role in southern Africa, where a thriving mining industry attracts workers from all over the region. Most miners live in single-sex dormitories, often hundreds of miles from their families. Many of these miners engage in sex with prostitutes, contract HIV, and transport the infection back home to their wives, who may in turn transmit the virus to infants during pregnancy. In the mining town of Carletonville, South Africa, close to six of every 10 women in their early 20s are infected with HIV.

**People in Conflict and Complex Emergencies**

War and instability are conducive to the spread of AIDS. The military can have a powerful impact on the general population’s exposure to HIV, whether through commercial sex, casual and consensual sex with other soldiers or civilians, or rape in times of conflict. Moreover, war and conflict often weaken or destroy public health systems, legitimate commerce, safe food supplies, and stable social arrangements. In some cases (Sierra Leone is an example), war has had the effect of putting a brake on the spread of HIV. This is likely because the conflict restricted movement within the country, and cross-border migration and trade became extremely difficult. In these situations, AIDS prevention efforts are a critical part of the reconstruction and normalization process.
Cultural Norms and the Status of Women
Cultural barriers often prevent women from taking necessary precautions to protect themselves and their babies from HIV. Domestic violence reduces women’s control over their exposure to HIV. In settings where supremacy and violence are regarded as a man’s right, women are seldom able to question their husbands about extramarital encounters, negotiate condom use, or refuse sex. In a recent study from Soweto, South Africa, 1366 women who presented for antenatal care were interviewed privately about their experiences of partner violence and their perceived power in sexual relationships. Their HIV status was also determined. Researchers found that women who reported having been physically or sexually assaulted by an intimate male partner were more likely to be HIV-infected. A high degree of male control in relationships was also associated with increased risk of HIV infection among women.11

People in Poverty
AIDS tends to disproportionately affect the politically and economically disenfranchised. All over the world, HIV has settled into communities where people are poorly educated and living in poverty. Sadly, it is often poor, uneducated, and unempowered women and children who are most susceptible to this disease. Millions of people are vulnerable to HIV because they do not know the basic facts or because their life choices are constrained by poverty. Poverty can force women into situations where prostitution or “transactional sex” (sex exchanged for gifts and favors) become their only sources of income.

Stigma and Denial
In many regions, denial and silence regarding HIV have been the norm for years. People are reluctant to admit that a fatal disease spread by behavior branded “immoral” is rampaging through their community or their country. People who purport to explain the transmission of HIV among different populations but limit their analysis to such factors as sexual promiscuity and drug use tend to stigmatize or blame certain groups while failing to explain or understand larger issues involved in disease transmission. As mentioned earlier, it is not necessary to have multiple partners to acquire HIV, and nor is everyone who has multiple partners HIV-infected.

Stigma and fear are fueled by ignorance. Failure to provide accurate information about HIV leaves an information vacuum that is often filled by malevolent rumors and misinformation regarding disease spread, prevention, and treatment.

Denial about HIV can have the effect of stigmatizing HIV/AIDS and creating an environment conducive to the continued spread of the virus. People living in such circumstances are less likely to want to know their HIV status, even if counseling and testing are offered. For example, people may be less likely to raise the issue of condom use before sex because they fear that their partner might interpret this as an indication of possible HIV infection. Fear of revealing her HIV status to friends and family may prevent an infected woman from giving her baby replacement feeding as a way to avoid transmitting the virus through breast milk. Prevention efforts are severely undermined by an atmosphere of persecution, denial, and misinformation.

Prevention and Control
While there is hope that an effective anti-HIV treatment will be made available on a wide scale in the future, a cure or vaccine for AIDS is unlikely within the next several years. Therefore, prevention and treatment remain the most realistic strategies for dealing with the HIV epidemic.

Success in prevention requires consistent and persistent intervention over time, a clear understanding of the realities of target populations, and empowered participation by those affected by the interventions. A number of barriers to successful prevention efforts have been identified around the world. These include:
- Regional and national political instability
- A combination of growing populations and
shrinking resources

- The presence of other endemic health problems (including childhood diseases, malaria, and tuberculosis)
- Poor governance, including inefficiency and corruption
- Apathy and silence at the international, national, and local organizational and governmental levels
- Lack of domestic spending on health care

HIV is clearly a preventable disease. If everyone who is currently infected did not transmit the virus to anyone else, the disease would eventually burn out and disappear. Stopping transmission through behavior change is a complicated challenge, but data indicate that HIV prevention and counseling efforts can be effective. A longitudinal study in Zambia of about 12,000 heterosexual couples evaluated the impact of prevention education and counseling on disease transmission. At baseline, 57 percent of the couples were concordant (both partners) HIV-negative, 23 percent were concordant HIV-positive, and 20 percent were serodiscordant (one partner was HIV-negative, the other HIV-positive). All couples were counseled about HIV prevention and provided with condoms. Long-term follow-up showed reduced HIV acquisition rates among concordant negative couples, from approximately 3 percent to approximately 0.5 percent per year, and among serodiscordant couples, from about 23 percent to less than 10 percent per year.

Uganda, which has a strong prevention and control campaign, has been successful in reducing rates of HIV transmission. President Yoweri Museveni is widely credited for his political leadership in Uganda’s efforts against the AIDS pandemic. The ABC Campaign, as it is known, emphasizes the following prevention messages: “Abstain, Be faithful, and use Condoms.” Museveni has urged other African leaders to follow his example and speak out on AIDS to help contain the spread of the disease. He is quoted as saying: “I encourage all the leaders in Africa to make alarm, a loud one. In our villages, when there’s danger, you make alarm. So when you see a lion coming and you don’t make alarm, you’re not helping the village.”

**Treatment and Its Influence on the Epidemic**

Fortunately, antiretroviral therapy is becoming increasingly available to people in developing countries. UNAIDS has launched an ambitious “3x5” program aimed at providing 3 million HIV-infected people with highly active antiretroviral therapy (HAART) by 2005. However, with an estimated 38 million people infected with HIV/AIDS, even the most ambitious international program to date has only the modest goal of serving less than 8 percent of the world’s HIV-infected population. Nevertheless, access to treatment is clearly on the rise.

Some health professionals believe that treatment itself can help eliminate stigma. When treatment is available and AIDS is no longer considered a death sentence, more people may be motivated to seek counseling and testing. Knowing one’s status is more acceptable when treatment can improve and prolong life. We have seen evidence of this at the Botswana-Baylor Children’s Center of Excellence (BBCCOE), an outpatient clinic for HIV-infected children and their families in Gaborone, Botswana. Prior to its opening, some members of the community were concerned that the clinic would be labeled an “AIDS clinic” and families would be reluctant to bring their children for treatment for fear of being recognized and stigmatized. After two years of operation, the BBCCOE is providing comprehensive health services to more than 1200 HIV-infected children in the Gaborone area, and the number is growing. In this case, access to treatment overshadowed concerns about stigma. As more treatment centers are able to offer HAART therapy, this phenomenon may be repeated throughout the developing world.

**Discussion**

The global HIV epidemic is not under control. More people are becoming infected with the virus than are dying from it on an annual basis, resulting in more people living with the disease every day. The numbers
Review Questions

1. What is the major route of transmission of HIV throughout the world?
   2. What are the three major modes of HIV transmission?
   3. Why are some groups of people known to be at high risk of infection with HIV? Discuss how people who are not in these high-risk groups also become infected.
   4. Name at least three societal factors that contribute to the spread of HIV.

Exam Questions

1. A majority of HIV-positive children under age 15 became infected with HIV:
   a. From contaminated water
   b. At birth or through breast milk
   c. From a blood transfusion
   d. During surgery

2. HIV can be transmitted by all of the following EXCEPT:
   a. Breast milk
   b. Blood
   c. Semen
   d. Saliva

3. Which of the following is true?
   a. More people are dying from AIDS than are acquiring HIV.
   b. Fewer people are living with HIV/AIDS today than five years ago.
   c. HIV is a preventable disease.
   d. The global epidemic of HIV is now under control.
of incident infections and deaths remain unnecessarily high. Education, prevention, and treatment are currently the most promising strategies to slow the spread of the disease. Achieving greater levels of education, prevention, and treatment globally and curbing the growth of the HIV/AIDS pandemic may well be one of the greatest challenges of our time, and it is one we must embrace with a sense of total commitment and immediacy.

Case Study

Unusually high rates of HIV have been documented in a particular gold-mining town in South Africa. Sixty percent of the miners are migrant workers from other parts of South Africa or from nearby countries. These miners make good wages in U.S. dollars. Most of them live lonely lives in single-sex dormitories, often hundreds of miles from their families. About 400-500 sex workers service these mines.

Question: The situation in this mining town makes it easy for HIV to be transmitted from one person to another. Which of the following mechanisms of HIV transmission is not increased due to the circumstances in this mine town?

a. Sexual transmission caused by miners having sex with prostitutes
b. Sexual transmission caused by miners returning home and having sex with their wives
c. Mother-to-child transmission when sex workers who service the mines become pregnant
d. Transmission through tainted blood transfusions

Answer: d. Transmission through tainted blood transfusions is not a mechanism that is enhanced due to the circumstances in this mine town. Donated blood is routinely screened for HIV in southern Africa, and HIV-contaminated blood is discarded. Although a limited number of HIV transmissions may occur due to tainted transfusions or improperly screened blood, there is nothing unique to this mining town that would suggest increased transmission through this mechanism.


Objectives

The purposes of this module are to:
1. Provide an overview of the normal immune system.
2. Describe the human immunodeficiency virus.
3. Describe the major components of the HIV life cycle.
4. Identify the various HIV types and HIV subtypes.
5. Discuss the effects of HIV on the immune system.

Key Points

1. The immune system protects the body by recognizing invading antigens on bacteria and viruses and reacting to them.
2. T-lymphocytes regulate the immune system and destroy antigens.
3. HIV is continuously using new host cells to replicate itself.
4. The HIV life cycle can be divided into six phases: binding and entry, reverse transcription, integration, replication, budding, and maturation.
5. Once HIV is in the circulatory system, it targets the CD4+ lymphocyte.
6. There are two types of HIV that cause AIDS: HIV-1 and HIV-2.
7. Primary infection refers to the period of time when HIV first enters the body.
8. Clinical latency refers to the period of time before onset of symptoms and complications in the HIV-infected individual. In HIV-infected adults, this phase may last eight to 10 years.
9. Early signs and symptoms of HIV can include candidiasis, lymphadenopathy, cervical carcinoma, herpes zoster, and peripheral neuropathy.
10. Late signs and symptoms of HIV and AIDS-defining illnesses can include the development of life-threatening infections and malignancies.

Overview

The human immunodeficiency virus (HIV) is a retrovirus belonging to the family of lentiviruses. Retroviruses have the ability to use their RNA and host DNA to make viral DNA and are known for their long incubation periods. Like other retroviruses, HIV infects the body, has a long incubation period (clinical latency), and ultimately causes the signs and symptoms of disease, in this case AIDS.1 HIV causes severe damage to the immune system and eventually destroys it. HIV accomplishes this by utilizing the DNA of CD4+ cells to replicate itself. In that process, the virus eventually destroys the CD4+ cells.

The Normal Immune System

The immune system protects the body by recognizing antigens on invading bacteria and viruses and reacting to them. An antigen is any substance that induces a state of sensitivity and immune responsiveness. These
antigens interact with antibodies and immune cells initiating an immune response. This results in destruction of the antigen, allowing the body to be free of infections. Types of antigens include bacteria, viruses, fungi, and parasites. When the immune system is weakened or destroyed by a virus such as HIV, the body is left vulnerable to infections.2

The immune system consists of lymphoid organs and tissues, including the bone marrow, thymus gland, lymph nodes, spleen, tonsils, adenoids, appendix, blood, and lymphatic vessels (Figure 1). All of the components of the immune system are vital in the production and development of lymphocytes or white blood cells. B- and T-lymphocytes are produced from stem cells in the bone marrow. B-cells stay in the bone marrow to complete the maturation process, but T-lymphocytes travel to the thymus gland to complete their maturation. It is in the thymus that T-lymphocytes become immunocompetent, multiply, and become more differentiated.

B-lymphocytes:
The main function of B-lymphocytes or B-cells is humoral (antibody) immunity.3 Each B-cell can recognize specific antigen targets and is capable of secreting specific antibodies. Antibodies function by coating antigens, making them more vulnerable to phagocytosis (attack by leukocytes or macrophages that engulf and ingest invading organisms), or by coating the antigen and triggering the complement system, leading to an inflammatory response. Antibodies are highly specialized serum protein molecules. Antibodies are grouped into five classes, each having a specialized function. These five classes are IgG, IgA, IgM, IgE, and IgD.

T-lymphocytes:
T-lymphocytes or T-cells have two major functions: regulation of the immune system and killing of cells that bear specific target antigens. Each T-cell has a surface marker, such as CD4+, CD8+, and CD3+, that distinguishes it from other cells. CD4+ cells are helper cells that activate B-cells, killer cells, and macrophages when a specific target antigen is present. There are two main types of CD8+ cells. The first type, cytotoxic CD8+ cells, kills cells infected by viruses or bacteria, as well as cancer cells. The second type of CD8+ cells, T-suppressor cells, inhibits or suppresses immune responses. Normal CD8+ cell count is between 300 and 1000 cells in adults and children. Normal CD4+:CD8+ ratio is between 1.0 and 2.0.

T-cells are capable of secreting cytokines (chemicals that kill cells), such as interferon. Cytokines can bind to target cells and activate the inflammatory process. They also promote cell growth, activate phagocytes, and destroy target cells. Interleukins are cytokines that serve as messengers between white blood cells. Recombinant (laboratory-synthesized) interleukins are currently being studied in clinical trials for patients with HIV infection.

Phagocytes:
Phagocytes include monocytes and macrophages, large white blood cells that engulf and digest cells carrying...
PATHOPHYSIOLOGY OF THE HUMAN IMMUNODEFICIENCY VIRUS

Figure 2: Cells of the Immune System

- Stem Cell
- Myeloid Precursor
- Lymphoid Precursor
- Platelets
- Eosinophil
- Neutrophil
- Basophil
- Mast Cell
- Monocyte
- H-Cell
- Cytotoxic T-Cell
- Helper T-Cell
- Suppressor T-Cell
- Plasma Cell
- Macrophage

Figure 3: Immune Response by White Blood Cells

- White Blood Cells
  - Neutrophils
  - Lymphocytes
  - Eosinophils
  - Basophils
    - B-Cells
    - T-Cells
      - CD4+
        - In charge of the army
        - Summons B-cells, natural killer (NK) cells, macrophages
        - Plans for a direct attack
      - CD8+
        - Binds directly to antigen and kills it
HIV CURRICULUM FOR THE HEALTH PROFESSIONAL

antigenic particles. Found throughout the body, phagocytes rid the body of worn-out cells, initiate the immune response by presenting antigen to lymphocytes, are important in immune response regulation and inflammation, and carry receptors for cytokines. Dendritic cells, another type of phagocyte, also are antigen-presenting cells. They have long thread-like extensions that help trap lymphocytes and antigens and are found in the spleen and lymph nodes. Neutrophils are granulocytic phagocytes that are important in the inflammatory response.

Complement:
The complement system consists of 25 proteins. Complement is capable of inducing an inflammatory response when it functions with antibodies to facilitate phagocytosis or weaken the bacterial cell membrane. The complement proteins interact with one another in a sequential activation cascade, promoting the inflammatory process.

Despite the heavy artillery the immune system has against foreign predators (see Figure 2 and Figure 3), over time it is defeated by HIV.

The Human Immunodeficiency Virus

The human immunodeficiency virus (HIV) consists of a cylindrical center surrounded by a sphere-shaped lipid bilayer envelope. There are two major proteins in this lipid bilayer, gp120 and gp41. The major function of these proteins is to mediate recognition of CD4+ cells, thereby enabling the HIV virus to attach to and invade the CD4+ cells. The inner sphere contains two single stranded copies of the
genomic material – ribonucleic acid (RNA) – as well as multiple proteins and enzymes necessary in the process of HIV replication and maturation: p24, p17, reverse transcriptase, integrase, and protease (Figure 4). Unlike other retroviruses, HIV utilizes nine genes to code for the necessary proteins and enzymes. The three principal genes are gag, pol, and env. The gag gene encodes core proteins. The pol gene encodes the enzymes reverse transcriptase, protease, and integrase. The env gene encodes the HIV structural components known as glycoproteins. The remainder of the genes – rev, nef, vif, vpu, and vpr – are important for viral replication and enhancing the infectivity rate of the HIV virus.

The HIV Life Cycle
Host cells infected with HIV have a shortened life span because the HIV virus uses them as “machines” to produce multiple copies of new HIV. Thus, HIV is continuously using new host cells to replicate itself. As many as 10 million to 10 billion virions (individual viruses) are produced daily. In the first 24 hours after exposure, HIV attacks or is captured by dendritic cells in the mucous membranes and skin. Within five days after exposure, these infected cells make their way to the lymph nodes and eventually to the peripheral blood, where viral replication becomes very rapid. CD4+ lymphocytes that are recruited to respond to viral antigen migrate to the lymph nodes. These become activated and then proliferate via complex interaction of cytokines released in the microenvironment of the lymph nodes. This sequence of events makes the CD4+ cells more susceptible to HIV infection, and it also explains the generalized lymphadenopathy characteristic of the acute retroviral syndrome seen in adults and adolescents. In contrast, monocytes that

This depiction of the HIV life cycle shows the sites of action of some antiretroviral agents.
are infected by HIV allow viral replication but resist killing. Thus monocytes act as reservoirs of HIV and as effectors of tissue damage in organs such as the brain.

The HIV life cycle can be divided into six phases: binding and entry, reverse transcription, integration, replication, budding, and maturation (Figure 5).

**Binding and Entry:**
The envelope proteins gp120 and gp41 bind to CD4+ cell receptors and co-receptors on the outside of the CD4+ cell. The joining of the proteins and the receptors results in the fusion of the HIV membrane with the CD4+ cell membrane, and the virus enters the CD4+ cell. The HIV membrane and the envelope proteins stay on the outside of the CD4+ cell, while the core of the HIV enters the CD4+ cell. CD4+ cell enzymes interact with the core of the HIV and stimulate the release of viral RNA and the viral enzymes reverse transcriptase, integrase, and protease.

**Reverse Transcription:**
The HIV RNA must be converted to DNA before it can be incorporated into the DNA of the CD4+ cell. This incorporation is required for the virus to multiply. The conversion of HIV RNA to DNA is known as the process of reverse transcription and is mediated by the HIV enzyme reverse transcriptase. The result is the production of a single strand of DNA from the viral RNA. The single strand of this new DNA then undergoes replication into double-stranded HIV-DNA.

**Integration:**
Once reverse transcription has occurred, the viral DNA can enter the nucleus of the CD4+ cell. The viral enzyme integrase then inserts the viral DNA into the CD4+ cell’s DNA. This process is known as integration. The CD4+ cell has now been changed into a “machine” used to produce more HIV.

**Replication:**
The new DNA, which has been formed by the integration of the viral DNA into the CD4+ cell, causes the production of messenger DNA that initiates the synthesis of HIV proteins.

**Budding:**
The HIV proteins and viral RNA, all the components needed to make a new virus, gather at the CD4+ cell membrane to form new viruses. These new viruses push through the different parts of the cell wall by budding. Many viruses can push through the wall of one CD4+ cell. These new viruses leave the CD4+ cell and contain all the components necessary to infect other CD4+ cells.

**Maturation:**
The new virus has all the components necessary to infect other CD4+ cells but cannot do so until it has undergone a maturation process. During this process, the HIV protease enzyme cuts the long HIV proteins of the virus into smaller functional units that then reassemble to form a mature virus. The virus is now ready to infect other cells.

**HIV Types**

There are two types of HIV that cause AIDS: HIV-1 and HIV-2. Very little is known about HIV-2. Studies have shown striking similarities but also important differences between HIV-1 and HIV-2. They have the same modes of transmission and are associated with the same opportunistic infections, but HIV-2 appears to progress at a slower rate. A majority of HIV-2 cases are found in western Africa.

Various subtypes of HIV-1 have been found in specific geographic areas and in specific high-risk groups. A person can be co-infected with different subtypes. The following are HIV-1 subtypes and their geographic distributions:

- **Subtype A:** Central Africa, sub-Saharan Africa
- **Subtype B:** South America, Brazil, U.S.A., Thailand, Europe, Caribbean, India, Japan
- **Subtype C:** Brazil, India, South Africa
- **Subtype D:** Central Africa, sub-Saharan Africa
- **Subtype E:** Thailand, Central African Republic, Southeast Asia
- **Subtype F:** Brazil, Romania, Democratic Republic of Congo (Zaire)
Subtype G: Democratic Republic of Congo (Zaire), Gabon, Thailand, Russia, Central Africa
Subtype H: Democratic Republic of Congo (Zaire), Gabon, Russia, Central Africa
Subtype I: Cyprus
Subtype O: Cameroon, Gabon

Subtypes are very unevenly distributed throughout the world. Subtype C currently accounts for more than half of all new HIV infections worldwide. Africa has most subtypes, although subtype B is less prevalent. There are no known subtypes of HIV-2.

**Effects on the Immune System**

The pathogenesis of HIV is basically a struggle between HIV replication and the immune responses of the patient, via cell-mediated and immune-mediated reactions. The HIV viral burden directly and indirectly mediates CD4+ T-cell destruction. There is destruction of mature CD4+ cells; CD4+ progenitor cells in bone marrow, thymus, and peripheral lymphoid organs; as well as CD4+ cells within the nervous system, such as microglia. The end result of this destruction is failure of T-cell production and eventual immune suppression.

There are many mechanisms of CD4+ cell depletion by HIV infection. Direct HIV-mediated cytopathic effects include single-cell killing as well as cell fusion or "syncytium" formation. The syncytium is a fusion of multiple uninfected CD4+ cells with a single HIV-infected CD4+ cell via CD4-gp120 interaction. This results in a multinucleated syncytium or giant cell, which may ultimately serve as a means to produce many HIV virions. The host’s natural immune responses also play a role in CD4+ cell depletion, mainly through cytotoxic CD8+ T-cells (CTL), antibody-dependent cellular cytotoxicity (ADCC), and natural killer (NK) cells. Other mechanisms include autoimmune responses, anergy, superantigen-mediated activation of T-cells, and programmed cell death, or apoptosis.

Many types of cells can be infected with HIV. The spread of HIV outside of lymphoid organs to brain, spinal cord, lung, colon, liver, and kidney usually occurs late in the course of the illness. Table 1 gives a partial list of cells susceptible to HIV infection.

The immune systems of children infected with HIV undergo changes that are similar to those in adults. B-cell activation occurs in most children early in the infection, evidenced by the presence of hypergammaglobulinemia (greater than 1.750 g/L) with high levels of anti-HIV-1 antibody. This reflects both dysregulation of T-cell suppression of B-cell antibody synthesis as well as active CD4+ enhancement of B-lymphocyte humoral response. Also, as HIV disease progresses through more severe immunosuppression and depletion of CD4+ cells, the CD8+ count increases, yielding an overall decrease in the CD4+:CD8+ ratio.

**Classification System for HIV-Infected Adults and Adolescents**

The U.S. Centers for Disease Control and Prevention (CDC) categorizes HIV-infected adults and adolescents based on their CD4+ counts and clinical conditions.

<table>
<thead>
<tr>
<th>System</th>
<th>Cell</th>
</tr>
</thead>
</table>
| Hematopoietic      | • T-cells (CD4+ or CD8+)
|                    | • Macrophages/monocytes
|                    | • Dendritic cells
|                    | • Fetal thymocytes and thymic epithelium
|                    | • B-cells
|                    | • NK cells
|                    | • Megakaryotic cells
|                    | • Stem cells
| Central Nervous    | • Microglia
|                    | • Capillary endothelial cells
|                    | • Astrocytes
|                    | • Oligodendrocytes
| Large Intestine    | • Columnar epithelium
| Other              | • Kupfer cells (liver)
|                    | • Synovial cells
|                    | • Placental trophoblast cells

Adapted from Levy J.A. Microbiological Reviews, 57:183-289, March 1993.
The classification system is used to guide health care professionals in making treatment decisions for HIV-infected patients. The system is based on three ranges of CD4+ T-lymphocyte counts and three clinical categories and is represented by a matrix of nine mutually exclusive categories (Table 2). The CD4+ categories are listed below and correspond to the number of CD4+ cells per microliter of blood.

Category 1: \( \geq 500 \) cells/uL
Category 2: 200-499 cells/uL
Category 3: <200 cells/uL

The classification is based on the patient's lowest CD4+ count at any given time, not on the most recent count. Once a patient has achieved a Category 2 or 3 classification, he or she cannot be reassigned to a lower category if the CD4+ count increases. However, this policy is currently under review.

### Classification System for HIV-Infected Children

Children infected with HIV often have severe disease when first evaluated, or they may develop AIDS over time, much like adults infected with HIV. Infants and young children normally have higher CD4+ counts than do adults. The normal CD4+ count in children varies with age, but it is equal to the adult value by the time the child is 6 years old. The CDC has developed a system to classify pediatric HIV based on clinical and immunologic categories (Table 3 and Table 4). Immunologic and clinical categories are used to evaluate the HIV disease status in children and to make treatment decisions.

### Clinical Categories of HIV Infection

**Primary Infection or Acute Retroviral Syndrome (Clinical Category A)**

Primary infection refers to the period of time when HIV first enters the body. \(^3\) At the time of primary infection...
infection with HIV, a person’s blood demonstrates a very high viral load, which means that there are many individual viruses in the blood. The number of copies of virus per milliliter of plasma or blood can exceed 1,000,000. Newly infected adults often experience an acute retroviral syndrome. Signs and symptoms of acute retroviral syndrome include fever, myalgia (muscle pain), headache, nausea, vomiting, diarrhea, night sweats, weight loss, and rash. These signs and symptoms usually occur two to four weeks after infection, subside after a few days, and often are misdiagnosed as influenza or infectious mononucleosis.

During primary infection, the CD4+ count in the blood decreases remarkably. The virus targets CD4+ cells in the lymph nodes and the thymus during this time, making the HIV-infected person vulnerable to opportunistic infections and limiting the thymus’ ability to produce T-lymphocytes. HIV-antibody testing using an enzyme-linked immunosorbent assay (ELISA) or enzyme immunoassay (EIA) will yield positive results.

**Clinical Latency** *(Clinical Category A)*

Although patients recently infected with HIV usually experience a “clinically latent” period of years between HIV infection and clinical signs and symptoms of AIDS, evidence of HIV replication and host immune-system destruction exists from the onset of infection.

During latency, HIV-infected patients do not have signs and symptoms of HIV infection. In HIV-infected adults, this phase may last eight to 10 years. The HIV ELISA and Western blot or immuno-fluorescence assay (IFA) will be positive. The CD4+ count is greater than 500 cells/mm³.

**Early Signs and Symptoms of HIV** *(Clinical Category B)*

HIV-infected people may appear to be healthy for years, and then minor signs and symptoms of HIV infection begin to appear. They may develop candidiasis, lymphadenopathy, cervical carcinoma, herpes zoster, and/or peripheral neuropathy. The viral load increases, and the CD4+ count falls to about 500 cells/mm³. Once patients develop a Category B condition, they remain in Category B. They can be reassigned to Category C if a condition from that category occurs, but they cannot be reassigned to Category A if they become asymptomatic.

**Late Signs and Symptoms of HIV** *(Clinical Category C)*

HIV-infected patients develop life-threatening infections and malignancies. The development of *Pneumocystis jiroveci* pneumonia, toxoplasmosis, cryptosporidiosis, and other opportunistic infections is common. Patients may be wasting or losing weight. The viral load continues to increase, and the CD4+ count falls to less than 200 cells/mm³. These patients have met the definition of AIDS. Once a Category C condition has occurred, the person remains in the category even if the condition resolves.

**Advanced HIV Disease** *(Clinical Category C)*

HIV-infected patients continue to develop new opportunistic infections, such as cytomegalovirus infection, *Mycobacterium avium* complex, cryptococcal meningitis, progressive multifocal leukoencephalopathy, and other infections that commonly occur secondary to a severely depressed immune system. The viral load is very high, and the CD4+ count is less than 50 cells/mm³. Death is imminent.
### Review Questions

1. Identify the major components of the immune system and their role in combating infection.
2. State the specific functions of T- and B-lymphocytes.
3. Review the life cycle of HIV.
4. Define the five phases of the HIV life cycle.
5. Identify the HIV-1 subtypes that are indigenous to your geographic area.
6. Describe the clinical signs and symptoms of a primary infection with HIV.
7. Define clinical latency.
8. Describe the early clinical signs and symptoms of HIV.

### Exam Questions

1. The major function of the B-lymphocyte is to:
   a. Secrete specific antibodies to foreign antigens.
   b. Activate phagocytes to destroy cells carrying antigens.
   c. Produce cytokines to bind antigens.
   d. Promote cell growth.
2. Which cell does HIV use to replicate itself, destroying this cell in the process?
   a. B-cell
   b. CD4+ cell
   c. CD8+ cell
   d. Phagocyte
3. What are the types of HIV that cause AIDS?
   a. HIV-1
   b. HIV-1 and HIV-2
   c. HIV-1, HIV-2, HIV-3, and HIV-4
   d. Phagocyte
4. Which of the following occurs in the individual at the time of primary infection with HIV?
   a. Signs and symptoms similar to influenza
   b. Extremely low viral load
   c. Virus targets the liver and spleen
   d. ELISA and EIA will have negative results
5. During the clinical latency period, the HIV-infected individual may not develop signs and symptoms of AIDS for as long as:
   a. Eight to 10 weeks
   b. Three to six months
   c. Three to five years
   d. Eight to 10 years
Case Study #1
A 30-year-old man goes to see his doctor with complaints of fever, myalgia, headache, nausea, vomiting, diarrhea, night sweats, weight loss, and rash. The man has a history of multiple sex partners.

Question: What is the most likely diagnosis?

a. Retroviral syndrome
b. Influenza
c. Mononucleosis

Answer: a. A newly HIV-infected adult will often experience an acute retroviral syndrome. Signs and symptoms of acute retroviral syndrome include fever, myalgia, headache, nausea, vomiting, diarrhea, night sweats, weight loss, and rash. These signs and symptoms usually occur two to four weeks after infection, subside after a few days, and often are misdiagnosed as influenza or infectious mononucleosis.

Case Study #2
A woman brings her 8-month-old HIV-infected baby to the clinic. The baby has a CD4+ count of 850 cells/mm³ and has had oral candidiasis and some mild upper-respiratory infections in the past, but no other infections. The mother is worried that the baby now has AIDS.

Question: In which immunologic and clinical classification category does the baby fit?

a. C3 c. B2
b. N1 d. A2

Answer: d. The normal CD4+ count for an 8-month-old child is ≥1500 cells/mm³. At the current level, the child is in Immunologic Category 2. Candidiasis and upper-respiratory infections are considered mild signs or symptoms of HIV infection and fall into Clinical Category A.

References
Objectives

The purposes of this module are to:
1. Identify the screening tests used to diagnose HIV.
2. Describe why it is difficult to diagnose HIV infection in an infant.
3. Review the CDC staging system for HIV disease in infants and children.
4. Define the WHO clinical staging system for HIV infection.
5. Discuss the clinical and laboratory criteria for the diagnosis of HIV disease in adults.
6. The WHO clinical diagnostic system is based on dividing signs and symptoms into major and minor criteria.
7. Diagnosing HIV follows the same principles in adults as in children.

Key Points

1. HIV disease is diagnosed by the presence of clinical signs and symptoms and specific laboratory tests.
2. The ELISA (enzyme-linked immunosorbent assay) is the screening test used to diagnose HIV infection.
3. The Western blot and PCR (polymerase chain reaction) tests help to confirm HIV infection.
4. Maternal antibodies are present in an infant's blood for up to 18 months after birth, making it difficult to establish the diagnosis of HIV by ELISA and Western blot.
5. The CDC has established a staging system for HIV disease in infants and children based on the CD4+ lymphocyte count and clinical signs and symptoms.

Overview

Human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS) can be defined by clinical signs and symptoms as well as by several laboratory tests. This lecture will discuss the types of tests that can be done to diagnose HIV infection and will review age-specific criteria for the diagnosis and classification of HIV infection and AIDS.

Diagnostic Tests

ELISA

One screening test used to diagnose HIV is the ELISA (enzyme-linked immunosorbent assay), which is an enzyme immunoassay (EIA). When this test is performed on a patient's serum or blood, it identifies antibodies to HIV. ELISA tests are highly sensitive but not always specific. This means that other illnesses besides HIV can cause a positive test. Among these illnesses are autoimmune diseases, certain viral infections, syphilis, and hematologic malignancies. Pregnancy may also cause a false-positive ELISA.
The ELISA test has some limitations. Because maternal antibodies are present in an infant’s blood for up to 18 months after birth, the ELISA is accurate only in patients over 18 months of age. Further, because the test is based on the detection of antibodies to HIV, there is a “window period” during which an infected patient may have a negative ELISA. This is usually in the first six to 12 weeks after infection. Some newer ELISA tests utilize improved technology that can shorten this time. It is important to know which ELISA test is being used in your institution so that you can counsel patients appropriately. The ELISA is designed for screening large numbers of patients. This makes it suitable for centralized laboratories, but it may not be cost-effective in other circumstances. Because the ELISA is a screening test, all positive results must be confirmed by a secondary test. This will be discussed in detail in the section titled “HIV Diagnosis in Adults.”

**Western Blot**

A Western blot is a polyacrylamide gel electrophoresis that detects bands of proteins specific to HIV antibodies. If no bands are seen, the Western blot is negative. If most or all of the protein bands are seen, the Western blot is positive. The Western blot test can be inconclusive or indeterminate. In the event that an indeterminate test result is found, the test should be repeated on the same serum sample and then repeated again in two weeks. If the indeterminate pattern persists, the Western blot needs to be repeated periodically for the next six months. If the pattern persists after six months, the person is most likely not infected with HIV.

**Rapid Tests**

Several rapid tests detect anti-HIV antibodies, much like the ELISA. Many are as accurate as an ELISA. Like the ELISA, these tests are accurate only in those over 18 months of age, and they have the same window period of six to 12 weeks. Like the ELISA, all positive rapid HIV tests must be confirmed by another test. Among advantages of rapid tests is that results are available in just a few minutes to hours.

Most rapid tests can be performed on blood obtained from a finger stick. Performing them requires little training. Many different commercial rapid tests are available, and most are 99-100 percent sensitive and specific. Some rapid tests can use saliva or urine samples instead of blood samples. While these tests offer a clear advantage in that the specimens can be obtained in a non-invasive manner, their quality and reliability have not been validated adequately. One study by the World Health Organization (WHO) and UNAIDS did not find the urine and saliva test kits they investigated to be sufficiently sensitive or specific. Other saliva tests have been found to be highly reliable. One should understand the accuracy of any rapid test before using it.

In 1997, a study in South Africa found that in areas with a high prevalence of HIV infection, the rapid tests performed well when used to diagnose HIV. In addition, when two different rapid test kits (testing for two different HIV-associated antibodies) were used, the combination of two positive rapid diagnostic tests was almost 100 percent sensitive and specific for diagnosing HIV infection. Because the results were available promptly, the effectiveness of post-test counseling was increased.

**DNA/RNA PCR**

Finally, polymerase chain reactions (PCR) for the DNA or RNA of the HIV virus can be performed. These tests are highly sensitive and specific for HIV infection. They are often used if the results of other diagnostic tests are unclear. DNA PCR is most commonly utilized to diagnose HIV infection in children under the age of 18 months. P24 antigen, RNA PCR, and HIV culture can also be used for diagnosis. These options will be discussed in more detail in sections on HIV diagnosis in infants and children. Clinicians must decide which test will be used to determine whether a patient has HIV (Figure 1).
HIV Diagnosis in Adults

Diagnosing HIV in adults follows specific principles. Both clinical and laboratory diagnostic criteria have been developed to determine positive and negative diagnoses. Signs and symptoms of early HIV infection can be very non-specific and similar to many viral infections: lethargy, malaise, sore throat, myalgias (muscle soreness), sweating, and fever. A patient may have some but not all of these signs and symptoms. At this early stage, laboratory testing is the best way to determine whether a patient is HIV-infected. The ELISA and rapid test are good, but they may not be positive until six to 12 weeks after the patient has been infected. If a patient has acute symptoms that suggest HIV infection and the ELISA or rapid test is negative, the test will need to be repeated later. These early flu-like symptoms will resolve, and the patient may have no other signs or symptoms of being infected with HIV for several years. This clinically latent period of HIV infection may last as long as eight or 10 years. During the latent period, HIV continues to attack the immune system even if there are no signs or symptoms of HIV infection. The late stage of HIV infection begins when a patient starts to develop illnesses consistent with AIDS. The most common signs at this late stage are weight loss, diarrhea, and weakness.

Once a patient is diagnosed with HIV, the extent of damage to the immune system needs to be determined. CD4+ lymphocyte (T-helper cell) counts are one way to quantify a patient's immune function. CD4+ lymphocyte counts are also useful in determining the clinical stage of HIV infection for a patient. This is part of the U.S. Centers for Disease Control and Prevention (CDC) classification system (Table 1). If such testing is not available, a total lymphocyte count can be helpful. The World Health Organization (WHO) has developed AIDS staging criteria for adults that use the total lymphocyte count to follow changes in a patient's immune system over time (Table 2). Many countries use a combination of both systems.

**CDC Classification**

The CDC's revised classification for adults and adolescents (>13 years old) is a two-tier system. One tier looks at the amount of immune suppression a patient is experiencing. The amount of immune suppression is determined by the CD4+ lymphocyte count; each patient is assigned a number based on his or her CD4+ lymphocyte count. The second tier is clinical staging: HIV-infected patients are assigned a letter based on their clinical symptoms.

The CDC classification system can also be used for surveillance case definition of AIDS. Any person in classes A3, B3, or C3 is considered to have AIDS. Once classified, a person may not be reclassified in a less severe category, even if improvement in clinical or immunological status occurs in response to antiretroviral therapy or other factors. Table 1 displays the CDC classification system for HIV infection and AIDS surveillance case definition for adolescents and adults.
Table 1: CDC Revised Classification System for HIV Infection and Expanded AIDS Surveillance Case Definition for Adolescents and Adults*

<table>
<thead>
<tr>
<th>CD4+ Cell Categories</th>
<th>CLINICAL CATEGORIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>1: &gt;500 cells/uL</td>
<td>A1</td>
</tr>
<tr>
<td>2: 200-499 cells/uL</td>
<td>A2</td>
</tr>
<tr>
<td>3: &lt;200 cells/uL</td>
<td>A3**</td>
</tr>
</tbody>
</table>

**AIDS**

*Modified from MMWR, Vol. 41, 1992 RR-17

**WHO Classification – Adults**

In many parts of the world, laboratory testing such as CD4+ lymphocyte counts are not available. In these cases, patients can be diagnosed and classified clinically, based on major and minor signs and symptoms. Two major signs or symptoms plus two minor signs or symptoms define symptomatic HIV infection. The WHO has also developed a system to categorize the immunosuppression of adults by their total lymphocyte counts. The WHO staging system can be applied to adults, and several studies have shown its reliability for predicting morbidity and mortality in infected individuals.7 Table 2 shows the WHO staging system based on laboratory and clinical criteria.

**Major Signs/Diseases**

- Weight loss of 10 percent or more of body weight
- Chronic diarrhea
- Prolonged fever for more than one month
- Tuberculosis
**HIV/AIDS Diagnostic Criteria**

### Table 2: WHO Clinical Staging for Adults and Adolescents*

<table>
<thead>
<tr>
<th>PRIMARY HIV INFECTION</th>
<th>CLINICAL STAGES</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Asymptomatic</td>
<td>1</td>
</tr>
<tr>
<td>• Persistent generalized lymphadenopathy (PGL)</td>
<td></td>
</tr>
<tr>
<td>• Moderate unexplained weight loss (&lt;10% of presumed or measured body weight)</td>
<td>2</td>
</tr>
<tr>
<td>• Recurrent upper respiratory tract infections (sinusitis, bronchitis, otitis media, pharyngitis)</td>
<td></td>
</tr>
<tr>
<td>• Angular cheilitis</td>
<td></td>
</tr>
<tr>
<td>• Recurrent oral ulcerations (2 or more episodes in 6 months)</td>
<td></td>
</tr>
<tr>
<td>• Papular pruritic eruptions</td>
<td></td>
</tr>
<tr>
<td>• Seborrheic dermatitis</td>
<td></td>
</tr>
<tr>
<td>• Fungal nail infections of fingers</td>
<td></td>
</tr>
<tr>
<td>• Severe weight loss (&gt;10% of presumed or measured body weight)</td>
<td>3</td>
</tr>
<tr>
<td>• Unexplained chronic diarrhea for longer than 1 month</td>
<td></td>
</tr>
<tr>
<td>• Unexplained persistent fever (intermittent or constant, for longer than 1 month)</td>
<td></td>
</tr>
<tr>
<td>• Oral candidiasis</td>
<td></td>
</tr>
<tr>
<td>• Oral hairy leukoplakia</td>
<td></td>
</tr>
<tr>
<td>• Pulmonary tuberculosis (diagnosed in past 2 years)</td>
<td></td>
</tr>
<tr>
<td>• Severe presumed bacterial infections (e.g., pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteremia)</td>
<td></td>
</tr>
<tr>
<td>• Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis</td>
<td></td>
</tr>
<tr>
<td>• Unexplained anemia (&lt;8 gm/dl), neutropenia (&lt;1000/mm^3) or thrombocytopenia (&lt;30 000/mm^3) for more than 1 month</td>
<td></td>
</tr>
</tbody>
</table>

### Conditions for which a presumptive diagnosis can be made using clinical signs or simple investigations:

- HIV wasting syndrome
- Pneumocystis pneumonia
- Recurrent severe or radiological bacterial pneumonia (2 or more episodes within 1 year)
- Chronic orolabial, genital, or anorectal herpes simplex infection (of more than 1 month's duration)
- Candidiasis of the esophagus
- Extrapulmonary tuberculosis
- Kaposi's sarcoma
- Central nervous system toxoplasmosis
- HIV encephalopathy

### Conditions for which confirmatory diagnostic testing is necessary:

- Cryptococcal meningitis
- Disseminated non-tuberculous mycobacteria infection
- Progressive multifocal leukoencephalopathy (PML)
- Candida of trachea, bronchi, or lungs
- Extrapulmonary cryptococcosis
- Cryptosporidiosis (diarrhea more than 1 month)
- Isosporiasis
- Cytomegalovirus (infection of an organ other than liver, spleen, or lymph nodes)
- Any disseminated mycosis (e.g. histoplasmosis, coccidiomycosis, penicilliosis)
- Recurrent non-typhoidal salmonella septicemia (2 or more episodes in 1 year)
- Lymphoma (cerebral or B-cell non-Hodgkin's)
- Invasive cervical carcinoma
- Leishmaniasis, visceral
- American trypanosomiasis reactivation

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**Minor Signs/Diseases**

- Oropharyngeal candidiasis
- Persistent cough for more than one month
- Body weakness
- Night sweats
- Loss of appetite
- Kaposi's sarcoma

- Generalized skin infection
- Generalized lymphadenopathy
- Herpes zoster
- Chronic herpes simplex infection
- Pneumonia

**HIV Diagnosis in Infants**

An infant may acquire HIV from the mother during pregnancy, labor, or breastfeeding. Infants with vertically transmitted (from the mother) HIV may be clinically normal during the neonatal period. The most common AIDS-defining illness in infants is pneumonia caused by *Pneumocystis carinii*. Common signs of HIV in infancy include failure to thrive, oral candidiasis (thrush), chronic diarrhea, and hepatosplenicomegaly (enlarged liver and spleen). All ELISA and rapid-test kits are based on the detection of antibodies to HIV. Because maternal IgG can cross the placenta and may remain detectible in an infant's serum up to 18 months of age, the ELISA and rapid tests are not reliable diagnostic tests for HIV-exposed
infants. Several other diagnostic tests are currently in use and under study for the purpose of early diagnosis of HIV in infants. According to the CDC, an infant less than 18 months of age is considered HIV-infected if he or she has “positive results on two separate determinations (excluding cord blood) from one or more of the following HIV detection tests: HIV culture, HIV polymerase chain reaction, HIV antigen (P24), or meets criteria for acquired immunodeficiency syndrome (AIDS) diagnosis based on the 1987 AIDS surveillance case definition.”

Cord blood is excluded because it has a high likelihood of being contaminated with maternal blood. Two tests are required because none of the current testing methods is 100 percent sensitive and specific, particularly during the first two weeks of life. For infants who are not breastfed, HIV infection can be excluded if HIV DNA PCR assay results obtained at birth, 4-6 weeks of age, and 8-16 weeks of age are negative. If an infant is breastfed, HIV infection cannot be definitively excluded until the infant has a negative diagnostic test six months after breastfeeding has ceased completely.

It is common practice to confirm any diagnosis or exclusion of HIV infection with a negative ELISA, rapid EIA test, and/or Western blot at age 18 months. Recently published data suggest, however, that this approach is neither necessary nor cost-effective.

Each of the tests employed in the diagnosis of infants with HIV will now be discussed.

**DNA PCR**

DNA PCR technology has allowed for the rapid, accurate diagnosis of HIV-infected infants. In developed countries, DNA PCR has replaced HIV cultures as the primary methodology used for the diagnosis of HIV infection in children under the age of 18 months. The sensitivity of DNA PCR for diagnosis of HIV infection increases from 38 percent at 48 hours of life to 93 percent at 2 weeks of life. These tests have a sensitivity of 90-100 percent and a specificity of 95-100 percent in infants 1 month of age or older. If maternal HIV status is known at the time of delivery, current recommendations include DNA PCR at delivery, 1-2 months, and 2-4 months. Cord blood should not be used.

**RNA PCR**

The sensitivity of HIV RNA measurements has been compared to that of DNA PCR for the diagnosis of neonatal HIV infection. In one study, for example, specimens obtained from 49 HIV-infected infants and eight uninfected infants were tested by both assays. In this study, quantitative plasma RNA testing was equivalent to DNA PCR in terms of specificity and equivalent or better in terms of sensitivity.

Only two of the 49 HIV-infected infants had received antiretroviral therapy before plasma specimens were collected. This is a potentially important issue, because the sensitivity of HIV RNA measurements for the diagnosis of neonatal HIV infection may be decreased if specimens are collected while the infant is receiving antiretroviral therapy. However, most infants have very high plasma HIV-1 RNA measurements, so even if antiretroviral therapy decreases their viral load, HIV RNA testing should be sensitive enough to detect the virus. These results suggest that measurement of plasma HIV-1 RNA may be a useful test for the early diagnosis of perinatal HIV-1 infection.

**P24 Antigen**

P24 is a major core protein of HIV. Several enzyme immunoassays that detect P24 antigen have been developed. These assays are simple to perform and inexpensive. However, they have not been found to be appropriately sensitive for the diagnosis of HIV in the first six months of life. A large study in Uganda found the sensitivity to be low (6-53 percent), especially in the first several months of life. In part, routine P24 antigen tests are less sensitive because they do not detect P24 antigen that is bound to antibody. Heating plasma or serum or incubating it in acid can cause the denaturing of antibody-antigen complexes and increase the sensitivity of the P24 antigen test. Because of its lack of sensitivity, P24 antigen testing is currently not recommended for diagnosis of HIV in infancy.
HIV Peripheral Blood Lymphocyte Co-Culture
Before polymerase chain reaction technology became available for the diagnosis of HIV, cultures were used to diagnose infection in infants. Cultures are expensive and labor-intensive, and they require several weeks to obtain results. Hence, this methodology has been replaced by those described above.

Infants With Non-Subtype B HIV Infection
Because many of the diagnostic tests for HIV detect antigens and/or genetic material, test sensitivity and specificity may be compromised in populations where HIV subtype B does not predominate. A recent study in Thailand, however, found that in a population where 92 percent of mothers were infected with subtype E, DNA and RNA PCR specifically designed to be sensitive to subtype E were 100 percent sensitive at 2 months of age. Further studies are needed to delineate the extent of this problem.

HIV Diagnosis in Children
Children over the age of 18 months can be diagnosed using a combination of clinical signs and symptoms and laboratory tests. Children often present with recurrent bacterial infections, failure to thrive or wasting, persistent lymphadenopathy, developmental delay, or oral and pharyngeal thrush. Like adults, children over the age of 18 months can be diagnosed using an ELISA or rapid serum test and a confirmatory test. Two systems of diagnosis and classification will be discussed.

CDC Classification
The CDC definition of an HIV-infected child is as follows: “any child over the age of 18 months who was born to an HIV-infected mother, or who has been exposed to infected blood or blood products, or other known methods of transmission who is HIV-antibody positive by ELISA and a confirmatory test.”

Once infection has been established, infants and children are classified under the CDC staging system based on their CD4+ lymphocyte count and the clinical manifestations of disease (Tables 3 and 4). A patient’s disease status can be classified by determining the degree of immunosuppression (1, 2, or 3) and the clinical category (N, A, B, C, or E). This classification allows for better surveillance and patient care. In the pediatric classification system, E refers to infants who are vertically exposed but whose status is still unclear.

Any of the CDC category C illnesses are considered AIDS-defining illnesses in children. Certain types of lung disease are considered AIDS-defining illnesses in children but not in adults. These are lymphoid interstitial pneumonitis (LIP) and pulmonary lymphoid hyperplasia (PLH). Both of these are CDC category B illnesses but are considered AIDS-defining as well. Several other conditions, including certain types of cytomegalovirus and herpes simplex virus infections and toxoplasmosis of the brain, are AIDS-defining only for adults and children over the age of 1 month.

Use of the CDC revised classification system is relatively straightforward. For example, a 3-month-old

<p>| Table 3: 1994 Revised Human Immunodeficiency Virus Pediatric Classification System: Immune Categories Based on Age-Specific CD4+ T-Lymphocyte Count and Percentage* |</p>
<table>
<thead>
<tr>
<th>Immune Category</th>
<th>No./µL</th>
<th>&lt;12 months (%)</th>
<th>No./µL</th>
<th>1-5 years (%)</th>
<th>No./µL</th>
<th>6-12 years (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1: No suppression</td>
<td>≥1500</td>
<td>(&gt;25%)</td>
<td>≥1000</td>
<td>(&gt;25%)</td>
<td>≥500</td>
<td>(&gt;25%)</td>
</tr>
<tr>
<td>2: Moderate suppression</td>
<td>750-1499</td>
<td>(15%-24%)</td>
<td>500-999</td>
<td>(15%-24%)</td>
<td>200-499</td>
<td>(15%-24%)</td>
</tr>
<tr>
<td>3: Severe suppression</td>
<td>&lt;750</td>
<td>(&lt;15%)</td>
<td>&lt;500</td>
<td>(&lt;15%)</td>
<td>&lt;200</td>
<td>(&lt;15%)</td>
</tr>
</tbody>
</table>

*Modified for CDC. 1994 Revised classification system for human immunodeficiency virus infection in children less than 13 years of age. MMWR 1994;43 (no. RR-12):1-10.
Table 4: 1994 Revised Human Immunodeficiency Virus Pediatric Classification System: Clinical Categories*

<table>
<thead>
<tr>
<th>Not Symptomatic – Children who have no signs or symptoms considered to be the result of HIV infection or who have only one of the conditions listed in category A.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mildly Symptomatic – Children with 2 or more of the following conditions but none of the conditions listed in categories B and C:</td>
</tr>
<tr>
<td>• Lymphadenopathy (&gt;0.5 cm at more than 2 sites; bilateral at 1 site)</td>
</tr>
<tr>
<td>• Hepatomegaly</td>
</tr>
<tr>
<td>• Splenomegaly</td>
</tr>
<tr>
<td>• Dermatitis</td>
</tr>
<tr>
<td>• Parotitis</td>
</tr>
<tr>
<td>• Recurrent or persistent upper respiratory infection, sinusitis, or otitis media</td>
</tr>
<tr>
<td>Moderate Symptomatic – Children who have symptomatic conditions other than those listed in category A or category C that are attributed to HIV infection. Conditions in clinical category B include but are not limited to:</td>
</tr>
<tr>
<td>• Anemia (&lt;8 gm/dl), neutropenia (&lt;1000/mm&lt;sup&gt;3&lt;/sup&gt;), or thrombocytopenia (&lt;100000/mm&lt;sup&gt;3&lt;/sup&gt;) persisting &gt;30 days</td>
</tr>
<tr>
<td>• Bacterial meningitis, pneumonia, or sepsis (single episode)</td>
</tr>
<tr>
<td>• Candidiasis, oropharyngeal (thrush), lasting &gt;2 months</td>
</tr>
<tr>
<td>• Cardiomyopathy</td>
</tr>
<tr>
<td>• Diarrhea, recurrent or chronic</td>
</tr>
<tr>
<td>• Hepatitis</td>
</tr>
<tr>
<td>• Herpes simplex virus, stomatitis, recurrent (&gt;2 episodes in 1 year)</td>
</tr>
<tr>
<td>• Herpes zoster (shingles) involving at least 2 distinct episodes or more than 1 dermatome</td>
</tr>
<tr>
<td>• Leukosarcoma</td>
</tr>
<tr>
<td>• Lymphoid interstitial pneumonia (LIP) or pulmonary lymphoid hyperplasia (PLH) complex</td>
</tr>
<tr>
<td>• Nephropathy</td>
</tr>
<tr>
<td>• Nocardiosis</td>
</tr>
<tr>
<td>• Fever lasting &gt;1 month</td>
</tr>
<tr>
<td>• Toxoplasmosis with onset before age 1 month</td>
</tr>
<tr>
<td>• Varicella, disseminated</td>
</tr>
<tr>
<td>Severe Symptomatic - Children who have any condition listed in the 1987 surveillance case definition for acquired immunodeficiency syndrome, with the exception of LIP.</td>
</tr>
<tr>
<td>• Serious bacterial infections, multiple or recurrent (any combination of at least 2 culture-confirmed infections in a 2-year period), of the following types: septicemia, pneumonia, meningitis, bone or joint infection, or abscess of internal organ or body cavity (excluding otitis media, superficial skin or mucosal abscesses, and in-dwelling catheter-related infections)</td>
</tr>
<tr>
<td>• Candidiasis, esophageal or pulmonary (bronchi, trachea, or lungs)</td>
</tr>
<tr>
<td>• Coccidiomycosis, disseminated (at site other than or in addition to lungs or cervical or hilar lymph nodes)</td>
</tr>
<tr>
<td>• Cryptococcosis, extrapulmonary</td>
</tr>
<tr>
<td>• Cryptosporidiosis or Isosporiasis with diarrhea persisting &gt;1 month</td>
</tr>
<tr>
<td>• Cryptosporidiosis or Isosporiasis with diarrhea persisting &gt;1 month</td>
</tr>
<tr>
<td>• Cytomegalovirus disease with onset of symptoms at age &gt;1 month (at site other than liver, spleen, or lymph nodes)</td>
</tr>
<tr>
<td>• Histoplasmosis, disseminated (at a site other than or in addition to lungs or cervical or hilar lymph nodes)</td>
</tr>
<tr>
<td>• Kaposi’s sarcoma</td>
</tr>
<tr>
<td>• Lymphoma, primary, in brain</td>
</tr>
<tr>
<td>• Lymphoma, small, noncleaved cell (Burkitt’s), or immunoblastic or large-cell lymphoma of B-cell or unknown immunologic phenotype</td>
</tr>
<tr>
<td>• Mycobacterium tuberculosis, disseminated or extrapulmonary</td>
</tr>
<tr>
<td>• Mycobacterium, other species or unidentified species, disseminated (at a site other than or in addition to lungs, skin, or cervical or hilar lymph nodes)</td>
</tr>
<tr>
<td>• Mycobacterium avium complex or Mycobacterium kansasii, disseminated (at site other than or in addition to lungs, skin, or cervical or hilar lymph nodes)</td>
</tr>
<tr>
<td>• Mycobacterium, other species or unidentified species, disseminated (at a site other than or in addition to lungs, skin, or cervical or hilar lymph nodes)</td>
</tr>
<tr>
<td>• Nephropathy</td>
</tr>
<tr>
<td>• Lymphoid interstitial pneumonia (LIP) or pulmonary lymphoid hyperplasia (PLH) complex</td>
</tr>
<tr>
<td>• Leimyosarcoma</td>
</tr>
<tr>
<td>• Lymphoma, primary, in brain</td>
</tr>
<tr>
<td>• Lymphoma, small, noncleaved cell (Burkitt’s), or immunoblastic or large-cell lymphoma of B-cell or unknown immunologic phenotype</td>
</tr>
<tr>
<td>• Mycobacterium tuberculosis, disseminated or extrapulmonary</td>
</tr>
<tr>
<td>• Mycobacterium, other species or unidentified species, disseminated (at a site other than or in addition to lungs, skin, or cervical or hilar lymph nodes)</td>
</tr>
<tr>
<td>• Mycobacterium avium complex or Mycobacterium kansasii, disseminated (at site other than or in addition to lungs, skin, or cervical or hilar lymph nodes)</td>
</tr>
<tr>
<td>• Pneumocystis carinii pneumonia</td>
</tr>
<tr>
<td>• Progressive multifocal leukoencephalopathy</td>
</tr>
<tr>
<td>• Salmonella (nontyphoid) septicemia, recurrent</td>
</tr>
<tr>
<td>• Toxoplasmosis with onset before age 1 month of age</td>
</tr>
<tr>
<td>• Wasting syndrome in the absence of a concurrent illness other than HIV infection that could explain the following finding: a) persistent weight loss &gt;10% of baseline OR b) downward crossing of at least 2 percentile lines on the weight-for-age chart (95th, 75th, etc.) in a child &gt;1 year of age OR c) &lt;5th percentile on weight-for-height chart on 2 consecutive visits PLUS either a) diarrhea (at least 2 loose stools per day for &gt;30 days) OR b) documented fever for &gt;30 days, intermittent or constant</td>
</tr>
</tbody>
</table>

*Modified for CDC. 1994 Revised classification system for human immunodeficiency virus infection in children less than 13 years of age. MMWR 1994;43 (no. RR-12):1-10.

Table 5: Criteria for the Clinical Diagnosis of HIV in Children

<table>
<thead>
<tr>
<th>Pediatric Major Signs/Diseases</th>
<th>Pediatric Minor Signs/Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Failure to thrive or weight loss</td>
<td></td>
</tr>
<tr>
<td>• Chronic diarrhea</td>
<td></td>
</tr>
<tr>
<td>• Prolonged fever without a known source</td>
<td></td>
</tr>
<tr>
<td>• Tuberculosis</td>
<td></td>
</tr>
<tr>
<td>• Generalized lymphadenopathy</td>
<td></td>
</tr>
<tr>
<td>• Oral candidiasis (thrush)</td>
<td></td>
</tr>
<tr>
<td>• Persistent cough</td>
<td></td>
</tr>
<tr>
<td>• Respiratory distress/pneumonia</td>
<td></td>
</tr>
<tr>
<td>• Repeated common infections</td>
<td></td>
</tr>
<tr>
<td>• Generalized skin infections</td>
<td></td>
</tr>
</tbody>
</table>

30
**HIV/AIDS Diagnostic Criteria**

### Table 6: IMCI HIV Assessment Algorithm

<table>
<thead>
<tr>
<th>Ask*</th>
<th>Then Look and Feel*</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Has the child had a chest infection requiring hospital admission in the past 3 months?</td>
<td>• Is the child’s weight below the 3rd percentile?</td>
</tr>
<tr>
<td>• Has the child had 2 or more episodes of diarrhea in the past 3 months?</td>
<td>• Does the child have poor weight gain according to his or her history or health card or standard growth curves?</td>
</tr>
<tr>
<td>• Has the child had any episode of persistent diarrhea (lasting 14 days) in the past 3 months?</td>
<td>• Does the child have any enlarged lymph glands in more than 1 of the following sites: neck, axillae, or groin?</td>
</tr>
<tr>
<td>• Has the child had a fever for 1 month or more?</td>
<td>• Is there oral thrush that extends to the back of the mouth or throat?</td>
</tr>
<tr>
<td>• Does the child have a poor appetite?</td>
<td><strong>(If the answer to any question is “yes,” consider symptomatic HIV infection.)</strong></td>
</tr>
<tr>
<td>• Does the child have a chronic ear infection (ear discharge 14 days)?</td>
<td></td>
</tr>
<tr>
<td>• Does the child have a history or evidence of past or present herpes zoster?</td>
<td></td>
</tr>
<tr>
<td>• Is there a history of past or present tuberculosis?</td>
<td></td>
</tr>
<tr>
<td>• Is a parent or sibling known to have tuberculosis?</td>
<td></td>
</tr>
<tr>
<td>• Is a parent or sibling known to be HIV-positive?</td>
<td></td>
</tr>
</tbody>
</table>

*Classify as suspected symptomatic HIV infection if the 2 columns combined produce at least 3 positive findings.

An infant with *Pneumocystis carinii* pneumonia and a CD4+ lymphocyte count of less than 750 cell/mm³ has a classification code of C3 to indicate severe signs or symptoms and severe immunosuppression. An asymptomatic 6-month-old infant with CD4+ lymphocyte count and percentage of at least 1500 cells/mm³ and 25 percent is classified as N1 to indicate no signs or symptoms and no evidence of immunosuppression.

These clinical and immunological classification categories are mutually exclusive. Once classified, an infant or child may not be reclassified in a less severe category even if improvement in clinical or immunological status occurs in response to antiretroviral therapy or other factors. An infant with HIV vertical exposure and indeterminate (unconfirmed) infection status has E (for vertically exposed) placed as a prefix to the appropriate classification code (e.g. EN1).

**WHO Classification – Children**

The WHO has developed several systems for diagnosing probable HIV infection in children based on dividing signs and symptoms into major and minor criteria. A child who is found to have at least two major and two minor symptoms can be diagnosed with HIV, even in the absence of any HIV laboratory testing (Table 5). In addition, the WHO has developed an HIV screening tool that can be incorporated into primary-care settings as part of the Integrated Management of Childhood Illness (IMCI) program (Table 6). This tool utilizes questions that can be asked of the caregiver as well as clinical signs and symptoms in order to identify suspected HIV cases. Different settings may find that this screening tool needs to be modified to highlight their most common HIV-defining illnesses. A study in South Africa found that with region-specific modifications, the sensitivity and specificity of the IMCI tool was improved. If a suspected case of HIV is identified using the IMCI tool, it is recommended that the child be sent to a specialist for further evaluation. Once a diagnosis of HIV has been established, the WHO clinical staging system for children (Table 7) can be used.
### Table 7: WHO Pediatric Clinical Staging

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
</table>
| **1** | Asymptomatic  
Persistent generalized lymphadenopathy (PGL)  
Hepatosplenomegaly |
| **2** | Recurrent or chronic upper respiratory tract infections (otitis media, otorrhea, sinusitis, 2 or more episodes in any 6-month period)  
Poplar pruritic eruptions  
Herpes zoster (1 or more episodes in 6 months)  
Recurrent oral ulcerations (2 or more episodes in 6 months)  
Lineal gingival erythema (LGE)  
Angular cheilitis  
Parotid enlargement  
Seborrheic dermatitis  
Extensive human papilloma virus infection or molluscum infection (more than 5% of body area or disfiguring)  
Fungal nail infections |
| **3** | Unexplained moderate malnutrition not adequately responding to standard therapy  
Unexplained persistent diarrhea (more than 14 days)  
Unexplained persistent fever (intermittent or constant, for longer than 1 month)  
Oral candidiasis (outside neonatal period)  
Oral hairy leukoplakia  
Pulmonary tuberculosis  
Severe recurrent presumed bacterial pneumonia (2 or more episodes in 6 months)  
Acute necrotizing ulcerative gingivitis/periodontitis  
Lymphoid interstitial pneumonitis (LIP)  
Unexplained anemia (<8 gm/dl), neutropenia (<1000/mm3) or thrombocytopenia (<30 000/mm3) for more than 1 month  
Chronic HIV-associated lung disease, including bronchiectasis  
HIV-related cardiomyopathy or HIV-related nephropathy |
| **4** | Conditions for which a presumptive diagnosis can be made using clinical signs or simple investigations:  
Unexplained severe wasting or severe malnutrition not adequately responding to standard therapy  
Unexplained severe bacterial infections (2 or more episodes within 1 year, e.g. empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia)  
Chronic oral or cutaneous herpes simplex infection (of more than 1 month’s duration)  
Extrapulmonary tuberculosis  
Kaposi’s sarcoma  
Esophageal candida  
Central nervous system toxoplasmosis  
HIV encephalopathy |
| Conditions for which confirmatory diagnostic testing is necessary:  
CMV infection (CMV retinitis or infection of an organ other than liver, spleen, or lymph nodes, onset at age 1 month or more)  
Cryptococcal meningitis or other extrapulmonary disease  
Any disseminated endemic mycosis (e.g. extra-pulmonary histoplasmosis, coccidiomycosis, penicilliosis)  
Cryptosporidiosis  
Isosporiasis  
Disseminated non-tuberculous mycobacteria infection  
Candida of trachea, bronchi, or lungs  
Acquired HIV-related recto-vesico fistula  
Cerebral or B-cell non-Hodgkin’s lymphoma  
Progressive multifocal leukoencephalopathy (PML) |
| Presumptive Stage 4 diagnosis in children less than 18 months of age where virological confirmation of infection is not available:  
Severe immunosuppression should be suspected and ARV treatment is indicated in an HIV-seropositive infant less than 18 months of age who is symptomatic with 2 or more of the following: oral thrush, +/- severe pneumonia, +/- severe wasting/malnutrition, +/- severe sepsis  
CD4+ values, where available, should be used to guide decision-making. CD4+ % below 24% requires urgent ARV treatment.  
Other factors that support the diagnosis of Clinical Stage 4 HIV infection in an HIV-seropositive infant are recent maternal death or advanced HIV disease in mother.  
Presumptive diagnosis of Stage 4 disease in seropositive children less than 18 months of age requires confirmation with HIV virological tests as soon as possible or repeat HIV antibody test after 18 months of age. |
HIV/AIDS DIAGNOSTIC CRITERIA

**Review Questions**

1. How does the ELISA determine the presence of HIV in an individual?
2. Which tests are used to confirm rapid test findings, and how do they work?
3. Why is it difficult to diagnose HIV in infants?
4. How are the degree of immunosuppression and presence of clinical signs and symptoms used to classify a patient’s disease status?
5. List the major and minor signs and symptoms from the WHO classification system, and describe how HIV is established using this algorithm.

**Exam Questions**

1. Screening tests such as the ELISA and rapid test kits measure:
   a. Bands of proteins specific for the virus
   b. Antibodies to HIV in the serum
   c. Chain reactions to DNA or RNA in the virus
   d. CD4+ lymphocyte counts

2. Maternal antibodies can be detected in an infant’s blood until:
   a. 1 year of age
   b. 3 months of age
   c. 18 months of age
   d. 6 months of age

3. Amadu is a 3-year-old boy vertically infected with HIV. As an infant he had *Pneumocystis carinii* pneumonia and a CD4+ cell count of 1000. Since then he has been well, experiencing only normal childhood illness. His current CD4+ cell count is 1200. Based on the CDC classification system for children, what would be his current classification?
   a. B3
   b. C2
   c. A1
   d. C1

4. The WHO staging system uses which of the following symptoms as a major sign to establish the diagnosis of HIV in children?
   a. Oral candidiasis
   b. Chronic diarrhea
   c. Pneumonia
   d. Lymphadenopathy

5. Which of the following conditions is NOT part of the 1993 CDC AIDS surveillance case definition for adults?
   a. Cytomegalovirus retinitis (with loss of vision)
   b. Cervical dysplasia
   c. Wasting syndrome due to HIV
   d. Mycobacterium tuberculosis

Answers: 1b, 2c, 3b, 4b, 5b
Case Study #1

A mother brings her 3-year-old son to clinic. She tells you that over the past several months he has bruised easily and bled from the nose frequently. She states that she has been told in the past that his blood doesn’t clot well. Reviewing the boy’s chart, you find that he had a positive ELISA test at 2 years of age, which was confirmed by Western blot. Also, his platelet count has been 50,000 cells/mm³ for the past three months. On his last visit to the clinic, his CD4+ count was 750 cells/mm³ (20 percent).

**Question:** What would this boy’s CDC classification be?

- a. N1
- b. B2
- c. C2
- d. B3

**Answer:** b. This child is HIV-infected, because he had a positive ELISA test over the age of 18 months, which was confirmed by Western blot. He is considered clinical category B. In Table 4, clinical category B lists “thrombocytopenia (<100,000/mm³) persisting >30 days.” His immunologic category is 2, because at age 3 his CD4+ count is 500-999 cells/mm³ (Table 3).

**Question:** Does this child have AIDS?

**Answer:** No. In order to meet the definition of AIDS, a child must have either a CD4+ count below 15 percent for his or her age group (Table 3) or one of the clinical illnesses that define AIDS. All of the category C illnesses define AIDS (Table 4). The only category B illnesses considered AIDS-defining illnesses are lymphoid interstitial pneumonia (LIP) and pulmonary lymphoid hyperplasia (PLH) complex. LIP and PLH are AIDS-defining illnesses only in children, not in adults.

**Question:** What recommendations would you give this boy’s mother because of his thrombocytopenia?

- a. He should never blow his nose.
- b. He should avoid activities that may involve contact injuries (e.g. football)
- c. Contact the clinic immediately if the child starts vomiting, is difficult to wake up, or has a seizure.
- d. b and c.
- e. None of the above.

**Answer:** d. HIV-associated thrombocytopenia can be difficult to manage. Parents should be advised of the increased risk of internal bleeding, especially with a very low platelet count (less than 20,000 cells/mm³). The family should be taught appropriate methods for stopping a nosebleed and be made aware of the importance of contacting the clinic or a health professional immediately if the child has a nosebleed that cannot be stopped. The family should also be told to contact the health care provider if the child has increasing bruising or shows signs of an intracranial bleed. Signs or symptoms of an intracranial bleed include seizures, focal motor weakness, and decreased alertness.

Case Study #2

A 6-month-old infant comes to clinic for immunizations. His mother is HIV-infected. The infant is a good weight and length for his age and has had only one episode of infectious diarrhea since he was born. The diarrhea resolved in two days. His physical exam is completely normal. The infant’s rapid test is positive, and his CD4+ cell count is 2200 (38 percent).

**Question:** According to CDC guidelines, how would the infant be classified?

- a. N1
- b. A2
- c. EN1
- d. EN2
Answer: c. By clinical criteria, this infant would be categorized as N, because he has had no signs or symptoms of HIV infection (Table 4). Because his CD4+ count is >25 percent for his age group (Table 3), his immunologic category is 1. Finally, the infant is classified as E for exposed. Because he is younger than 18 months, his positive rapid test may only reflect the presence of maternal antibodies in his blood. DNA PCR (if available) would be the easiest and most economical test at this time to determine whether the infant is infected.

Question: List three topics you feel it is important to discuss with this mother before the end of her visit. Briefly explain why you feel these issues are important and what anticipatory guidance you would give the mother.

Answer: Topics may include breastfeeding, immunizations, adding soft foods to the infant’s diet, home safety, and signs and symptoms of dehydration. Where safe alternatives to breastfeeding are readily available, HIV-infected women are encouraged not to breastfeed. However, in places where formula and a clean water source may not be readily available, the WHO recommends explaining the risks of breastfeeding as well as the risks of improperly mixed formula to the mother so that she may make an informed choice about what to feed her infant. Live vaccines given to an immuno-compromised child may cause illness in some cases. However, the WHO recommends that HIV-infected children receive all immunizations, as the risk of contracting the vaccine-preventable disease is greater. The one exception is BCG; a severely immunocompromised child should not receive BCG. At 6 months, children should begin to eat a variety of soft foods to add more nutrients to their diet. As children begin to become mobile, it is important that families keep unsafe objects out of the children’s reach. Finally, all mothers should be taught to recognize and manage acute dehydration.

Case Study #3

A 2-year-old girl is brought to the rural clinic by her grandmother. The grandmother tells you that the girl’s mother died of “slim disease” two months ago. The girl has had diarrhea for three months with weight loss. Her current weight is 7 kg (<5 percent). On examination, you find oral thrush and generalized lymphadenopathy.

Question: According to the WHO guidelines for clinical diagnosis of HIV, would this child be considered HIV-infected?

Answer: Yes. A diagnosis of presumed HIV infection in a child requires identification of two major criteria and two minor criteria associated with infection by the virus. This girl has two major (weight loss and chronic diarrhea) and two minor (generalized lymphadenopathy and oral thrush). Moreover, her mother probably died from complications of HIV. This tells you that the girl was probably exposed to HIV perinatally.

Case Study #4

A 24-year-old student presents for anonymous HIV testing. She was raped three months ago. Two months ago she was seen in clinic for fever, malaise, fatigue, and swollen lymph nodes. At that time she was diagnosed with influenza. At present she has no complaints or symptoms.

Question: Assuming that her ELISA test is positive, in which CDC category would she be?

a. A1
b. B3
c. C2
d. None of the above

Answer: d. Because no CD4+ count was given, an immunologic category (1, 2, or 3) cannot be assigned.
Question: In which clinical category would she be according to the CDC guidelines?

a. N
b. A
c. C
d. B

Answer: b. The illness the student experienced 2 month prior to this clinic visit was probably secondary to her acute (primary) HIV infection, rather than influenza. In addition, the student is currently asymptomatic. Hence, she is clinical category A (Table 2).

References

6. CDC. 1993 revised classification system for human immunodeficiency virus infection in adolescents and adults. MMWR 41. 1993;(No. RR-17).
8. CDC. 1994 Revised classification system for human immunodeficiency virus infection in children less than 13 years of age. MMWR 43. 1994.


Objectives

The purposes of this module are to:
1. Discuss the goals of treatment for human immunodeficiency virus (HIV) infection.
2. Present the basic principles of antiretroviral (anti-HIV) therapy.
3. Review the antiretroviral medicines currently being used around the world to treat HIV infection.
4. Discuss barriers to effective antiretroviral therapy and some of the ways to overcome them.

Key Points

1. Many antiretroviral drugs are available for the treatment of HIV infection. However, none of these medications can cure HIV.
2. Medications used to treat HIV reduce the ability of the virus to replicate (or reproduce) within the body.
3. When HIV is unable to replicate, damage to the immune system and other vital organs is reduced, usually leading to improved health.
4. Patients receiving antiretroviral therapy are less susceptible to opportunistic infections, malignancies, and other illnesses.
5. Many patients live longer as a consequence of antiretroviral therapy.
6. One goal of antiretroviral therapy is to reduce the patient’s virus load, preferably to below levels that can be detected with available tests.
7. There are three main groups of antiretroviral drugs: nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs) and protease inhibitors (PIs). Each group of drugs works at a different point in the life cycle of the virus within the cell.
8. The decision to begin antiretroviral therapy in an HIV-infected person is determined by that person’s clinical, virologic, and immunologic condition.
9. Antiretroviral therapy often is changed when an HIV-infected child or adult experiences clinical, virologic, or immunologic failure.
10. Among the numerous barriers to treatment are cost, time commitment, compliance, and home environment.

Introduction

While many medicines are used to treat HIV infection, none can cure HIV/AIDS. Antiretroviral drugs can reduce the ability of the virus to replicate, and they can thus reduce the damage the virus does over time to the person’s immune system and other vital organs.

Therapeutic Goals

The primary goal of antiretroviral therapy is to improve the health and prolong the life of the HIV-infected child or adult. This is achieved by interfering with the ability of the virus to replicate or reproduce inside the body. When the virus is unable to replicate, damage to the immune system is minimized. Because the immune system is functioning more normally, the treated individual is less susceptible to opportunistic infections, malignancies, and other illnesses. HIV-infected patients receiving
Antiretroviral therapy also are less likely to develop other complications associated with HIV/AIDS, such as wasting syndrome and encephalopathy (a disorder of the brain). Most patients taking effective antiretroviral therapy will live longer than they would without medications.

The health professional can monitor how well the goals of treatment are being met by talking to and examining the patient as well as by performing laboratory tests. Clinically patients are evaluated for signs and symptoms of HIV disease progression, such as weight loss or new opportunistic illnesses. Children taking antiretroviral drugs will often have improved growth and development. The two laboratory tests used most commonly to monitor the success of antiretroviral therapies are measures of the viral load and the CD4+ cell count. A viral load (e.g. HIV DNA PCR) assay is a measurement of the concentration of the virus in the blood or plasma. With some types of highly active antiretroviral therapy (HAART), it is possible to reduce the amount of virus circulating in the blood or plasma to below levels of detectability. Unfortunately, in such cases, the virus is still present in the body, and the concentration of circulating virus will increase if treatment is stopped.

Antiretroviral therapy typically produces a significant drop in viral load. Viral-load test results may vary from week to week. Changes in viral load are often expressed by logarithms, or logs (see Table 1). A 1 log change is a drop or increase by a factor of 10. A 1 log drop means that the level of HIV in the blood has decreased by 90 percent; a 1 log increase means the level of HIV in the blood has increased 10-fold. In general, the larger the log drop, the stronger the sign that HIV replication is being slowed.

The significance of a change in viral load varies with the age of the patient. In patients younger than 2 years of age, only changes of 0.7 log or more from the baseline level (the viral load before medications are started) are considered significant. In children 2 years of age and older and in adults, only viral-load increases or decreases of more than 0.5 log are considered meaningful. The viral load should be monitored at regular intervals. If the viral load decreases but then begins to increase, this may be an indication of non-compliance with medications, resistance of the virus to the antiretroviral drugs, or treatment failure.

The CD4+ cell count measures the concentration of a particular type of lymphocyte, the T-helper cell, in a specified amount of the patient’s blood. The CD4+ cell is severely affected by HIV infection. In the body, HIV attaches to and enters CD4+ cells. Once inside, the virus subverts the CD4+ cell’s replication machinery, turning it into a virus factory. In the process of copying itself, the virus destroys the CD4+ cell. Often when a patient begins antiretroviral therapy, the CD4+ count will increase, a reflection of the immune system’s improved ability to fight infection. Determining a patient’s CD4+ cell count at regular intervals allows the health professional to monitor the strength of the patient’s immune system. Successful antiretroviral therapy will cause the CD4+ cell count to rise and then remain elevated during therapy. A decrease in the concentration of CD4+ cells may represent failure of antiretroviral therapy.

**Table 1: Guide to Logarithmic Changes**

<table>
<thead>
<tr>
<th>Log Drop</th>
<th>% Change</th>
<th>Resulting Viral Load in a Patient With a Baseline Viral Load of 100 000 Copies HIV RNA/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.3</td>
<td>55%</td>
<td>50 000</td>
</tr>
<tr>
<td>0.5</td>
<td>67%</td>
<td>33 000</td>
</tr>
<tr>
<td>0.6</td>
<td>75%</td>
<td>25 000</td>
</tr>
<tr>
<td>1.0</td>
<td>90%</td>
<td>10 000</td>
</tr>
<tr>
<td>1.5</td>
<td>97%</td>
<td>3 000</td>
</tr>
<tr>
<td>2.0</td>
<td>99%</td>
<td>1 000</td>
</tr>
<tr>
<td>2.3</td>
<td>99.5%</td>
<td>500</td>
</tr>
</tbody>
</table>
Principles of Therapy

When to Start Therapy
Antiretroviral therapy is not necessarily started when a patient is first infected with HIV. Although some evidence suggests that starting medicines before a patient is symptomatic can prolong life, there are many obstacles to such early treatment. Antiretroviral therapy can be costly. Also, the virus can develop resistance to these medications, in much the same way that bacteria can become resistant to the effects of antibiotics. The medicines can be difficult to take, causing many side effects. Patients who do not feel ill from their disease may not be motivated to take medicines. Once antiretroviral medicines are started, they need to be taken consistently, according to instructions, every day. Patient motivation is important to ensure that medication schedules are followed precisely.

With these caveats in mind, most clinicians who treat adults follow standard criteria for starting medications, which may include the following:
- Symptoms of HIV infection, such as candidiasis or weight loss
- Viral load (HIV RNA) of more than 55 000 copies/mL of plasma
- CD4+ count of less than 350 cells/uL of blood

Most studies relating viral load and immune status to HIV disease progression have been conducted in developed countries. Many developing countries have chosen to utilize a higher viral load and lower CD4+ cell count for initiating antiretroviral medications. These changes are based on drug availability as well as

Figure 1: The HIV Life Cycle

Life cycle of HIV virus with sites of action of some antiretroviral medications
growing concern regarding the potential side effects of long-term antiretroviral therapy.

Opinions also differ about when to start antiretroviral therapy in an HIV-infected child. An HIV-infected child’s clinical, virologic, and immunologic status should be evaluated at the time of diagnosis and monitored closely at regular intervals thereafter. Few experts would disagree that a symptomatic HIV-infected child should be treated. In particular, children who are experiencing growth failure or neurodevelopmental regression or who are failing to achieve developmental milestones normally should receive antiretroviral treatment. Similarly, any child with a high or rising viral load should be considered for antiretroviral therapy. Finally, any child whose immune system has been compromised should be treated. Immunologic compromise is reflected in a lower-than-expected CD4+ cell count or percentage (<25 percent).

Available evidence suggests that infants younger than 12 months should be treated as soon as they are diagnosed with HIV. The rationale is that it is very difficult to determine which infants will have rapid disease progression and which will have slow disease progression. A prediction of rate of disease progression cannot be made based on the viral-load determination or the CD4+ cell count or any other measure that is currently available.

**Which Therapy to Begin**

Antiretroviral drugs are grouped by how they work. Each class of medications interrupts HIV replication at a different point in the life cycle of the virus (Figure 1). The groups of drugs are nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), and protease inhibitors (PIs). Each of these groups will be discussed in more detail in the next section.

Patients with HIV infection almost always receive combinations of antiretroviral drugs, and typically these combinations include drugs from more than one group or class. The rationale for combination antiretroviral therapy is the same in adults and children: to target at least two points in the HIV life cycle. The more ways HIV is attacked by different drugs, the less likely it is that the virus will become resistant to treatment. This is similar to the use of combination therapy to treat tuberculosis.

Prevention of mother-to-child transmission is the one instance where single-drug antiretroviral therapy sometimes is given. Several studies have shown that treatment of the mother and infant with zidovudine (ZDV, AZT) can decrease transmission of the virus to the newborn. The same is true of the drug nevirapine. Regardless, one should not confuse these efforts to reduce mother-to-child HIV transmission with treatment of a child or adult with HIV/AIDS.

Many current guidelines suggest starting antiretroviral therapy with two NRTIs, usually in combination with an NNRTI or a PI. Table 2 shows some of the NRTIs that are often used in combination with one another.

In certain patients, a combination of three NRTIs may be appropriate. Adults with a viral load less than 50,000 copies/ml and a good CD4+ cell count (>200 cells/μL) may benefit from treatment with a single pill combining zidovudine (ZDV), lamivudine (3TC), and abacavir. Because this combination is in a single pill, compliance with the regimen is easier. However, this regimen is not as powerful as one containing an NNRTI or PI.

**When to Change Therapy**

Antiretroviral therapy should be changed when the child or adult experiences clinical, virologic, or immunologic failure. Evaluation for treatment failure should include a medical history and physical examination for evidence of disease progression, viral

<table>
<thead>
<tr>
<th>Table 2: NRTI Combinations</th>
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<tbody>
<tr>
<td>Common Combinations Used</td>
</tr>
<tr>
<td>ZDV + ddI</td>
</tr>
<tr>
<td>ZDV + 3TC</td>
</tr>
<tr>
<td>d4T + ddI</td>
</tr>
</tbody>
</table>
load, and CD4+ cell count. Adults who are responding well to treatment will maintain their weight and have few illnesses. Adults in whom the treatment is no longer as active will lose weight and develop more infections and illnesses. In children, it is important to measure growth and monitor neurodevelopment. Neurodevelopment is the way a child achieves normal milestones, such as sitting, walking, and feeding him-or herself. Monitoring this involves watching children closely during examinations and asking their caregivers about how they have changed since the last visit. Children who are responding well to antiretroviral therapy typically grow well and develop normally. Children who are failing antiretroviral therapy frequently fail to grow or experience developmental problems.

The definition of virologic failure differs for each individual. A patient whose viral load is undetectable after a first course of antiretroviral therapy but then rebounds to 10 000 or 20 000 copies/ml could be defined as having failed therapy. However, a patient who has had every available antiretroviral drug but whose viral load decreases from 1 000 000 copies/ml to 10 000 or 20 000 copies/ml after a new course of treatment would be considered a treatment success.

As in treatment initiation, the decision to change treatment because of failure should be put into clinical context. Children and adults may have an initial drop in viral load, followed by a slow increase. But if their CD4+ lymphocytes continue to increase over time, this could indicate that the treatment is holding the virus at bay, preventing it from destroying the immune system, and thus the best course of action might be to continue the current medications. Each case is different. Decisions about when to declare failure and change treatment require the judgment of experienced professionals.

**Antiretroviral Therapies**

Our discussion of the three groups of antiretroviral drugs includes tips for caregivers regarding difficulties that patients often have in taking medications and some suggestions for overcoming these barriers. Table 3 lists doses and common side effects of all three classes of medications.

**Nucleoside Reverse Transcriptase Inhibitors (NRTIs)**

NRTIs were the first class of antiretroviral medications approved by U.S. and European regulatory agencies, starting with zidovudine (ZDV, AZT) in 1987. NRTIs work by blocking an HIV protein called reverse transcriptase (Figure 1), thus preventing HIV RNA from changing into DNA. This is a critical point in the life cycle of HIV. NRTIs in combination with one another and with other classes of drugs are the cornerstone therapy for HIV-infected children and adults.

**Tips for Caregivers:**

- **ZDV (Retrovir or zidovudine or AZT)** can be taken with or without food and is available in oral solution, tablets, and capsules, all of which should be stored at room temperature. The capsules should be protected from moisture.
- **d4T (Zerit or stavudine)** can be taken with or without food. The oral solution needs to be refrigerated and shaken well before administering. The capsule can be opened and sprinkled over mashed potatoes or other soft foods. It should never be administered with ZDV, because the two medicines have the same mechanism of action and act at the same spot in the life cycle of HIV. Hence, giving d4T and ZDV together would be the same as giving just one drug.
- **ddl (Videx or didanosine)** should be given on an empty stomach one hour before or two hours after a meal. The suspension needs to be refrigerated and shaken well before administering. If the solid formulation is used, two tablets must be given to ensure adequate buffering. The tablets may be dissolved in water or chewed. A new formulation of ddl is available, an enteric coated capsule (Videx EC). This can be taken once a day by adults or twice a day by children. The EC formulation is often more palatable for patients.
### Table 3: Antiretroviral Medications

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation)</th>
<th>How Supplied</th>
<th>Dosing</th>
<th>Notes</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Didanosine (ddl) Videx</strong></td>
<td>Chew tablet (white, round): 25 mg, 50 mg, 100 mg, 150 mg&lt;br&gt;EC capsules: 125 mg, 200 mg, 250 mg, 400 mg&lt;br&gt;Powder for oral solution in packets and bulk bottles</td>
<td>Neo&lt;br&gt;• (&lt;90 days): 50 mg/m² q12hr&lt;br&gt;Pediatrics&lt;br&gt;• 90-150 mg/m² q12hr&lt;br&gt;Adolescent / Adults&lt;br&gt;• &lt;60 kg: 125 mg bid or 250 mg daily if EC&lt;br&gt;• &gt;60 kg: 200 mg bid or 400 mg daily if EC</td>
<td>ddi liquid: mixed with antacids&lt;br&gt;• Oral solutions: Shake well, refrigerate; stable for 30 days&lt;br&gt;• Take on empty stomach&lt;br&gt;• If using chew tabs, 2 tabs per dose recommended</td>
<td><strong>Common:</strong> Nausea/vomiting/diarrhea, abdominal pain&lt;br&gt;<strong>Severe:</strong> Peripheral neuropathy, electrolyte abnormalities, hyperuricemia, lactic acidosis with hepatic steatosis&lt;br&gt;<strong>Uncommon:</strong> Pancreatitis, increased liver-function tests, retinal depigmentation</td>
</tr>
<tr>
<td><strong>Lamivudine (3TC) Epivir</strong></td>
<td>Tablet: 100 mg, 150 mg&lt;br&gt;Oral solution: 10 mg/ml (strawberry/banana)</td>
<td>Neo&lt;br&gt;• (&lt;30 days): 2 mg/kg q12hr&lt;br&gt;Pediatrics&lt;br&gt;• 4 mg/kg q12hr&lt;br&gt;Adolescent / Adults&lt;br&gt;• &lt;50 kg: 2 mg/kg bid&lt;br&gt;• &gt;50 kg: 150 mg bid</td>
<td>With or without food&lt;br&gt;• Active against hepatitis B&lt;br&gt;• Store oral solution at room temperature</td>
<td><strong>Common:</strong> Nausea/diarrhea, headache, fatigue, skin rash, abdominal pain&lt;br&gt;<strong>Severe:</strong> Pancreatitis, lactic acidosis with hepatic steatosis</td>
</tr>
<tr>
<td><strong>Stavudine (d4T) Zerit</strong></td>
<td>Capsule: 15 mg, 20 mg, 30 mg, 40 mg&lt;br&gt;Oral powder for solution: 1 mg/ml</td>
<td>Pediatrics&lt;br&gt;• 1 mg/kg q12hr&lt;br&gt;• 30-60 kg: 30 mg bid&lt;br&gt;• &gt;60 kg: 40 mg bid&lt;br&gt;Adolescent / Adults&lt;br&gt;• &lt;60 kg: 30 mg bid&lt;br&gt;• &gt;60 kg: 40 mg bid</td>
<td>With or without food&lt;br&gt;• Oral solution: Shake well, refrigerate; stable for 30 days</td>
<td><strong>Common:</strong> Headache, nausea/vomiting/diarrhea, skin rash, increased liver-function tests&lt;br&gt;<strong>Severe:</strong> Peripheral neuropathy, pancreatitis, lactic acidosis with hepatic steatosis</td>
</tr>
<tr>
<td><strong>Zalcitidine (ddC) Hivid</strong></td>
<td>Film-coated oral tab: 0.375 mg (beige), 0.75 mg (gray)&lt;br&gt;Syrup (investigational): 0.1 mg/ml</td>
<td>Pediatrics&lt;br&gt;• 0.01 mg/kg q8hr&lt;br&gt;Adolescent / Adults&lt;br&gt;• 0.75 mg tid</td>
<td>Take on empty stomach</td>
<td><strong>Common:</strong> Headache, malaise&lt;br&gt;<strong>Severe:</strong> Peripheral neuropathy, pancreatitis, hepatic toxicity, rash, oral ulcers, hematologic toxicity, lactic acidosis with hepatic steatosis</td>
</tr>
<tr>
<td><strong>Zidovudine (ZDV) Retrovir</strong></td>
<td>Capsule: 100 mg (white with blue stripe)&lt;br&gt;Tablet: 300 mg (white, round, biconvex)&lt;br&gt;Syrup: 10 mg/ml&lt;br&gt;IV: 10 mg/ml</td>
<td>Premature&lt;br&gt;• 1.5 mg/kg q 12hr&lt;br&gt;Neo&lt;br&gt;• 2 mg/kg po q6hr&lt;br&gt;• 1.5 mg/kg IV q6hr&lt;br&gt;Pediatrics&lt;br&gt;• 60-180 mg/m² po q6-8hr (usual 160 mg/m² po q8hr)&lt;br&gt;• IV intermittent: 60-120 mg/m² q6hr&lt;br&gt;• IV continuous: 20 mg/m²/hr&lt;br&gt;Adolescent / Adults&lt;br&gt;• 200 mg tid or 300 mg bid</td>
<td>Take with food&lt;br&gt;• Hematoxicity: Interrupt therapy or decrease dose or use erythropoietin, filgrastim&lt;br&gt;• IV: Infuse over 1 hour; dilute with D5W to 4 mg/ml; refrigerated stable for 24 hours</td>
<td><strong>Common:</strong> Hematologic toxicity, headache&lt;br&gt;<strong>Other:</strong> Myopathy, myositis, liver toxicity, lactic acidosis with hepatic steatosis</td>
</tr>
<tr>
<td><strong>Abacavir (ABC) Ziagen</strong></td>
<td>Film-coated tablet: 300 mg&lt;br&gt;Oral solution: 20 mg/ml (strawberry/banana)</td>
<td>Pediatrics&lt;br&gt;• 8 mg/kg twice daily&lt;br&gt;Adolescent / Adults&lt;br&gt;• &gt;16 yrs: 300 mg bid</td>
<td>Store at room temperature&lt;br&gt;• Required: warning card and patient package insert</td>
<td><strong>Common:</strong> Nausea/vomiting/diarrhea, loss of appetite, malaise, headache, rash&lt;br&gt;<strong>Severe:</strong> Hypersensitivity: Do not rechallenge.</td>
</tr>
<tr>
<td>Table 3: Antiretroviral Medications Continued</td>
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<tr>
<td>---------------------------------------------------------------</td>
<td></td>
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</tr>
<tr>
<td><strong>Nucleoside Reverse Transcriptase Inhibitors (NRTIs) Continued</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Generic Name</strong> (Abbreviation)</td>
<td><strong>How Supplied</strong></td>
<td><strong>Dosing</strong></td>
<td><strong>Notes</strong></td>
<td><strong>Side Effects</strong></td>
</tr>
<tr>
<td>---------------------------------</td>
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<td>-------------</td>
<td>-----------</td>
<td>-----------------</td>
</tr>
<tr>
<td>Tenofovir Disoproxil Fumarate Virad</td>
<td>• Tablet: 300 mg</td>
<td><strong>Adolescent / Adult</strong></td>
<td>• 300 mg daily</td>
<td>• Take 2 hours before or 1 hour after didanosine</td>
</tr>
<tr>
<td>Zidovudine/ Lamivudine Combivir</td>
<td>• Tablet (white, capsule-shaped, coated)</td>
<td><strong>Adolescent / Adult</strong></td>
<td>• 1 tablet bid</td>
<td>• Store at room temperature</td>
</tr>
<tr>
<td>Zidovudine/ Lamivudine/ Abacavir Trizivir</td>
<td>• Tablet</td>
<td><strong>Adolescent / Adult</strong></td>
<td>• 1 tablet bid</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Generic Name</strong> (Abbreviation)</td>
</tr>
<tr>
<td>---------------------------------</td>
</tr>
<tr>
<td>Delavirdine (DVL) Rescriptor</td>
</tr>
<tr>
<td>Nevirapine (NVP) Viramune</td>
</tr>
<tr>
<td>Efavirenz Sustiva</td>
</tr>
<tr>
<td>Indinavir (IDV) Crixivan</td>
</tr>
<tr>
<td>Nelfinavir (NFV) Viracept</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Protease Inhibitors (PIs)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Generic Name</strong> (Abbreviation)</td>
</tr>
<tr>
<td>---------------------------------</td>
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<td></td>
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</tbody>
</table>

45
**Table 3: Antiretroviral Medications Continued**

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation)</th>
<th>How Supplied</th>
<th>Dosing</th>
<th>Notes</th>
<th>Side Effects</th>
</tr>
</thead>
</table>
| Ritonavir (RTV) Norvir      | Capsule: 100 mg (white, soft gel) | **Pediatrics** | • 400 mg/m² q12hr | • Take with food  
• Store liquid in refrigerator in original container; can be stored at room temperature for 30 days  
**Common:** Nausea/vomiting/diarrhea, abdominal pain, anorexia  
**Other:** Circumoral paresthesias, increased LFTs; spontaneous bleeding, pancreatitis; increase triglyceride and cholesterol, hyperglycemia |

| Saquinavir (SQV-H) Invirase | Hard gel capsule: 200 mg (opaque light brown/dark green) | **Adolescent / Adult** | • 400 mg bid with ritonavir  
• Otherwise not recommended | **Common:** Nausea/vomiting/diarrhea, abdominal pain, headache  
**Other:** Spontaneous bleeding, hyperglycemia |

| Saquinavir (SQV-S) Fortovase | Soft gel capsule: 200 mg (opaque, beige gel cap) | **Pediatrics** | • 50 mg/kg q 8 hr or 33 mg/kg q 8hr with nelfinavir (investigational)  
**Adolescent / Adult** | • Take within 2 hours of meal  
• Causes photosensitivity; protect against sun  
**Common:** Nausea/vomiting/diarrhea, abdominal pain, headache  
**Other:** Spontaneous bleeding, hyperglycemia |

| Amprenavir Agenerase | Capsule: 50 mg, 150 mg (white, oblong gel cap)  
Liquid: 15 mg/ml (grape, bubblegum, peppermint flavors) | **Pediatrics (6-3 years)** | • <50 kg: 22.5 mg/kg bid oral soln or 20 mg/kg bid capsules  
• >50 kg: 1200 mg bid  
**Adolescent / Adult** | • With or without food  
**Common:** Headache, nausea/vomiting/diarrhea, rash |

| Lopinavir/ritonavir Kaletra | Capsule: 133.3 mg lopinavir + 33.3 mg ritonavir  
Liquid: 80 mg lopinavir + 20 mg ritonavir/ml | **Pediatrics** | • 7-<15 kg: 12 mg/kg lopinavir + 3 mg/kg ritonavir bid  
• 15-40 kg: 10 mg/kg lopinavir + 2.5 mg/kg ritonavir bid  
• >40 kg: 400 mg lopinavir + 100 mg ritonavir bid  
**Adolescent / Adult** | • Take with food  
• Refrigerate; can be kept at room temperature up to 25 degrees C up to 2 months  
**Common:** Nausea/vomiting/diarrhea, headache  
**Other:** Hyperglycemia, increased liver-function tests |

Table courtesy of Stephanie Maciejewski, PharmD

- **3TC (Epivir or lamivudine)** can be given with or without food. It is available in a tablet or oral-solution formulation. The oral solution needs to be refrigerated.
- **Abacavir (Ziagen or ABC)** is available as a tablet or a yellow oral solution. It can be administered with or without food. The solution and tablets can be stored at room temperature. Abacavir has been known to cause severe hypersensitivity reactions, which may include rash, diarrhea, and respiratory symptoms. If such a reaction occurs, the drug must be stopped immediately and never restarted. Patients and parents should be taught the signs and symptoms of a hypersensitivity reaction.
- **ddc (Hivid or zalcitabine)** comes in two different tablet formations. It should be taken on an empty stomach.
- **Tenofovir (Viread)** is available in tablet form. It
is known to increase the concentration of didanosine, so these two should not be taken at the same time.

**Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)**
NNRTIs also work by blocking the HIV protein reverse transcriptase, but they do so in a slightly different way than NRTIs. These drugs have been used in combination with NRTIs and PIs and have been found to be generally well-tolerated and safe.

**Tips for Caregivers:**
- **Nevirapine (Viramune)** is available as a tablet and an oral solution. It can be administered with or without food. The tablets are scored and may be broken in half for ease of administration. The solution should be shaken well prior to use. Nevirapine sometimes produces a measles-like rash in the first six weeks after initiating therapy. The likelihood of rash can be reduced by giving the medicine at half-dose for the first 14 days. Patients and parents should be taught to contact the health care provider if a rash appears. The rash is usually self-limited. However, involvement of mucous membranes (eyes, mouth, and urethra) signals a more serious condition and may require permanent discontinuation of the drug. Antihistamines may help with the itching that often accompanies a nevirapine rash.
- **Efavirenz (Sustiva)** can be given with or without food, but high-fat meals should be avoided for best absorption. Efavirenz capsules can be opened and sprinkled over food. The drug may cause hyperactivity, impaired concentration, abnormal dreams, and other central nervous system effects. These side effects can be reduced by giving the once-daily dose at bedtime. Efavirenz can cause a rash similar to that seen with nevirapine.
- **Delavirdine (Rescriptor)** can be taken with or without food. It is not recommended for children. It can also cause a rash similar to that experienced with nevirapine. See Table 3 for dosing guidelines and common side effects.

**Protease Inhibitors (PIs)**
PIs are antiretroviral drugs that work differently from NRTIs and NNRTIs. PIs prevent the protease enzyme from cleaving large HIV precursor proteins into smaller functional units, a process that causes the production of defective virus particles incapable of infecting CD4+ cells and replicating. PIs are very powerful, but when they are taken alone, the virus quickly becomes resistant to their anti-HIV effects, and the benefit of therapy is short-lived. For this reason, PIs are always combined with other anti-HIV medications. Taking PIs in the correct dose and exactly on time is very important. Missed doses can lead to viral resistance and drug failure. Combining a small dose of one PI called ritonavir with a therapeutic dose of several other PIs can boost the concentration of those other PIs in the blood, improving the effectiveness of treatment. Kaletra (lopinavir/r) is a PI that combines one PI (lopinavir) with a small amount of ritonavir in a single pill.

**Tips for Caregivers:**
- **Nelfinavir (Viracept)** should be given with a light meal or snack. It is available as a blue tablet or a powder formulation. The tablets can be crushed, pulverized, or dissolved in water. It should not be given with citrus juices or applesauce. The powder has a very low bioavailability, so a large amount of the powder needs to be administered to equal one dose. Because the powder has the consistency of sand, the tablets are usually preferred if the weight-based dose required by the patient is at least equivalent to one tablet. The taste of the powder can be improved by mixing it with milk, chocolate milk, pudding, or vanilla ice cream.
- **Ritonavir (Norvir)** can be given with or without food, but food seems to make it more tolerable. It is available as an oral solution or a soft gelatin capsule. The solution needs to be refrigerated. Ritonavir has a bad taste and is not well tolerated by most patients. Several methods have been used to make it more palatable, including mixing it
with milk, chocolate milk, or vanilla or chocolate pudding; dulling the taste buds by giving ice or frozen treats prior to dosing; and coating the mouth with peanut butter.

- **Indinavir (Crixivan)** is available only in a capsule formulation. It should be administered one hour before or two hours after a meal. Those who take it should drink 48 ounces of fluid per day to prevent the formation of kidney stones (renal calculi). It should not be taken with grapefruit juice, but it can be taken with water, skim milk, or apple juice.

- **Saquinavir (Invirase, Fortovase)** should be given with a meal or no more than two hours after a meal. It is available as a tablet or capsule. Saquinavir is always given with ritonavir. Because saquinavir has been reported to cause photosensitivity, patients should wear protective clothing or sunscreen when outdoors.

- **Amprenavir (Agenerase)** can be administered with or without food. Because it contains high levels of vitamin E, patients should be advised against taking supplements of this vitamin. The solution has a bitter taste but is generally well tolerated.

- **Lopinavir/ritonavir (Kaletra)** should be administered with food. It comes as a capsule or an oral solution. The capsules should be refrigerated or kept in a cool place, although they can be left out of the refrigerator for one month if necessary.

### Monitoring During Therapy

Many of these medications have potentially serious side effects, which are summarized in Table 3. Many of them also have interactions with other medications, described in Table 4 and Table 5. It is important to carefully monitor patients taking antiretroviral medications. Current practice guidelines recommend evaluating patients at least every three months while they are receiving these medications. Side effects experienced by the patient should be reviewed. If available, a complete blood
count and routine blood chemistries should be checked. Urinalysis also should be checked at intervals.

When beginning antiretroviral therapy, patients should be advised not to stop their medications without first speaking with a health care provider. Many times, side effects can be minimized with simple interventions. Stopping one or two of the medications can increase the likelihood that the patients’ HIV will become resistant to treatment.

Adherence

Treatment success is highly dependent on patients’ ability to adhere to their medication schedule. Strict scheduling guidelines, side effects, and the need to take multiple (at times unpalatable) medications make it difficult for adults and children to take their medications at the right time and in proper coordination with their meals. Yet adhering to the medication schedule is critical to prevent the development of resistant forms of HIV. The health care team, family, and friends are vital components in the patient’s success in adhering to treatment.

Adherence needs to be discussed at every clinic visit and does not depend solely on the patient’s ability to remember to take his or her medications. Barriers to adherence can include lack of access to refills, insufficient food and water with which to take the medications, inability to get to the clinic for scheduled appointments because of problems with transportation, and lack of a personal support system. These are all issues that should be discussed with the patient before he or she starts antiretroviral medications and at every clinic visit after the patient has started antiretroviral therapy.

Nurses and others on the health care team can assist patients with adherence by using multiple interventions. Interventions should not be delayed until patients start having problems. Interventions should begin during the first discussions about starting antiretrovirals and should continue at every clinic visit. Interventions include education, counseling, assistance with problem-solving, and motivational strategies. Patients should be educated about the results of good adherence, problems that will result from non-adherence, and adverse events related to the medications. Counseling can help patients identify factors that may prevent them from taking their medications as scheduled. Health care providers can help by developing a written schedule that is individualized to a patient’s daily life and by assisting the patient to develop cues for remembering to take the medications. One way to achieve this is to incorporate taking medication into everyday activities. The patient may brush his or her teeth every morning and use this activity as a cue to take the morning dose of medication.

It is just as important for children to adhere to their antiretroviral medication schedule as it is for adults. Discussions of the importance of medication adherence should begin as early possible. The discussions should be based on the child’s developmental level. Parent-child interaction and discipline are critical to the

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<tr>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Substantial increases SQV</td>
<td>Antagonistic in vitro (one lab)</td>
<td>Increases SQV-S</td>
<td>Decreases SQV and APV</td>
<td>Decreases SQV-H</td>
<td>Increases SQV</td>
<td>Decreases SQV, don’t combine</td>
<td>Saquinavir (SQV-H/S)**</td>
</tr>
<tr>
<td>Increases SQV-S</td>
<td>Increases SQV</td>
<td>Decreases SQV and APV</td>
<td>Decreases SQV-H</td>
<td>Increases SQV</td>
<td>Decreases SQV, don’t combine</td>
<td>Saquinavir (SQV-H/S)**</td>
<td></td>
</tr>
<tr>
<td>Increases IDV</td>
<td>Increases NFV</td>
<td>Increases APV</td>
<td>No significant interaction</td>
<td>Increases RTV</td>
<td>Modest increase in both</td>
<td>Ritonavir</td>
<td></td>
</tr>
<tr>
<td>Increases APV</td>
<td>Increases IDV</td>
<td>Increases APV, decreases IDV</td>
<td>Decreases IDV</td>
<td>Increases IDV</td>
<td>Decreases IDV</td>
<td>Indinavir</td>
<td></td>
</tr>
<tr>
<td>Increases APV</td>
<td>Increases APV, decreases IDV</td>
<td>No significant interaction</td>
<td>Increases NFV</td>
<td>No significant interaction</td>
<td>Nelfinavir</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No data</td>
<td>No data</td>
<td>Decreases APV</td>
<td>Amprenavir</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Table adapted from Medscape, Inc., 2000  
** SQV-H: hard gel capsule; SQV-S: soft gel capsule
<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism of Interaction</th>
<th>Drug Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nevirapine</td>
<td>Potent CYP450 3A4 inducer</td>
<td>• Midazolam, oral contraceptives, protease inhibitors, rifampin, rifabutin, triazolam</td>
</tr>
<tr>
<td>Delavirdine</td>
<td>CYP450 3A4 inhibitor</td>
<td>• alprazolam, amphetamines, carbamazepine, cisapride, midazolam, nifedipine, phenobarb, phenotoin, rifampin, rifabutin, triazolam, midazolam, ergot derivatives</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Increases Levels of: • clarithromycin, dapsone, indinavir, quinidine, saquinavir, warfarin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Separate by at Least One Hour: • antacids or didanosine</td>
</tr>
<tr>
<td>Efavirenz</td>
<td>CYP450 3A4 inhibitor/inducer</td>
<td>• cisapride, midazolam, triazolam, ergot derivatives</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Increases Levels of: • nelfinavir, ritonavir</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Decreases Levels of: • indinavir, saquinavir, efavirenz, phenobarb, phenytoin, rifampin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Potentially Significant: • clarithromycin, ethinyl estradiol, rifampin, warfarin</td>
</tr>
<tr>
<td>Saquinavir (SQV)</td>
<td>Weak CYP450 3A4 inhibitor</td>
<td>• cisapride, ergot derivatives, lovastatin, simvastatin, midazolam, triazolam, rifampin (decreases SQV by 80%), rifabutin (decreases SQV by 40%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SQV Levels Increased by: • grapefruit juice, ketoconazole, nelfinavir, ritonavir</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SQV Levels Decreased by: • carbamazepine, dexamethasone, nevirapine, phenobarb, phenytoin, rifabutin, rifampin</td>
</tr>
<tr>
<td>Ritonavir (RTV)</td>
<td>Potent CYP450 3A4 inhibitor</td>
<td>• amiodarone, bepridil, bupropion, cisapride, clorazepate, clozapine, diazepam, encainide, ergot alkaloids, estazolam, midazolam, flurazepam, lovastatin, triazolam, simvastatin, flecaïnine, meperidine, piroxicam, propoxyphene, propafenone, quinidine, rifabutin, zolpidem</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Increases Levels of: • clarithromycin, desipramine, ketoconazole</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Decreases Levels of: • ZDV, ethinyl estradiol, sulfamethoxazole, theophylline</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RTV Levels Decreased by: • rifampin (35%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Separate by at Least Two Hours: • antacids, didanosine</td>
</tr>
<tr>
<td>Indinavir (IDV)</td>
<td>CYP450 3A4 inhibitor</td>
<td>• delavirdine, ketoconazole (consider 25% IDV decrease), nelfinavir</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IDV Levels Decreased by: • grapefruit juice, nevirapine, rifampin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Separate by at Least One Hour: • ddl (it decreases IDV absorption)</td>
</tr>
<tr>
<td>Nelfinavir (NFV)</td>
<td>CYP450 3A4 inhibitor</td>
<td>• amiodarone, lovastatin, midazolam, saquinavir, quinidine, TCAs, warfarin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Decreases Levels of: • ethinyl estradiol, norethindrone</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NFV Levels Decreased by: • rifabutin, rifampin</td>
</tr>
<tr>
<td>Amprenavir</td>
<td>CYP450 3A4 inhibitor</td>
<td>• bepridil, cisapride, ergot alkaloids, lovastatin, simvastatin, rifampin, triazolam, midazolam, vitamin E</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Increases Levels of: • amiodarone, lidocaine, nelfinavir, quinidine, TCAs, warfarin</td>
</tr>
<tr>
<td>Zidovudine (ZDV)</td>
<td></td>
<td>Increased ZDV Toxicity: • chemo agents, cinetidine, dapsone, ribavirin, ganciclovir, interferon, probenecid, valproic acid, fluconazole (increases ZDV level 74-84%)</td>
</tr>
<tr>
<td>Lamivudine (3TC)</td>
<td></td>
<td>Not significant</td>
</tr>
<tr>
<td>Didanosine (ddI)</td>
<td></td>
<td>ddI Levels Decreased by: • dapsone, itraconazole, ketoconazole, methadone</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ddI Levels Increased by: • ganciclovir, ribavirin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Use with alcohol contraindicated</td>
</tr>
<tr>
<td>Zalcitabine (ddC)</td>
<td></td>
<td>ddC, Toxicity Increased by: • aminoglycosides, amphotericin, ddI, stavudine, dapsone, metoclopramide, phenytoin, probenecid</td>
</tr>
</tbody>
</table>
effectiveness of long-term medication maintenance. Parents or guardians need to be taught how to intervene appropriately when a child refuses to take the medications. Coercion and bribery are not recommended. These methods may promote short-term but not long-term adherence. Parents should be taught that if their child refuses to take the medications, everything in the child’s life stops until the medications are taken. The parent should refrain from cajoling the child to take the medications. The child should simply not be allowed to do anything until the medicines are consumed. Children should be taught that medication taking is part of their daily lives. Motivational tools, such as videotapes of other children who take antiretrovirals, and personal medication calendars may be useful for children. By focusing on factors that will help the patient and family adhere to the demanding regimens of antiretrovirals over time, the entire team working together can help accomplish this difficult task.

**Drug Interactions**

Various antiretroviral drugs interact with one another as well as with other common medications (see Table 4 and Table 5). All medications a patient is taking should be reviewed periodically for possible interactions. There are also many interactions between antiretrovirals and the drugs used to treat tuberculosis. Before treating a patient for both conditions, a specialist should be consulted. See the module on tuberculosis for a more detailed discussion of the interactions between antiretroviral and antituberculosis treatment.

### Treatment Options for Patients If Antiretroviral Therapy Fails

It would be ideal to begin an entirely new treatment regimen for any patient who is not benefiting from antiretroviral therapy. This is not always possible, because some people have already received most of the antiretrovirals available. One antiretroviral may be changed or added, although this is not recommended because of concerns about the virus becoming resistant. Another option may be to continue the failing regimen. It is important to remember that the definition of failure is different for each individual. A patient who has been on many antiretroviral drugs and finds the viral load increasing while receiving HAART may still be deriving some clinical benefit from the drug combination. The failing treatment regimen may be continued even though full suppression of viral replication is not achieved. Antiretroviral drugs used in the patient’s past may be used again, but this is not generally considered as a first option. Rarely, antiretrovirals are completely discontinued in a person with very advanced disease who has been through all available therapies and in whom therapy is producing toxicity or intolerance but no benefits.
Limitations to Selection of Alternative Antiretroviral Therapy

A number of possible limitations to the selection of alternative antiretroviral therapy exist. There is cross-resistance among some agents. Hence, a patient who develops resistance to one protease inhibitor may have resistance to most protease inhibitors. There is cross-resistance among the non-nucleoside reverse transcriptase inhibitors. The nucleoside agents are less prone to this classwide type of cross-resistance. There is cross-resistance between ddI and ddC and some potential cross-resistance between ddI and 3TC, particularly if 3TC is used prior to ddI. D4T is unique among antiretroviral agents in that it does not have a genotypic marker for resistance, and high-grade resistance to d4T has been difficult to demonstrate in samples of virus taken from individual patients. In most cases, the virus retains susceptibility to d4T even in patients who have been treated with d4T monotherapy over a long period of time.

Accessory or secondary mutations of HIV invariably accumulate in patients who are treated with antiretroviral agents. They are considered accessory mutations because they usually need to combine with other mutations to cause enough resistance to prevent the drug from working. A primary mutation by itself can keep a drug from working effectively. An HIV virus that has accumulated a number of accessory mutations over time will be resistant to therapy.

Resistance testing may also have a role to play when changing antiretroviral therapy. Two types of resistance testing are available, genotyping and phenotyping. Genotyping is less expensive and can usually be completed in one to two weeks. Genotyping detects drug-resistance mutations that are present in the relevant viral genes. In contrast, phenotyping assays measure the ability of viruses to grow in the presence of various concentrations of antiretroviral drugs. They are more expensive and generally take two to three weeks to complete. Where available, resistance testing should be considered in cases of virologic failure while receiving HAART or suboptimal suppression of viral load after initiation of HAART. Resistance testing has several drawbacks, however. It is costly and lacks uniform quality assurance. Moreover, it is insensitive for minor viral species. For example, if a patient has not taken ZDV in several years, ZDV-resistant virus may represent only a small percentage of circulating virus. Resistance testing may inaccurately report this patient as having a virus susceptible to ZDV. Were the patient to be restarted on ZDV, the resistant virus would quickly become dominant.

Barriers to Treatment

Barriers to treatment can be found at both the community and the individual levels. At the community level, antiretroviral medications can be too expensive for a government or community to supply to everyone who needs them. Current studies are evaluating more cost-effective treatment regimens that may reduce this problem. Cost can also be a barrier for an individual. Lack of transportation and other logistical problems can hinder treatment. In addition, the toxicity of antiretrovirals may deter some people from taking the medications. Combination antiretroviral therapy can be complicated and time-consuming and may not be seen as compatible with some people’s lifestyles. Some medications need to be refrigerated, and this may limit their usefulness in areas where refrigeration is not available. The development of resistance can also be a barrier to treatment. Patients who are non-compliant with their medications can develop resistance and then spread the resistant virus. To overcome this, research is trying to develop simpler, once-daily therapies. Once such therapies are developed, it may become possible to institute programs of directly observed therapy (similar to those used in tuberculosis treatment) in which a health worker actually watches the patient take the medication.
ANTIRETROVIRAL TREATMENT

Review Questions

1. Review the goals of antiretroviral therapy.
2. What are the principles of antiretroviral therapy?
3. When should antiretroviral therapy begin?
4. Identify the specific medication groups available for HIV.
5. Identify the major side effects of the medications.

Exam Questions

1. The primary goal of antiretroviral therapy is to:
   a. Kill the virus
   b. Improve the patient’s health and prolong his or her life
   c. Improve the host’s immune system
   d. Prevent encephalopathy
2. Ideally, when is antiretroviral therapy initiated in infants (<1 year of age)?
   a. At diagnosis
   b. After the first opportunistic infection
   c. When they are failing to thrive
   d. None of the above

Answers: 1b, 2a
Case Study #1

You are seeing a 25-year-old man in clinic. He was diagnosed with HIV two years ago. Since that time, he has been treated for oral thrush twice and infectious diarrhea once. Now he is starting to lose weight. You decide to start him on dual therapy (two nucleoside reverse transcriptase inhibitors).

Question: Which combination of NRTIs is NOT recommended? Why not?

   a. d4T & ZDV
   b. 3TC & d4T
   c. ZDV & ddI
   d. ddI & d4T
   e. All of the above are acceptable combinations

Answer: a. d4T and ZDV is not one of the recommended dual therapies. Both d4T and ZDV inhibit HIV replication at the same spot in the life cycle. ZDV is the more “aggressive” of the two drugs. Hence, if you treat a patient with d4T and ZDV at the same time, it is the same as giving just ZDV. Any of the other combinations listed would be acceptable.

Question: Which of the following side effects is/are commonly seen with NRTIs? What suggestions might you give the patient for obtaining relief?

   a. Nausea
   b. Diarrhea
   c. Headache
   d. All of the above
   e. None of the above

Answer: d. Nausea, diarrhea, and headache are all common side effects seen with NRTIs. Vomiting can also be associated with medications. Usually, after the patient has taken the medications for a while, these side effects lessen. For nausea, patients can try eating small, frequent meals. Fresh lemon juice may relieve nausea. If the diarrhea is severe and a health practitioner has determined that the diarrhea is not caused by infection, medications such as Imodium can be used. Finally, paracetamol may relieve headaches. Patients should be counseled NOT to stop their medications if they experience side effects. Rather, they should contact their health care worker for assistance.

Case Study #2

Alex is 3 years old. He acquired HIV from his mother (vertical infection). For the past two years, he has been on HAART. He takes two NRTIs and a PI. Alex has a viral load and CD4+ count checked every six months. You have just received the results of his last lab tests. His viral load has increased from 1000 copies HIV RNA/ml to 10 000 copies HIV RNA/ml. His CD4+ count has remained stable at 890 cells/uL (23 percent). Alex has grown several centimeters since his last visit and has gained weight. He has not been ill since his last visit and is tolerating his medication well.

Question: What is the logarithmic change in Alex’s viral load? Is this significant?

   a. 0.3
   b. 0.6
   c. 1.0
   d. 1.5
   e. 2.0

Answer: c. A change from 1 000 to 10 000 is a 10-fold increase in Alex’s viral load. A 10-fold increase corresponds to a 1 log increase. Any change in viral load of more than 0.5 log is considered significant. The change in Alex’s viral load most likely represents a true clinical change and should not be attributed to the variability of viral-load testing.

Question: Would you change Alex’s antiretroviral therapy? Why or why not?
Case Studies Continued

Answer: No. It is true that Alex’s viral load has had a significant increase. However, his CD4+ count has not changed. This shows that his immune system is maintaining its strength. Alex has also not had any illnesses in the past six months. This is another sign that his immune system is functioning well. Lastly, he has grown taller and gained weight. His ability to continue to grow is a good indicator of his body’s strength. The goal of antiretroviral therapy is to allow patients to live longer and healthier. Currently, despite the change in viral load, Alex’s therapy is still helping him achieve these goals. One should consider more closely monitoring Alex over the next several months to ensure that his medications do continue to work well.

Question: What is the most likely cause of the increase in Alex’s viral load?

a. Non-adherence to the antiretroviral regimen
b. Development of resistance to the antiretroviral regimen
c. Alex was ill at the time the viral-load determination was performed

Answer: a. Non-adherence is the most likely cause for the increase in Alex’s viral load. Studies have demonstrated that lapses in adherence to antiretrovirals can lower the suppression of viral replication. The development of resistance to the antiretrovirals will cause an increase in the viral load, but the development of resistance usually follows a history of poor adherence. Intercurrent illness or the administration of vaccines can cause an intermittent rise in viral load. The family should be counseled about adherence, and the viral load should be repeated. If the rise was due to intercurrent illness, the viral load should come back down.

Bibliography


PREVENTION OF SEXUAL TRANSMISSION OF HIV/AIDS

Objectives

The purposes of this module are to:
1. Review factors associated with sexual transmission of HIV.
2. Evaluate risk factors related to sexual transmission of HIV.
3. Address the importance of safer-sex education.
4. Analyze key components of a successful prevention program to stop sexual transmission of HIV.

Key Points

1. HIV can be transmitted through exposure to any of four body fluids: blood, semen, vaginal fluids, and breast milk.
2. Sexual intercourse is the major route of transmission throughout the world.
3. Prevention of HIV transmission is the most realistic strategy for slowing the HIV epidemic.
4. To help sustain a sexually transmitted epidemic, an individual must have unprotected sex with at least two partners, becoming infected by one and passing the infection on to at least one other.
5. The presence of another sexually transmitted infection may increase the risk of HIV transmission.
6. Safer-sex practices reduce the risk of acquiring HIV.

7. Correct and consistent use of latex condoms during sexual intercourse can greatly reduce the chances of acquiring or transmitting HIV.
8. Even when both partners are infected, latex condoms should still be used to prevent transmission of different strains of HIV.

Overview

Sexual intercourse is the major route of transmission of HIV throughout the world. While we maintain hope that an effective anti-HIV treatment or vaccine will be made available on a wide scale in the future, a cure or vaccine for AIDS is unlikely within the next several years. Therefore, prevention remains the most realistic strategy for slowing the HIV epidemic. The power of preventive interventions makes it theoretically possible to eradicate HIV from the planet. If everyone who is currently infected with HIV did not transmit it to anyone else, the virus would burn out and disappear. Thus it is vitally important to design, implement, analyze, and continually improve our prevention efforts. This module reviews facts about the sexual transmission of HIV. These include risk factors for sexual transmission of the virus and specific interventions known to be effective in reducing its
spread. This module also provides evidence that prevention programs can be effective and describes essential elements found in most successful interventions.

Risk Factors for Sexual Transmission

The precise risk of HIV transmission from a single act of sexual intercourse is not known. While some people have had multiple sexual contacts with an infected person without acquiring HIV, others have become infected from a single sexual encounter. Repeated intercourse with an HIV-infected person increases the risk of infection. The risk of becoming infected with HIV as a result of sexual intercourse depends on:

- The probability that the sexual partner is infected
- The number of sexual partners
- The type of sexual contact involved
- The amount of virus present in the blood or secretions of the infected partner
- The presence in either partner of other sexually transmitted infections (STIs) and/or genital lesions, which increase the risk of HIV transmission

Probability That Sexual Partner Is HIV-Infected

The prevalence of HIV infection among sexually active people varies in different areas and among population subgroups within each area. The extent to which HIV spreads between groups with high-risk behavior and the larger population depends on whether members of those high-risk groups have sex with people who do not share their high-risk behaviors and on whether condoms are used in those sexual encounters. For example, a married man who has sex with a sex worker is engaging in a high-risk behavior. If that man also has sex with his wife without a condom, the wife is at risk of acquiring HIV. If the wife becomes HIV-infected, she may pass the virus to the couple’s children during pregnancy, birth, or breastfeeding. This is an example of how HIV spreads from high-risk groups into the general population. As infection rises in the general population, so does the likelihood of encountering an infected person early in one’s sexual career.

To help sustain a sexually transmitted epidemic, a person must have unprotected sex with at least two partners, becoming infected by one and passing the infection on to at least one other. In fact, since not every encounter between an HIV-positive and an HIV-negative partner results in a new infection, a sustained heterosexual epidemic suggests that a substantial proportion of the population, both male and female, have a number of sexual partners over their lifetimes. The risk of acquiring HIV from each sexual encounter depends, in part, on the likelihood that the partner is infected. This risk varies based on regional HIV prevalence rates and the type of risk behavior of each potential partner.

Number of Sexual Partners

The probability that a person has acquired an STI is, in general, proportional to the number of sexual partners that person has had in recent years. However, in areas where the prevalence of HIV is high, people may become infected who have had only one partner. This fact was illustrated in a study done to determine behavioral and demographic risk factors for HIV infection in Rwanda. Infection rates were higher among women who were single and reported more than one lifetime sexual partner. Women in legal marriages or monogamous partnerships had lower rates of infection, but even among “low-risk” women, the prevalence of HIV was about 20 percent. For most of these women, a steady male partner was the source of their HIV risk.

In places where efforts to reduce HIV prevalence have been successful, reducing the number of sexual partners has been a consistent element of prevention programs. Partner reduction was a key factor in the drop in HIV transmission in the homosexual populations of the United States and Europe in the mid-1980s. Community education and a dramatic
reduction in the number of gay bathhouses (where men often met for casual sex) were strategies that limited the spread of HIV. Partner reduction is also credited for the drop in HIV prevalence in Uganda in the 1990s. Slogans such as “zero grazing” (faithfulness to one partner) and “love faithfully” were an important part of Uganda’s early response to HIV.3

**Type of Sexual Contact Involved**

All types of sexual intercourse carry a risk of HIV transmission. While existing data suggest differences in the relative risks of various types of intercourse, the precise level of risk associated with each is not known. Trauma to the mucous membranes of the rectum or vagina may make transmission of HIV more efficient, but it is not essential for transmission to occur. The highest risk of HIV infection occurs among women and men who engage in receptive anal intercourse with an infected partner. Vaginal intercourse carries a higher risk for men and women than oral sex.

Sexual intercourse refers to penetration of the penis into an orifice: vagina, rectum, or mouth. Sexual behavior is any act of sexual gratification, whether between two or more individuals or by oneself. Sexual intercourse is a risk behavior for acquiring HIV and other STIs, but not all sexual behaviors promote risk. Sexual behavior in which the exposure of infectious body fluids is minimized, such as intercourse using a condom, is considered risk reduction or SAFER sex. Sexual practices with no exposure or exchange of infectious body fluids are considered prevention or SAFE sex. These include but are not limited to hugging, dry kissing, masturbation, and frottage (rubbing).

In summary, HIV can be transmitted through exposure to blood, semen, vaginal fluids, or breast milk. Any activity that directly exposes a person to any of these body fluids is risky. (Participant Activity I near the end of this chapter is designed to promote discussion of behaviors associated with HIV transmission.)

**Amount of Virus Present in the Blood or Secretions of the Infected Partner**

HIV-infected individuals are believed to become more infectious as they progress to AIDS. In theory, those who have fewer particles of virus circulating in their bodies have fewer particles of virus to pass to their partners during unprotected sex. However, even newly infected persons who show no overt signs of immune compromise can transmit HIV infection. In addition, they are more likely to have many sexual partners than are people who have clear symptoms of disease. Mathematical models suggest that the primary HIV infection interval – the time before an infected person shows symptoms of HIV – may account for as many as half of all infections.4 If this is true, the primary infection interval presents a special window within which it is possible to have a major impact on the spread of HIV.

**Presence of Other STIs**

There is increasing evidence that the presence of another STI in one or both partners increases the risk of HIV transmission. Genital ulceration, such as may occur with chancroid, syphilis, or herpes simplex virus infection, appears to increase susceptibility to infection.1 This may be because blisters, small tears, and other openings in the mucosal lining of the vagina or on the skin of the penis provide a “door” that allows HIV to enter the body. In the Rwanda study of behavioral and demographic risk factors for HIV infection,2 history of another STI in the past five years was the strongest risk factor for acquiring HIV infection. In other words, history of another STI within the past five years was a better predictor of HIV infection than marital status, income, or even the number of sexual contacts within the past five years. However, it is important to realize that HIV can be transmitted even in the absence of other STIs. Microscopic tears to the mucosal lining of the vagina or to the skin of the penis can occur during normal sexual activity. Although these may not be visible to the naked eye and may not be painful, they could provide a “door” for HIV to enter the body.
Prevention of Further Sexual Transmission Within the HIV-Positive Population

This module focuses on prevention of sexual transmission of HIV from an infected partner to an uninfected partner. However, even if both partners are infected, condoms still should be used to prevent further transmission. There are different types (strains) of HIV, and partners infected with different types might infect each other. Some researchers believe that certain types of HIV may be stronger and inflict more damage on the immune system than others. Reinfection occurs when a person gets more (different) HIV types in his or her system. If partners have different treatment histories with antiretroviral medications, medication-resistant strains could be transmitted from one partner to another. Safer-sex practices such as condom use help protect against reinfection. They also protect against other STIs, such as hepatitis, syphilis, gonorrhea, parasites, and herpes.

Safer-Sex Education

There are certain actions a person can take that are known to reduce the risk of acquiring HIV. Education about these actions is an essential element of every successful prevention campaign. Everyone must be made aware of how to avoid acquiring HIV and must be empowered to act on that information. The first three concepts below are widely known as the elements of ABC prevention campaigns.

Abstinence – Refraining from sexual intercourse is the best way to prevent transmission of HIV and other STIs. Abstinence means not engaging in any sexual activity in which there is a direct or theoretical risk of exposure to blood, semen, or vaginal fluid (see Participant Activity I).

Be Faithful – If two partners are tested for HIV and found to be uninfected, they may enter into a strictly monogamous sexual relationship, and neither will be at risk of contracting HIV infection sexually. However, if one partner engages in sex with a third party, even one time, both partners are at risk of acquiring the virus. Monogamy works as a prevention strategy only if both partners are known to be uninfected when their sexual relationship begins and if neither partner has sex, even one time, outside of this relationship.

Condoms – Correct and consistent use of latex condoms during sexual intercourse (vaginal, anal, and oral) can greatly reduce the chances of acquiring or transmitting HIV and other STIs. Natural-membrane condoms, often made from sheep gut, are
not recommended, because they have tiny pores through which HIV can pass.

Consistent use means using a condom with each act of intercourse. Correct condom use involves all of the following steps:

- Use a new condom for each act of vaginal, anal, or oral intercourse.
- Put on the condom as soon as erection occurs and before any vaginal, anal, or oral contact with the penis.
- Hold the tip of the condom and unroll the condom onto the erect penis, leaving space at the tip of the condom but ensuring that no air is trapped in the tip.
- Adequate lubrication is important to prevent condom breakage, but use only water-based lubricants, such as glycerin. Oil-based lubricants, such as petroleum jelly, cold cream, hand lotion, and baby oil, can weaken the condom.
- Withdraw from the partner immediately after ejaculation, holding the condom firmly at the base of the penis to keep it from slipping off.

The promotion and supply of condoms should be viewed as specific disease-control measures. Condoms should not be seen merely as contraceptives or as associated with a particular social or sexual lifestyle.

**Common Myths About Condom Use**

*See Participant Activity II:*

- Condoms don’t work: If used correctly and consistently (during every sexual encounter), latex condoms are highly effective in preventing transmission of HIV and other STIs.
- Condoms often break: Condom breakage is extremely rare when condoms are used correctly. Using oil-based lubricants can weaken latex, causing the condom to break.
- HIV can pass through condoms: Intact latex condoms provide a barrier to HIV and much smaller micro-organisms, such as hepatitis B. Natural-membrane condoms, often made from sheep gut, have tiny pores through which HIV can pass, so they are not recommended.

- Education about condom efficacy promotes sexual activity: The World Health Organization recently reviewed 19 studies and found no evidence that sex-education programs increased sexual activity among young people. In fact, five of the studies showed that such programs can lead young people to delay or decrease sexual activity.

**Postponement** - A fourth, potentially powerful prevention message is postponement. Postponement means delaying intercourse until two partners are tested and found to be uninfected. Postponement is an empowering concept, especially for young people, for whom abstinence may have an “eternal” or “forever” connotation.

**Microbicides** – Microbicides are topical formulations designed to block HIV infection when applied vaginally before intercourse. To date, there is no single vaginal microbicide that has proven to be safe and effective in preventing the transmission of HIV. To be successful, such agents will have to be cheap, stable, easy to use, and acceptable to target populations. Spermicidal compounds containing nonoxynol-9 (N-9) or other virucidal chemicals have been shown to inactivate HIV in vitro. However, a study conducted among high-risk commercial sex workers found that the women who used N-9 gel became infected with HIV at about a 50 percent higher rate than women who used a placebo gel. The reason for this increased transmission of HIV when N-9 was used is that the chemical also destroyed membranes of epithelial cells lining the vagina and the cervix, which provide an important natural barrier to HIV infection. This study is important, because health workers need to be aware that N-9 should NOT be recommended as a method of protection against HIV.

**Female Condom** – The recent marketing of the female condom has generated considerable interest, especially among those who are allergic to latex. The female condom is made of polyurethane, not latex, so someone who is allergic to latex can use it without reaction. Although laboratory studies indicate that
the device serves as a barrier to HIV, further research is needed to determine its effectiveness in preventing transmission of HIV. If a male condom cannot be used, consider using a female condom.

In settings where access to condoms is non-existent or limited (prisons, rural or remote areas), promoting “anything is better than nothing” with respect to risk reduction should always be encouraged. Helpful steps include limiting a person’s number of sexual partners, withdrawal prior to ejaculation, and abstaining from intercourse during menstruation.

Challenges for Sexual Prevention Programs

The design and implementation of interventions to reduce sexual HIV transmission confront several challenges:

- A reluctance to discuss sexual matters publicly has been a constant hindrance in the battle against HIV. An example of this is the failure of many political leaders of the most HIV-affected countries to embrace prevention through safer-sex education. This silence has been observed on national, regional, and local scales.
- Inaccurate risk perception often leads to unsafe sex. This has been described as the “downhill phenomenon,” in which people always compare their own risk with that of someone who is at much greater risk. This leads to an incorrect assessment in which the person sees himself or herself as being at lower risk for HIV than objective evidence would suggest.
- Most models of behavior change have been developed in North America and emphasize actions an individual can take to reduce his or her risk of HIV infection. However, much of the world’s population lives in collectivistic rather than individualistic societies. In this context, the emphasis on and opportunity for individual behavior change are decreased.
- Those most exposed to HIV-prevention messages often acquire “prevention fatigue.” In high-income countries, this phenomenon has been implicated in the rise of HIV-infection rates among risk groups who are well-educated and informed about HIV and HIV prevention.
- Myths about how to cure HIV exist in all parts of the world. There currently is no cure for HIV. One particularly damaging myth that is prevalent in southern Africa is that having sex with a virgin will cure a person of HIV infection. This myth is responsible for a growing epidemic of child sexual assault and rape. Having sex with a virgin WILL NOT cure HIV and will expose the virgin (in many cases a child) to acquiring the infection.
- In developed countries where access to effective treatments has dramatically improved healthy survival rates, prevention efforts have been stymied by attitudes among risk subpopulations that there is a “cure.” This will be a challenge in other regions as populations see a marked improvement in health outcomes due to access to antiretroviral therapy.

Aspects of Successful Sexual Prevention Interventions

Stopping HIV transmission through behavior change is a complicated challenge, but data indicate that HIV prevention efforts can indeed work. Even modest gains through behavior change in key subpopulations (e.g. commercial sex workers and at-risk adolescents) can produce substantial gains for the entire population. In Uganda, reduction of HIV transmission through behavior change has been equivalent to a vaccine of 80 percent effectiveness. Aspects of successful HIV prevention campaigns include:

- Education on how HIV is transmitted and how exposure to it can be minimized or eliminated is a central element of all HIV-prevention campaigns. Consistent and persistent education over time is important. Complicated behavior changes (such as those involving an person’s decision-making regarding sexual practices) are unlikely after a one-time-only intervention. Because sexual behavior is private and many sexual behaviors meet with
community disapproval, education must be provided for the entire population so as to reach all those at risk. Particular attention should be paid to adolescents and young adults, who are entering the age of sexual exploration.

- Successful interventions are usually based on a clear understanding of the realities of target populations and involvement of members of those populations in the development of prevention efforts. Support from the community is critically important. If HIV is so heavily stigmatized that people do not even discuss it, prevention interventions such as condom distribution are unlikely to be effective.

- Interventions that emphasize clarity, simplicity, and feasibility for the target population have the greatest chance of success. The concept of harm reduction is helpful in guiding feasible interventions. This concept emphasizes specific behaviors that can minimize risk when entirely eliminating risk is not feasible. For example, if it is not feasible to shut down the industry of sex workers completely in a region, providing education and condoms to sex workers and their customers may minimize the number of cases of HIV transmission that occur.

- Successful prevention programs often include training in interpersonal skills, such as talking about sexual practices, discussing the avoidance of risks with a partner, and asserting personal preference in a sexual relationship (including abstinence from sex, non-penetrative sex, or the use of condoms).

An example of a successful behaviorally based prevention model comes from Uganda. In Uganda, HIV prevalence nationally among pregnant women peaked in 1991 at 21.1 percent and by 1998 declined to 9.7 percent. By 2000, prevalence had declined further to 6 percent. Although population-based surveys show there was an increase in the age of sexual debut and an increase in condom use during this period of time, this striking reduction in HIV prevalence is believed to be due largely to a decrease in the number of casual or non-regular sexual partners. From the beginning of the Ugandan HIV/AIDS epidemic, the government communicated a clear warning and prevention recommendation: AIDS or “slim” was fatal and required an immediate population response based on “zero grazing” (faithfulness to one partner). In addition to the government’s efforts, data suggest that social networks played a crucial role in information dissemination in Uganda. By 1995, 91.5 percent of men and 86.4 percent of women in Uganda were aware of AIDS as having infected or killed someone they knew personally. This suggests that credible communication of alarm and advice had taken root in discussions in social networks to a greater extent in Uganda than in neighboring countries. Furthermore, the communication process may have provided greater personal exposure to the fear-evoking consequences of the epidemic and thus catalyzed the process of behavior change.

**Summary**

The purpose of this module is to provide factual information on the prevention of sexual transmission of HIV. Other modules go into more detail about issues such as counseling and common psychological responses to a positive HIV test result. The precise risk of HIV transmission from a single act of sexual intercourse is not known. The risk of becoming infected with HIV as a result of sexual intercourse depends on several factors, including the number of sexual partners a person has, the presence of other STIs, and the type of sexual contact involved. Refraining from sexual intercourse with an infected partner is the best way to prevent transmission of HIV and other STIs. Correct and consistent use of latex condoms during sexual intercourse (vaginal, anal, and oral) can greatly reduce the chances of acquiring or transmitting HIV and other STIs. Finally, there is the encouraging fact that HIV prevention programs can indeed work. At this point, prevention is the most realistic strategy for slowing the HIV epidemic. Thus it is vitally important to design, implement, analyze, and continually improve our prevention efforts.
Review Questions

1. What are the major risk factors associated with sexual transmission of HIV?

2. How important is the number of sexual partners in relation to the risk of HIV acquisition or transmission?

3. Which type of sexual contact poses the highest risk of HIV transmission?

4. How do sexually transmitted infections increase the risk of HIV transmission?

5. Describe safer-sex practices that decrease the risk of HIV transmission.

6. Review the correct use of a condom.

7. Name four common myths about condom use, and describe why they are inaccurate.

8. What interventions would you incorporate into a sexual HIV prevention program?

Exam Questions

1. Which type of sexual contact places a person most at risk of HIV?
   a. Oral intercourse
   b. Vaginal intercourse
   c. Anal intercourse
   d. Self-masturbation

2. Which of the following information about condom use is accurate and important to discuss with a couple in which both partners are HIV-positive?
   a. Condom use may cause irritation of the vagina.
   b. Condom use may prevent exposure to different strains of HIV.
   c. Natural-membrane condoms prevent transmission of HIV.
   d. Condoms can be used more than once to save cost.

3. Which of the following statements about condom education and use is true?
   a. Oil-based lubricants cause no concern about condom breakage.
   b. Latex condoms provide a barrier to HIV.
   c. Natural-membrane condoms provide an effective barrier to HIV.
   d. Education about condom use promotes sexual activity.

4. Which would be appropriate interventions to include in a sexual HIV prevention program?
   a. A one-time-only lecture about the morals of sex outside marriage
   b. Basic education regarding the facts of HIV transmission
   c. Provision of information regarding personal hygiene
   d. Publishing a 20-question sexual-health quiz a partner should be given before considering sexual contact.
Case Study

Patrick, 26, and Winnie, 20, were recently married. The couple come to clinic because Patrick has not been feeling well for two weeks. He complains of fatigue and intermittent diarrhea. In taking a history, you discover that Patrick had sex with six partners before the marriage. Winnie does not report any previous sexual partners. You get their consent and draw blood for HIV tests for both partners.

**Question:** How should you counsel them about sexual relations until the test results come back?

a. Carry on sexual relations as usual. If one partner is infected, the other is probably already infected anyway.
b. Practice safer sex by using a condom until the test results come back.

c. Don’t counsel them at all. What goes on in a marriage happens behind closed doors, and you shouldn’t get involved.
d. Encourage the couple to get the marriage annulled immediately.

**Answer:** b. The couple should practice safer sex by using a condom, because until the test results come back, it is impossible to know whether either partner is infected. Having sex without a condom would be dangerous until both partners are shown to be uninfected, because even if transmission has not occurred in the past, it is possible that it could occur the next time. As a health care provider, you should not miss this opportunity to educate Patrick and Winnie about HIV transmission and advise the safest course of action for both partners.

**References**

The following three participant activities are designed to increase student/participant awareness of how to prevent HIV. **Activity I** can be used in small-group sessions to promote discussion of behaviors associated with the sexual transmission of HIV.

**Activity II** is a small-group activity related to the use of condoms to prevent the spread of HIV. Participation can increase awareness about common myths associated with condom use. The activity also may help prepare participants to deal with situations in which one partner is reluctant or unwilling to use a condom during sexual intercourse.

**Activity III** also relates to condom use. It is intended to teach about the appropriate sequence of steps in using a condom. Activity III is adapted from material developed by AIDS Foundation Houston.

### Participant Activity I

**Read the following list of behaviors. Circle the ones you believe are compatible with abstinence.**

- Dry kissing
- Holding hands
- Hugging with hands on arms and back
- Flirting using eye contact
- Open-mouth kissing
- Vaginal intercourse
- Hand contact with another person’s penis or vagina
- Hugging with hands on other person’s hips
- Mouth contact with someone’s breasts
- Penis-to-anus contact (used by some to “preserve a girl’s virginity”)
- Hand contact with someone’s anus
- Hand contact with someone’s breasts
- Touching another person’s upper body with clothes on
- Mouth on someone’s penis or vagina
- Touching another person’s lower body with clothes on
- Kissing while pressing your body against another person’s
- Touching another person’s lower body with clothes off
- Outercourse (penis-to-body contact outside the vagina, anus, or mouth)
**Participant Activity II**

Read the list of reasons not to wear a condom.

In small groups, discuss responses to each of these reasons that are compatible with safer sex.

- **Intimacy** – I just don’t feel close enough to my partner when we use a condom.
- **Trust** – If I use a condom, my partner will think I don’t trust him/her.
- **Convenience** – I mean to use a condom, but when I start having sex, I don’t want to stop to put it on.
- **Sensation** – Sex doesn’t feel as good with a condom.
- **Frustration** – I am just sick of having to wear a condom all the time.
- **Love** – If my partner is going to die, then I want to die, too.
- **Fate** – We’re all going to die someday.

**Participant Activity III**

Write each of the following steps related to condom use on a separate card. Shuffle the cards, and distribute them among participants. Tell participants that the task is to arrange the cards in the order of proper condom use. If there are enough people, have them hold one card each and stand or sit in the proper order. Tell them they have three minutes to complete the task. The tasks are listed below in proper order.

- Discuss and agree upon condom use.
- Check expiration date on condom package, and make sure package is not damaged.
- Erect penis.
- Open condom package.
- Check direction in which condom unrolls.
- Dab water-based lubricant on tip of penis.
- Unroll condom onto shaft of penis (all the way down).
- Check condom for damage (properly rolled/no holes).
- Apply water-based lubricant.
- Sexual intercourse.
- Hold condom at base (before pulling out).
- Withdraw penis.
- Take condom off and discard.
- Loss of erection.
STANDARD PRECAUTIONS
AND HIV POST-EXPOSURE PROPHYLAXIS

EXPOSURE

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Objectives

The purposes of this module are to:
1. Define standard precautions recommended by the World Health Organization (WHO) for protection against the transmission of infectious pathogens.
2. Review infectious versus non-infectious types of body fluids.
3. Describe examples of protective barriers that can be used to prevent exposure to HIV.
4. Evaluate the management of HIV exposure in the health care setting.
5. Explore options for post-exposure management.
6. Review recommendations for follow-up and monitoring after an HIV exposure.

Key Points

1. WHO standard precautions recommend that all individuals be treated as if they were infected with HIV or other infectious pathogens.
2. Exposures that place health care workers at risk of infection include injuries, such as needle sticks, and contact of infectious fluids with mucous membranes or non-intact skin (skin that has a cut or abrasion).
3. The most effective infection-control measure that can be performed by health care workers is handwashing with soap and water before and after patient contact.
4. Precautions should be taken to avoid having the skin, eyes, and mucous membranes come into contact with blood.
5. Needles should never be recapped, bent, or broken; they should be discarded into sealed, puncture-resistant containers.
6. Spills of blood or other infectious fluids should be cleaned while wearing gloves, using a solution of one part household bleach to 10 parts water.
7. When exposure occurs, the source patient and health care worker should be tested for HIV and hepatitis B and C.
8. Treatment to reduce the risk of contracting HIV from the exposure depends on the risk of exposure and information about the exposure source.
9. Seroconversion after six months following the exposure is very rare.

Overview

All health care workers, defined by the U.S. Centers for Disease Control and Prevention (CDC) as all persons (employees, students, contractors, attending clinicians, public-safety workers, or volunteers) whose activities include contact with patients or blood or
other body fluids from patients in a health care or laboratory setting, should be taught how to practice infection control in all health care settings.1 Health care workers must be educated about appropriate measures to be taken if an exposure to a potentially infectious substance occurs. All health care settings should have a written plan of action for infection control, including counseling and follow-up for exposures. All health care workers should be made aware of the plan.1 One option for assuring that all health care workers are aware of infection-control measures is to make review of infection-control policies mandatory for all health care workers on an annual basis. This lecture addresses the importance of following standard precautions when caring for individuals with HIV/AIDS.

**Standard Precautions**

Universal Blood and Body Fluid Precautions, or universal precautions, were developed in 1995 by the CDC and covered fluids containing blood. These precautions have been revised and now include all potentially infectious pathogens.2 The precautions are now called standard precautions. The WHO also recommends the use of these precautions. The precautions recommend that all people should be treated as if they were infected with HIV or other infectious pathogens. The guidelines consider certain body fluids as potential sources of infection, while others are not considered infectious1 (Table 1). As a general rule, any body fluid that contains visible blood is potentially infectious, but body fluids that do not appear to contain blood also may be infectious. These fluids include vaginal secretions, semen, pericardial fluid, pleural fluid, cerebrospinal fluid, amniotic fluid, peritoneal fluid, and synovial fluid. Body fluids considered non-infectious are tears, feces, urine, saliva, nasal secretions, sputum, vomit, and sweat. Health care worker exposure to breast milk is not considered a threat for HIV transmission, but gloves should be worn when breast milk is handled for an extended period of time, such as in a milk bank.

<table>
<thead>
<tr>
<th>Infectious Body Fluids</th>
<th>Non-Infectious Body Fluids</th>
</tr>
</thead>
<tbody>
<tr>
<td>• All body fluids containing visible blood</td>
<td></td>
</tr>
<tr>
<td>• Vaginal secretions</td>
<td></td>
</tr>
<tr>
<td>• Semen</td>
<td></td>
</tr>
<tr>
<td>• Pericardial fluid</td>
<td></td>
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<tr>
<td>• Pleural fluid</td>
<td></td>
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<tr>
<td>• Cerebrospinal fluid</td>
<td></td>
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<tr>
<td>• Amniotic fluid</td>
<td></td>
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<tr>
<td>• Peritoneal fluid</td>
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<tr>
<td>• Synovial fluid</td>
<td></td>
</tr>
<tr>
<td>• Tears</td>
<td></td>
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<tr>
<td>• Feces</td>
<td></td>
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<tr>
<td>• Urine</td>
<td></td>
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<tr>
<td>• Saliva</td>
<td></td>
</tr>
<tr>
<td>• Nasal secretions</td>
<td></td>
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<tr>
<td>• Sputum</td>
<td></td>
</tr>
<tr>
<td>• Vomit</td>
<td></td>
</tr>
<tr>
<td>• Sweat</td>
<td></td>
</tr>
</tbody>
</table>

*Adapted from World Health Organization, Regional Office for the Western Pacific, Manila. HIV/AIDS Reference Library for Nurses: Infection Control. (1993);3,14.*
Exposures that most often put a health care worker at risk of infection include percutaneous injuries, such as needle sticks, or contact of infectious fluids with mucous membranes or non-intact skin. The risk of HIV transmission from a percutaneous exposure is very low, approximately 0.3 percent. The risk after a mucous-membrane exposure is about 0.09 percent. Transmission of HIV from exposure to intact skin has not been documented. Studies suggest that several factors may affect the risk of HIV transmission through percutaneous exposure. These include the quantity of blood to which the person was exposed, the viral load of the patient, and the stage of disease of the patient. The risk of HIV transmission is higher if the health care worker is exposed to a larger quantity of blood through injury from a needle that has been in a vein or artery, or through a deep injury, or through a device that is visibly contaminated with blood. It is also believed that exposure to the bodily fluid of a patient who has end-stage AIDS carries a higher risk of transmission because the patient will most likely have a very high viral load. However, the presence of a low viral load cannot guarantee that transmission will not occur. HIV is very fragile and will survive for only a short time outside the human body. Studies have been done that indicate that HIV can live for up to one day outside of the body, but in these studies the amount of virus that was used was very high. Thus, it seems that the survival time of the virus outside the human body depends on the viral load of the person. Other factors that affect the viability of the virus outside the human body include conditions in the environment, such as temperature and chemicals.

How to Prevent Exposure
Exposure can be prevented through the use of standard precautions supplemented by simple infection-control measures (Figure 1). The most effective infection-control measure that can be taken by health care workers is handwashing with soap and water or alcohol-based disinfectant products before and after all patient contact. For effective cleaning, the hands and forearms should be wet, and soap should be applied over all surfaces using friction; they should then be rinsed completely of soap using running water and dried with a paper towel. If paper towels are not available, a cloth towel that is laundered after each use can be used. Communal towels should never be used. If paper towels and cloth towels are not available, allow the hands and forearms to air-dry. Wet hands should not be dried on clothes. Soap bars can be used but should be cut into small pieces and put into soap dishes that allow water drainage. When running water is not available, hands can be washed using soap and a clean bowl of water, then rinsed using a clean water source that is poured from a cup or bucket over the arms and forearms. The water in the bowl should be discarded after each use, and the bowl should be washed. An alcohol-based handrub can be prepared by adding together 2ml of glycerin, propylene glycol, or sorbitol and 100 ml of 60-90 percent alcohol. To use this handrub, pour 3-5 ml into the palm of one hand and vigorously rub it into all parts of both hands until dry.

Protective Barriers
Examples of protective barriers include gloves, gowns, goggles, and masks. The use of all of these barriers in all situations is impractical; judgment as to when they are needed should be used. If a procedure will be performed in which the eyes could be splashed (such as removing a chest tube or preparing a body for embalming), gloves, gown, and eye protection are indicated. Gloves should be changed and hands should be washed between patients. Gloves should never be washed, because washing can cause breakdown of the gloves. If barriers such as gloves and gowns are not available, other items may be used as a barrier. For example, a clean, thick cloth can be used to put pressure on a bleeding wound. Precautions should always be taken to avoid contact of blood with the skin, eyes, and mucous membranes. Hands should be washed with soap and water after all direct patient contacts.
If a phlebotomy is to be performed, the use of gloves is the only necessary barrier. Remember that gloves only protect a health care worker from getting blood on the skin or in cuts. They do not protect against percutaneous injuries. Percutaneous injuries usually occur when the phlebotomist is inexperienced, in a hurry, or tired, or when the patient is uncooperative.6

**Handling Potentially Infectious Items**

Contaminated waste, such as disposable needles, disposable syringes, and bloody bandages, should be discarded appropriately. Needles should be discarded into sealed puncture-resistant containers. Needles should not be removed from the syringe and should never be recapped, bent, or broken. Puncture-resistant containers should be kept within easy access of medical procedure areas, thereby decreasing the handling of needles and sharps and reducing the risk of accidental injury.

Reusable needles and syringes should be disinfected after each use. The needles and syringes should be washed as quickly as possible after use to prevent the formation of clots, which can be difficult to remove. There are two methods of cleaning used needles and syringes. For the first method, take the needle and syringe apart and clean them with soap and water, paying special attention to the area around the fittings. Put the needle and syringe back together. Fill the syringe with water through the needle, shake it, and expel the water through the needle; repeating these steps until the water that is expelled looks clear. For the second method, fill a clean cup with undiluted bleach. Fill the syringe with the bleach through the needle, and let the syringe and needle sit in the bleach-filled cup for 30 seconds. After the 30 seconds have elapsed, expel the bleach out of the syringe through the needle, and rinse the syringe with water at least three times to remove all bleach.7 The bleach in the cup should be discarded and not reused.

Bloody bandages should be discarded according to local guidelines. All trash should be discarded into leak-proof plastic bags. Heavily contaminated trash, such as used bandages, which may be very wet with blood or other infectious fluid, should be put into a separate plastic bag prior to being put into a general trash container. Soiled linens and clothes do not need to be separated from other linen or laundry before washing. Laundry workers should always wear gloves when handling dirty laundry. Spills of blood or other infectious fluids should be cleaned while wearing gloves, using a solution of one part household bleach to 10 parts water. If gloves are not available, use some type of barrier between the hands and the spill, such as paper towels. Hands should be washed with soap and water immediately after the cleanup.

**HIV Exposure in the Health Care Setting**

**Background**

Health care workers are often at risk of exposure to HIV and other infectious diseases because of the environment in which they work. Following standard precautions easily minimizes this risk. All health care settings should have a written plan of action for handling HIV exposures. All health care workers should be familiar with this plan of action and should know where a copy of it can be found. The plan should include instructions for reporting the exposure, instructions for managing the exposure, information on testing and counseling, and information on post-exposure prophylaxis (PEP), follow-up, and monitoring.

Data on time to HIV seroconversion is limited because of the low prevalence of infection after work-related exposure among health care workers. Among those health care workers who do seroconvert, available data indicates that 81 percent will seroconvert at a mean interval of 65 days after exposure, and an estimated 95 percent will seroconvert by six months after initial exposure.1

In theory, there is a short time interval between HIV exposure and infection, during which transmission of
HIV may be prevented.1 In the first 24 hours after exposure, HIV attacks dendritic-like cells in the mucous membranes and skin.1 Within five days after exposure, these infected cells then make their way to the lymph nodes and eventually to the peripheral blood, where viral replication becomes very rapid. Based on this theory of pathogenesis, it should be possible to prevent HIV infection if antiretrovirals are used prior to 24-48 hours post-exposure.

**Reporting Exposures**

All exposures to potentially infectious fluids should be reported so that appropriate action can be taken. The report should include the date and time of the exposure, details of the procedure being performed, details of the exposure, and details about the exposure source. The wound or skin site should be washed immediately with soap and water, and exposed mucous membranes should be flushed with water. The use of caustic agents or antiseptics or disinfectants at the wound site is not recommended. Squeezing the site to encourage bleeding has not been shown to affect transmission. The source patient and the health care worker should then be tested for HIV and hepatitis B and C, and the need for HIV post-exposure prophylaxis (treatment to try to prevent the acquisition of HIV infection) should be assessed.

**Management of Exposure**

The exposure should be assessed for potential to transmit HIV based on the type of fluid, the route of the exposure, and the severity of the exposure (see Appendix 1).1,4 Exposure to fluids containing visible blood or other fluids known to transmit or contain HIV should be considered sources of possible infection. Evaluation of human bites should take into account the HIV status of both the person who was bitten and the biter. Transmission through a bite is very rare, but if a bite draws blood, post-exposure prophylaxis may be considered.

The person who is the source of the exposure should be evaluated for the presence of HIV (see Appendix 2).1,9 The evaluation should include information on risk factors for HIV, questions about HIV-related symptoms, and HIV testing. If the source is known to be HIV-infected, information about viral load and CD4+ count should be obtained.3 This information may be used in the consideration of post-exposure prophylaxis, but post-exposure prophylaxis should not be held pending these results. Changes to post-exposure prophylaxis can always be made after the treatment has been started. If the source of the exposure is unknown, then an epidemiologic evaluation should be done. An epidemiologic evaluation includes assessing the geographic area in which the exposure occurred for its prevalence of HIV. The geographic area would include the country, the province, the city, the village, the hospital, and the hospital ward. If HIV exists at a high rate in any of these areas, the exposure should be considered high-risk, and post-exposure prophylaxis should be started. Testing of needles and other sharp instruments for the presence of HIV is not recommended, since the reliability of this type of testing is unknown.

Occupational exposure to HIV among pediatricians was previously underestimated. New studies suggest that pediatricians represent a high-risk group.13

**Evaluation and Testing**

Health care workers who are exposed to potentially infectious fluids should have baseline testing performed within hours of the exposure to check for the presence of HIV antibodies. Evaluation of the health care worker also should include questions about medications and current or past medical conditions. All women should be offered pregnancy testing. If the woman is pregnant, her evaluation for the risk of acquiring HIV should not be different from that of any other health care worker. Pregnancy is not a contraindication to exposure prophylaxis. PEP should be explained to the health care worker. The health care worker should be informed about the rationale for using PEP and about the risks and benefits of receiving it.

**Post-Exposure Prophylaxis (PEP)**

Factors that have influenced the recommendation of
post-exposure prophylaxis include knowledge about the pathogenesis of the infection, experience in preventing perinatal transmission, and studies of the risks vs. benefits of receiving PEP.10 Animal and human studies have provided direct and indirect information indicating that post-exposure treatment with zidovudine (ZDV, AZT) is effective in preventing infection. Some animal studies have shown that treatment with other antiretrovirals also works, but human study data are not available.

Three types of antiretroviral drugs currently exist for the treatment of HIV. They are 1) nucleoside reverse transcriptase inhibitors, such as ZDV, stavudine (d4T), lamivudine (3TC) and didanosine (ddI); 2) non-nucleoside reverse transcriptase inhibitors, such as nevirapine and delavirdine; and 3) protease inhibitors, such as saquinavir, nelfinavir, and ritonavir. ZDV and nevirapine are the only drugs proven to prevent perinatal HIV transmission as indicated by the ACTG 076 trial and HIVNET 012 trial in Uganda.11,12 No data are available to indicate that addition of other antiretrovirals is additive or synergistic in preventing transmission, but the use of combination therapy in HIV-infected patients has been shown to suppress viral replication more completely. Thus, it is assumed that use of combination therapy in PEP might be even more effective than single-agent treatment in reducing the risk of transmission.

Current HIV treatment guidelines recommend the use of at least three drugs for HIV-infected adults, but the use of all three drugs in PEP is not always considered necessary. The decision to use two or three drugs is based on the risk of transmission after exposure. The nucleosides recommended for post-exposure prophylaxis include ZDV and 3TC, 3TC and d4T, and ddI and d4T. ZDV is recommended because of the ACTG 076 results, and 3TC is recommended because experts believe that the combination of ZDV and 3TC results in more potent suppression of HIV replication than does ZDV alone, with less chance of developing viral resistance.1 The other combinations may be preferred when resistance to ZDV and/or 3TC is thought to be present. The third drug that can be used can be chosen from any of the medications currently approved for use for HIV by the U.S. Food and Drug Administration. These include the protease inhibitors nelfinavir, indinavir, saquinavir, ritonavir, and lopinavir/ ritonavir. The non-nucleoside reverse transcriptase inhibitor Efavirenz can be used when there is suspicion of protease-inhibitor resistance.1 It is not recommended for use during pregnancy. Abacavir can also be used, but because it has been associated with very serious hypersensitivity reactions, patients taking this medication should be closely monitored. PEP needs to be taken for at least four weeks. It is important to minimize the possibility of side effects when choosing which medications to use.

The selection of which post-exposure regimen to use, the basic regimen (two drugs) or the expanded regimen (three drugs), should be based on the risk of exposure and information about the exposure source1 (see Appendix 3 and Appendix 4). Information about the exposure source would include information about antiretroviral history, the presence of possible resistance to anti-HIV drugs, CD4+ count, viral load, and disease stage. Most exposures will require only the basic regimen of two nucleoside reverse transcriptase inhibitors. In exposures in which the risk of transmission is considered great, or when resistance may be an issue, a protease inhibitor should be added.

Pregnant women should be informed of the possible risks of receiving and of not receiving PEP. They should be informed that there are very limited data about the effects of many of these medications on the fetus. Efavirenz has been shown to be teratogenic in primates and thus is not recommended for use in pregnant women. Indinavir can cause hyperbilirubinemia and renal stones and should be used cautiously in pregnant women. Reports of the development of fatal and non-fatal lactic acidosis with concomitant use of d4T and ddI during pregnancy suggest that this combination should be used only when the benefits are believed to outweigh the risks. Studies with women who received ZDV
after 14 weeks of gestation suggest that the drug is safe.11 The decrease in risk of transmission of HIV to the baby outweighs any risk associated with receipt of ZDV.

PEP should be started as soon as possible. If the HIV status of the source is not known, the basic regimen may be started based on the source and geographic prevalence of HIV. The regimen can be stopped when it is proven that the source is not HIV-infected. Some animal studies have shown that PEP is not effective when started more than 24-36 hours after exposure. However, in current practice, PEP is begun as late as two weeks after exposure in cases where the risk of transmission is very great. Once PEP is started, it should be given for at least four weeks.

Follow-Up and Monitoring
HIV counseling, medical follow-up, and HIV testing after exposure should be done for a minimum of six months following the exposure. Recommended testing intervals are six weeks, 12 weeks, and six months after exposure. Seroconversion after six months is very rare. However, any health care worker who experiences acute retroviral syndrome (fever, rash, pharyngitis, lymphadenopathy) should be tested for HIV, even if it has been longer than six months since the known exposure. HIV-antibody tests using enzyme immunoassay (EIA) should be used to test for seroconversion, and Western blot can be used to confirm any positive results. Direct virus assays such as cultures or polymerase chain reaction (PCR) are not recommended in cases of exposed health care workers because very few actually acquire the virus this way and direct virus assays are very expensive.

If PEP is used in health care workers, it is important to monitor the individual with laboratory tests for drug-associated toxicities. Baseline screening including a complete blood count and liver- and renal-function tests should be done prior to starting therapy and again two weeks after the initiation of therapy. Serum glucose should be tested in individuals receiving a protease inhibitor. Some patients cannot complete the course of medication required for PEP because of medication side effects, including nausea and diarrhea. Administration of antidiarrheals and antiemetics often help to prevent or relieve these symptoms.

Counseling
Health care workers who are exposed to HIV need to be counseled about the impact the exposure will have on their lives. This includes the possibility of HIV seroconversion, the importance of starting prophylaxis, and behavioral changes that will have to be made for at least six months to prevent the possibility of transmission of HIV to others. These changes include sexual abstinence or condom use and cessation of breastfeeding, if appropriate. Access to information about HIV/AIDS should be provided, and appropriate referrals should be made for further counseling and medical care.

It is not necessary for HIV-infected health care workers to discontinue patient contact. HIV-infected health care workers should be allowed to continue to work without fear of stigmatization or discrimination. The diagnosis of HIV infection should be strictly confidential. HIV-infected health care workers should continue to follow infection-control measures and standard precautions to prevent acquiring other infections and prevent transmitting HIV to others.

Summary of Management of HIV Exposure in the Health Care Setting
Following standard precautions can prevent exposure to HIV. If an exposure does occur, the exposure site should be washed with soap and water or flushed with water immediately. The exposure should be
reported as soon as possible so that appropriate interventions can be started. The exposure should be assessed for potential to transmit HIV based on the type of fluid involved, the route of the exposure, and the severity of the exposure. The person who is the source of the exposure should be evaluated for the presence of HIV. The evaluation should include information on risk factors for HIV and questions about HIV-related symptoms. The health care worker should have baseline HIV testing performed and receive counseling on HIV, and the risks and benefits of receiving post-exposure prophylaxis should be evaluated. PEP should be initiated if warranted. The health care worker needs to be an active participant in the decision of whether to start PEP. HIV testing is repeated for a minimum of six months following the exposure, usually at the intervals of six weeks, 12 weeks, and six months.

Appendix 1: Factors to Be Assessed After Possible Occupational Exposure to HIV

<table>
<thead>
<tr>
<th>Type of Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Percutaneous injury</td>
</tr>
<tr>
<td>• Mucous-membrane exposure</td>
</tr>
<tr>
<td>• Non-intact skin exposure</td>
</tr>
<tr>
<td>• Bites resulting in blood exposure to either person involved</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type and Amount of Fluid/Tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Blood</td>
</tr>
<tr>
<td>• Fluids containing blood</td>
</tr>
<tr>
<td>• Potentially infectious fluid or tissue (sperm, vaginal secretions, and cerebrospinal, synovial, pleural, peritoneal, pericardial, and amniotic fluids)</td>
</tr>
<tr>
<td>• Direct contact with concentrated virus</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Infectious Status of Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Presence of HIV antibody</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Susceptibility of Exposed Person</th>
</tr>
</thead>
<tbody>
<tr>
<td>• HIV immune status</td>
</tr>
</tbody>
</table>

Appendix 2: Evaluating the Occupational Exposure Source

**Known Sources**
- Test known sources for HIV antibody.
- Direct virus assays for routine screening of source patients are not recommended.
- Consider using a rapid HIV-antibody test.
- If the source person is not infected with HIV, baseline testing or further follow-up of the exposed person is not necessary.
- For sources whose infection status remains unknown (e.g. if the source person refuses testing), consider medical diagnoses, clinical symptoms, and history of risk behaviors.
- Do not test discarded needles for HIV.

**Unknown Sources**
- For unknown sources, evaluate the likelihood of exposure to a source at high risk of infection.
- Consider the likelihood of HIV infection among patients in the exposure setting.
## Appendix 3: Recommended HIV Post-Exposure Prophylaxis for Percutaneous Injuries

<table>
<thead>
<tr>
<th>Exposure Type</th>
<th>HIV Status of Source</th>
<th>HIV Status of Source Is Unknown+</th>
<th>Unknown Source†</th>
<th>HIV-Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less Severe‡</td>
<td>Basic 2-drug PEP</td>
<td>Expanded 3-drug PEP</td>
<td>Generally, no PEP warranted; however, consider basic 2-drug PEP** if source has HIV risk factors++</td>
<td>Generally, no PEP warranted; however, consider basic 2-drug PEP** in settings where exposure to HIV-infected persons is likely</td>
</tr>
<tr>
<td>More Severe††</td>
<td>Expanded 3-drug PEP</td>
<td>Expanded 3-drug PEP</td>
<td>Generally, no PEP warranted; however, consider basic 2-drug PEP** if source has HIV risk factors++</td>
<td>Generally, no PEP warranted; however, consider basic 2-drug PEP** in settings where exposure to HIV-infected persons is likely</td>
</tr>
</tbody>
</table>

* HIV-Positive Class 1: Asymptomatic HIV infection or known low viral load (e.g. <1,500 copies/ml). HIV-Positive Class 2: Symptomatic HIV infection, AIDS, acute seroconversion, or known high viral load. If drug resistance is a concern, obtain expert consultation. Initiation of PEP should not be delayed pending expert consultation, and, because expert consultation alone cannot substitute for face-to-face counseling, resources should be available to provide immediate evaluation and follow-up care for all exposures.
† Source is of unknown HIV status (e.g. deceased source person with no samples available for HIV testing).
‡ Less severe (e.g. solid needle and superficial injury)
** The designation “consider PEP” indicates that PEP is optional and should be based on an individualized decision by the exposed person and the treating clinician.
++ If PEP is offered and taken and the source is later determined to be HIV-negative, PEP should be discontinued.
†† More severe (e.g. large-bore hollow needle, deep puncture, visible blood on device, or needle used in patient’s artery or vein)

## Appendix 4: Recommended HIV Post-Exposure Prophylaxis for Mucous-Membrane Exposures and Non-Intact Skin Exposures

<table>
<thead>
<tr>
<th>Exposure Type</th>
<th>HIV Status of Source</th>
<th>HIV Status of Source Is Unknown+</th>
<th>Unknown Source†</th>
<th>HIV-Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small Volume‡</td>
<td>Consider basic 2-drug PEP **</td>
<td>Basic 2-drug PEP</td>
<td>Generally, no PEP warranted; however, consider basic 2-drug PEP** if source has HIV risk factors++</td>
<td>Generally, no PEP warranted; however, consider basic 2-drug PEP** in settings where exposure to HIV-infected persons is likely</td>
</tr>
<tr>
<td>Large Volume††</td>
<td>Basic 2-drug PEP</td>
<td>Expanded 3-drug PEP</td>
<td>Generally, no PEP warranted; however, consider basic 2-drug PEP** if source has HIV risk factors++</td>
<td>Generally, no PEP warranted; however, consider basic 2-drug PEP** in settings where exposure to HIV-infected persons is likely</td>
</tr>
</tbody>
</table>

* For skin exposures, follow-up is indicated only if there is evidence of compromised skin integrity (e.g. dermatitis, abrasion, or open wound).
† Source is unknown (e.g. splash from inappropriately disposed blood).
‡ Small volume (i.e. a few drops)
** The designation “consider PEP” indicates that PEP is optional and should be based on an individualized decision by the exposed person and the treating clinician.
++ If PEP is offered and taken and the source is later determined to be HIV-negative, PEP should be discontinued.
†† Large volume (i.e. major blood splash)
Review Questions

1. Define “standard precautions” in relation to caring for a person with HIV/AIDS.
2. Name at least three examples of protective barriers for use in patient care.
3. Describe the proper handling of potentially infectious items in the health care setting.
4. What considerations exist when assessing the risk of an HIV exposure?
5. Describe HIV post-exposure prophylaxis.
6. Review the current practice for managing HIV post-exposure prophylaxis in the U.S.

Exam Questions

1. A new nurse working in the hospital is concerned about exposure to HIV. Which of the following body fluids should she be concerned about?
   a. Amniotic fluid
   b. Urine
   c. Saliva
   d. Sputum

2. Which of the following are appropriate interventions to protect oneself from an HIV exposure?
   a. Cleanse patient wounds before bandaging.
   b. Avoid contact of blood with the eyes.
   c. Wash patient linens in hot soapy water.
   d. Boil all water before drinking.

3. Which of the following is an example of proper handling of potentially infectious materials?
   a. Isolating soiled linen prior to washing
   b. Discarding needles in puncture-resistant containers
   c. Recapping needles prior to discarding
   d. Cleaning blood spills with soapy water

4. A physician has experienced a percutaneous needle stick from an HIV-infected patient. He is concerned about the waiting period to determine whether he will be infected. What is known about the length of time for seroconversion to occur?
   a. He will know within three weeks, since seroconversion occurs rapidly.
   b. Seroconversion after six months is very rare.
   c. It will be years before he is confirmed HIV-negative.
   d. There is no risk of seroconversion.

Answers: 1a, 2b, 3b, 4b
Case Study #1

A student nurse has started working on your shift. She has been assigned eight patients with different medical diagnoses. You notice that each time you see her, she is wearing gloves. You ask her if she is changing her gloves between patients. She replies that she has been wearing the same gloves all day to avoid infecting herself with anything.

**Question:** The appropriate response to her actions would be all of the following EXCEPT:

a. “That’s a good idea. I do the same thing, but you should wash your gloves between patients.”

b. “You should change gloves between patients, but they are only needed if you are going to come into contact with potentially infectious body fluids.”

c. “You should wash your hands between patients.”

d. “Washing your gloves can cause them to break down.”

**Answer:** a. Gloves should be discarded after contact with each patient and should never be washed and reused. Washing gloves can cause them to break down, putting the health care worker at risk of exposure to the patient’s potentially infectious body fluids. Gloves should be used as a protective barrier if there is a risk of coming into contact with potentially infectious body fluids. The most effective infection-control measure that can be taken by the health care worker is handwashing before and after all patient contact.

The student nurse is getting ready to start a line for intravenous fluids on a patient with a diagnosis of HIV. You notice that she is putting on gloves, a gown, and a mask. She has started intravenous lines on other patients and never used all of these barriers.

**Question:** Which of the following would be an appropriate response?

a. Do not say anything. This patient has HIV and should be treated differently from other patients.

b. Tell the student nurse she should also wear eye protection.

c. Tell the student that resources are scarce and she does not need to use any protective barriers when starting an intravenous line.

d. Tell the student that she should follow the World Health Organization’s recommended standard precautions with all patients.

**Answer:** d. Standard precautions recommend that all people should be treated as if they were infected with HIV or other infectious fluids. Protective barriers can protect the health care worker from exposure, but the use of all barriers in all situations is impractical. In this situation, the student only needed to wear gloves to protect herself. It is unlikely that any other part of her body was at risk of exposure to HIV by placing an intravenous line.

Case Study #2

A nurse you work with accidentally punctures her finger with a large-bore needle after starting an intravenous line on a patient who is HIV-positive. The patient has *Pneumocystis jiroveci* pneumonia.

**Question:** What should you tell the nurse?

a. Be quiet and do not report the exposure to anyone.

b. Wash the site with soap and water.

c. Pour bleach on the site and squeeze the site to force the blood out.

d. Wash the site with soap and water and report the exposure to the supervisor.
**Answer:** d. The nurse should immediately wash the site with soap and water. The use of bleach and other caustic agents is not recommended. Squeezing the site to encourage bleeding has not been shown to affect transmission of HIV. The nurse should report the exposure as soon as possible so the risk can be evaluated and appropriate interventions can be initiated. As part of the post-exposure evaluation, the nurse should be tested for pregnancy.

**Question:** Her test is positive for being pregnant. What advice would you give her?

a. Tell her to go home because there is nothing that can be done if she is pregnant.

b. Tell her she needs to be evaluated for her risk of acquiring HIV from the exposure, just as any other health care worker would be evaluated.

c. Tell her that it is never recommended that pregnant woman start post-exposure prophylaxis.

d. Tell her she should start post-exposure prophylaxis and that the medications will cause no harm to her baby.

**Answer:** b. All women who are exposed to potentially infectious body fluids should be offered pregnancy testing. If the woman is pregnant, she should be evaluated for her risk of acquiring HIV, just like any other health care worker. Pregnancy is not a contraindication to post-exposure prophylaxis. PEP should be explained to the health care worker. She should be informed about the rationale for using PEP and the risks and benefits of receiving it based on existing knowledge of post-exposure prophylaxis in the perinatal setting.

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**References**


10. Almeda J. et al. Proposed recommendations for the management of HIV postexposure


Objectives

The purposes of this module are to:

1. Describe the prevalence of HIV in women.
2. Review the risk factors associated with transmission of HIV from a woman to her baby.
3. Identify interventions currently being investigated to prevent HIV mother-to-child transmission.
4. Discuss the use of ZDV, ZDV plus 3TC, nevirapine, and ZDV plus nevirapine for prevention of mother-to-child transmission.
5. Explain the risk of transmitting HIV by breastfeeding.

Key Points

1. Almost half of all adults living with HIV globally are women. In Africa, women represent about 57 percent of adults living with HIV.
2. Growing numbers of HIV-infected young women suggest that more infants will be exposed to HIV.
3. Infants are infected with HIV through the perinatal route: in utero, during labor and delivery, or postpartum through breast milk.
4. Risk factors for mother-to-child (or vertical) transmission of HIV include a low CD4+ count, a high viral load, placental inflammation, and prolonged duration of ruptured membranes.
5. Antiretroviral treatments are effective in reducing mother-to-child transmission.
6. Non-pharmacologic interventions to reduce mother-to-child transmission include Caesarean section and choosing not to breastfeed.
7. Nevirapine is inexpensive and effective in reducing mother-to-child transmission.

Overview

According to data from the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the World Health Organization (WHO), HIV/AIDS is affecting more young people around the world than ever before, and the numbers continue to rise. At the end of 2004, an estimated 39.4 million people around the world were living with HIV.1 Almost half of them were between 15 and 24 years old. The proportion of young women with HIV also continues to rise. Women now account for nearly half of all adults living with HIV. In sub-Saharan Africa, the region most severely impacted by HIV/ AIDS, about 57
percent of HIV-infected people are women. This rise in HIV infection among women suggests that more infants will be exposed to HIV. Most infants are infected with HIV through the perinatal route: in utero (in the womb), during labor and delivery, or after birth through breast milk. Unless an effective intervention to interrupt mother-to-child transmission (also called vertical transmission) is implemented on a global scale, it is predicted that the rate of new childhood infections will increase at the same rate as HIV infection among young women.1

This module focuses on the prevention of HIV transmission to fetuses or infants from pregnant women with established HIV infection. However, it is important to emphasize that the single most effective way to prevent HIV infection in children is to prevent HIV infection in girls and young women. Strategies to prevent mother-to-child transmission should be linked to primary prevention programs that provide education about safer sex, condoms, diagnosis and treatment of other sexually transmitted diseases, and safe medical practices (see modules on prevention of sexual transmission and prevention of occupational exposure to HIV). It is also important to emphasize that many of the interventions described below are dependent on the pregnant woman’s being accurately diagnosed as HIV-infected. Voluntary or routine counseling and testing services are an important part of any effort to reduce HIV transmission (see modules on counseling and testing).

Transmission of HIV can occur at any point in pregnancy as well as after birth while the mother breastfeeds. In non-breastfeeding populations, most transmissions (50 percent to 75 percent) are believed to occur near or during the time of delivery, when membranes have ruptured and the infant is exposed to fluids in the maternal genital tract. At this point, the infant may ingest maternal secretions from the cervix or vagina through the nose or mouth. A study in Thailand showed a very strong association between the presence of HIV in infant nasal/oral secretions and mother-to-child transmission.2 In regions where HIV-infected women are likely to breastfeed, as much as 44 percent of HIV infection of infants can be attributed to breastfeeding.3

Prevention of mother-to-child transmission is one of the most powerful methods available to reduce the global impact of this deadly virus. Fortunately, there are several successful strategies for the prevention of mother-to-child transmission. These include both non-pharmacologic interventions and antiretroviral treatment. Behavioral interventions emphasize reducing maternal behaviors that are known to increase mother-to-child transmission, such as cigarette smoking and illicit drug use. Other non-pharmacologic interventions include methods such as delivery by Caesarean section and the provision of infant formula as an alternative to breastfeeding. Finally, antiretroviral treatment regimens, given to the mother during gestation, labor, and delivery as well as to the newborn, have proven to be highly effective in reducing mother-to-child transmission of HIV. This module provides an overview of the most recent data describing some of these effective strategies and outlines future challenges to health care providers and public health specialists.

**Risk Factors for HIV Perinatal Transmission**

Maternal immunologic and virologic factors are known to influence the risk of HIV transmission in a predictable way. There is an inverse linear relationship between maternal CD4+ lymphocyte count and perinatal transmission risk. In other words, lower CD4+ counts are associated with a higher risk of mother-to-child transmission, and higher CD4+ counts are associated with a lower risk of mother-to-child transmission. This makes sense, because low CD4+ counts usually are associated with more advanced disease; sicker mothers are more likely to transmit the virus than HIV-infected mothers who are still clinically healthy.
There is a direct linear relationship between maternal viral load and perinatal transmission risk – the higher the viral load, the higher the transmission risk. This also makes sense, because a high viral load is usually associated with more advanced disease. In a study of 552 HIV-infected women, mother-to-child transmission did not occur among 57 women with RNA levels of less than 1000 copies per milliliter. However, there are other reports of mother-to-child transmission among women whose viral loads were too low to be counted. Therefore, it cannot be concluded that there is a viral-load threshold below which there is no risk of perinatal transmission.

Any type of placental inflammation can increase the risk of mother-to-child transmission. A study from Mombasa, Kenya, showed that chorioamnionitis (inflammation of the lining of the amniotic sac and the womb) increased the risk of mother-to-child transmission of HIV. In this study of 298 HIV-infected mothers who were not receiving antiretroviral therapy, the rate of transmission of HIV was found to be 25.4 percent, which is similar to the rate of transmission observed in other studies in the region. This study showed that if chorioamnionitis could be eliminated, cases of mother-to-child transmission of HIV would drop by 3 percent.

Ordinarily, the placenta forms a barrier between maternal and fetal circulation. Although nutrients and waste products are exchanged between the mother and fetus, their circulatory systems are separate. The reason HIV transmission is increased when there is placental inflammation or chorio-amnionitis is that the barrier that separates the mother’s and baby’s blood and other secretions is compromised. This could provide a “door” for HIV to enter the baby’s circulation. Several maternal behaviors can cause placental inflammation, including frequent sex with multiple partners (which increases the risk of sexually transmitted diseases), cigarette smoking, and illicit drug-taking.

Delivery is a time of high risk of HIV transmission, and a long duration of ruptured membranes increases this risk. During delivery, the baby of an HIV-infected woman is exposed to secretions in the maternal genital tract, which are known to contain HIV. An analysis of 15 studies involving 4721 deliveries to HIV-infected women illustrates this point. This analysis showed that the risk of mother-to-child transmission of HIV increased by about 2 percent for every additional hour of duration of ruptured membranes. For women diagnosed with AIDS (not simply HIV infection), the probability of transmission increased by 8 percent with duration of ruptured membranes of two hours, and by 31 percent with duration of 24 hours. This association remained even after controlling for other risk factors, such as mode of delivery, receipt of antiretroviral therapy, and maternal CD4+ count.

**Prevention of HIV Perinatal Transmission With Antiretroviral Therapy**

Prior to the use of antiretroviral prophylaxis to prevent perinatal HIV transmission beginning in the mid-1990s, rates of transmission ranged from 15 percent to 25 percent in Western countries and from 25 percent to 40 percent in Africa. Studies examining different regimens of anti-retroviral treatment have shown that drug therapy is remarkably effective in reducing the rate of mother-to-child transmission. With current antiretroviral strategies to prevent mother-to-child transmission of HIV, rates of transmission have dropped to about 2 percent in Western countries.

**Use of Chemoprophylaxis in Resource-Rich Communities: ZDV**

**PACTG 076**, the Pediatric AIDS Clinical Trials Group Protocol 076, was the first major study of perinatal-transmission prevention. This randomized, double-blind, placebo-controlled study evaluated the use of antiretroviral prophylaxis with zidovudine monotherapy (ZDV, also known as AZT). In this
study, neither the woman nor her doctor knew whether she was receiving ZDV or a placebo (a sugar-pill substitute). Women with CD4+ counts greater than 200 cells/μL who had not received prior HIV treatment were randomized to a three-part regimen of ZDV vs. placebo. The sample size was 409. ZDV was given to the mother beginning at 14-34 weeks of pregnancy, at a dose of 100 mg, by mouth, five times per day. Therapy was avoided during the first trimester to reduce the risk of possible birth defects. During labor, intravenous ZDV was given to the mother as a loading dose of 2 mg/kg over one hour followed by a continuous infusion of 1 mg/kg per hour until delivery. Finally, oral ZDV was given to the newborn for the first six weeks of life, at a dose of 2 mg/kg every six hours. Women in this study were instructed not to breastfeed their infants.

At 18 months, there was a dramatic relative-risk reduction of 67.5 percent in mother-to-child transmission in the ZDV treatment group compared to the placebo group. HIV transmission occurred with 25.5 percent of women receiving the placebo and with 8.3 percent of women receiving ZDV. Patients receiving ZDV also showed a slight reduction in viral load, but the researchers estimated that reduction in viral load accounted for only 17 percent of the reduction in HIV transmission. Experts speculate that ZDV may also exert its effect by reducing the concentration of HIV within cervico-vaginal secretions. Furthermore, unlike other HIV medications, ZDV becomes fully active within the placenta. This may also explain some of its protective capacity.

Infants in the ZDV group experienced temporarily lower hemoglobin concentrations compared to infants in the placebo group; however, this resolved without requiring treatment. No significant differences were observed between the study groups in growth, neurodevelopment, or other developmental indicators. No unexpected ophthalmologic, cardiac, or other organ-system problems were observed, and no malignancies have been observed in follow-up to 10 years of age. Although the short-term toxicity of this regimen for infants appears minimal, long-term effects are unknown. Follow-up safety information continues to be collected.

Use of Chemoprophylaxis in Resource-Poor Communities

While the results of the PACTG 076 trial were a dramatic breakthrough in the search for an effective means of preventing the vertical transmission of HIV, this method unfortunately remains limited to resource-rich areas of the world. In resource-poor regions, where 95 percent of the world's AIDS cases occur, funding has not been made available for the complex protocol employed in the PACTG 076. Instead, research regarding prevention of vertical transmission of HIV has focused on the discovery of cheaper and simpler methods.

Short-Course ZDV

The first study to address the needs of resource-poor settings was a trial conducted in Thailand in 1998. In this study, a shorter course of ZDV therapy was provided than was used in the PACTG 076 protocol. This was a randomized, double-blind, placebo-controlled trial of 397 HIV-infected women from two Bangkok hospitals. Oral ZDV (300 mg twice daily) was given to pregnant women, beginning at 36 weeks of gestation. This was followed by oral ZDV given to the mother during labor, at a dose of 300 mg administered every three hours until delivery. Unlike PACTG 076, this trial had no newborn treatment component. The mothers did not breastfeed. Results from this study showed that a shortened course of ZDV therapy can reduce the risk of mother-to-child transmission by approximately 50 percent. The rate of HIV transmission was 18.9 percent in the placebo group and 9.4 percent in the ZDV group. The study also confirmed that a majority of cases of vertical transmission occur during the intrapartum period.

Because most HIV-infected women in Africa do not have the resources to provide formula for their
children, it has been essential to assess the efficacy of prophylaxis in sites where breastfeeding is unavoidable. The short-course regimen of ZDV used in Thailand was replicated in Abidjan, Cote d’Ivoire, in a population of 260 breastfeeding women. The use of ZDV resulted in a 37 percent reduction in the transmission of HIV by the time the infants were 3 months old. The Cote d’Ivoire study showed that the regimen of ZDV was effective in a breastfeeding population, although the reduction in transmission was not as large as in the Thailand study, most likely because of postnatal transmission through breast milk.

The DITRAME trial evaluated the use of a short course of ZDV prophylaxis in a breastfeeding population in Burkina Faso and Cote d’Ivoire. A postpartum maternal course of ZDV was given for one week with the goal of reducing the transmission of HIV through breast milk. At six months, the treated group showed a 38 percent reduction in HIV transmission compared with the group receiving a placebo. Hence, the added week of ZDV did not contribute to any further reduction in the transmission of HIV. Analysis of data from the Cote d’Ivoire and DITRAME trials at 24 weeks revealed a persistent effect of short-course ZDV prophylaxis despite continuation of breast-feeding. At 24 weeks, the relative decrease in HIV transmission was 26 percent compared with placebo.

As a result of these studies, the WHO recommends short-course ZDV as an option for the prevention of mother-to-child transmission of HIV in resource-limited settings. Although the short course of ZDV offered in this study is much less expensive than the long course of ZDV therapy offered in the PACTG 076 study (about $170 USD vs. $800 USD), it still far exceeds annual per-capita health care expenditures in most developing nations.

**ZDV Plus 3TC**

Once short courses of ZDV were found to be effective, subsequent trials evaluated the efficacy of antiretroviral prophylaxis combining ZDV with 3TC (lamivudine). A randomized, double-blind, placebo-controlled trial known as the PETRA trial, which was conducted in South Africa, Uganda, and Tanzania, evaluated the use of ZDV with 3TC in a resource-poor setting.

Between June 1996 and January 2000, 1797 HIV-infected pregnant women were randomized to one of four regimens (see Table 1). Almost all of these mothers breastfed their infants. Results showed that regimens A and B were effective in reducing HIV transmission by six weeks postpartum, though the benefits had diminished considerably after 18 months. As in other studies in resource-poor settings, this likely reflected continued HIV transmission via breastfeeding. Nevertheless, short-course ZDV with 3TC remains a valid option for the prevention of mother-to-child transmission of HIV in resource-poor settings and is recommended by the WHO.

**Single-Dose Nevirapine**

Nevirapine, a non-nucleoside reverse transcriptase inhibitor (NNRTI), may provide a less expensive and logistically more feasible alternative for developing countries than ZDV or ZDV plus 3TC. The effects of nevirapine were assessed in a study known as HIVNET 012, conducted among 619 HIV-infected...
pregnant women and their infants in Kampala, Uganda. In one arm of the study, a single 200 mg oral dose of nevirapine was given to mothers at the onset of labor, and a single 2 mg/kg oral dose of nevirapine was given to infants within 48-72 hours after birth. The other study arm consisted of an ultra-short course of ZDV. Oral ZDV was given to mothers beginning at the onset of labor, at an initial dose of 600 mg, followed by 300 mg every three hours during labor. Oral ZDV was given to infants at a dose of 4 mg/kg twice per day for the first seven days of life. In both arms of the study, infants were breastfed by their mothers. Infant infection status was analyzed at 6-8 weeks, 14-16 weeks, and 18 months of life. Results showed that the two doses of nevirapine reduced transmission by 47 percent compared to an ultra-short course of ZDV by 14-16 weeks postpartum. No significant adverse effects were noted. HIV transmission rates among the 311 infants receiving nevirapine and the 308 infants receiving ZDV were:

- 8.1 percent vs. 10.3 percent at birth
- 11.8 percent vs. 20.0 percent at 6-8 weeks
- 13.6 percent vs. 22.1 percent at 14-16 weeks (47 percent reduction)
- 15.7 percent vs. 24.1 percent at 18 months (42 percent reduction)

As a result of this study, the WHO recommends the HIVNET 012 regimen as an option for the prevention of mother-to-child transmission of HIV in resource-limited settings.

Advantages of the nevirapine regimen are that it is suitable for women who first come to medical attention at the onset of labor; the medication is administered orally and can easily be stored at room temperature; and, most significantly, the cost of the entire nevirapine regimen is only about $4.

Because this intervention with nevirapine is inexpensive, safe for both the mother and the baby, and highly effective, two studies have looked at the cost-effectiveness of giving nevirapine to all pregnant women who live in areas with a high prevalence of HIV infection, even if the women have not been tested for HIV. These studies show that it would be less expensive to provide nevirapine to all pregnant women than to counsel and test all women. Another study looked at the attitudes of Zambian women toward this mass-therapy strategy. It showed that most Zambian women would support such mass therapy as a policy if it would make the drug available to a larger proportion of the at-risk population.

**Combination ZDV/3TC vs. Single-Dose Nevirapine**

After PETRA and HIVNET 012 demonstrated the efficacy of short courses of medication in reducing mother-to-child transmission, a study called SAINT (South African Intrapartum Nevirapine Trial) compared these two regimens. Results showed similar efficacy for intrapartum nevirapine and for combination ZDV/3TC in reducing mother-to-child transmission of HIV.

**Combination Nevirapine and ZDV**

To evaluate the efficacy of adding single-dose nevirapine to a short course of ZDV (300 mg by mouth twice a day starting at 28 weeks of gestation, 300 mg by mouth every three hours intrapartum, and to the newborn 2 mg/kg by mouth every six hours for one week), Perinatal HIV Prevention Trial investigators in Thailand in 2001-2003 randomized 1844 non-breastfeeding women to ZDV alone or ZDV combined with nevirapine. Results at six months revealed a transmission rate of 6.3 percent in the ZDV-alone group and 1.1 percent in the ZDV/nevirapine group. This confirmed that adding nevirapine to short-course ZDV further reduces mother-to-child transmission of HIV in non-breastfeeding women.

To assess the same regimen in a breastfeeding population, investigators in Cote d’Ivoire and Burkina Faso conducted an open-label study, called DITRAME-Plus 1, in which single-dose nevirapine was given along with short-course ZDV (similar to the Thai study). Combination therapy resulted in a
transmission rate of 7 percent at three months post-partum, compared to 13 percent in previously documented cases without the addition of nevirapine. Thus, even in a population of breastfeeding women, the addition of single-dose nevirapine to short-course ZDV appears to be efficacious.\textsuperscript{19}

Because of the success of the Thai and DITRAMA-Plus 1 trials, the WHO recommends short-course ZDV with single-dose nevirapine as an option for the prevention of mother-to-child transmission of HIV in resource-limited settings. The WHO recommendations are discussed below.

Recently, investigators in Malawi tried adding a one-week neonatal course of ZDV to the HIVNET 012 nevirapine protocol in a predominantly breastfeeding population. However, giving the newborn ZDV did not result in a statistically significant difference in the rates of transmission. At six weeks, the rate of transmission was 14.1 percent in infants who received only nevirapine and 16.3 percent in infants who received both nevirapine and ZDV.\textsuperscript{20}

The effects of combining intrapartum/newborn nevirapine with standard ZDV-based antenatal prophylaxis in resource-rich communities was recently studied in the PACTG 316 trial. Non-breastfeeding women in the United States, Europe, Brazil, and the Bahamas were randomized to standard ZDV-based antiretroviral therapy (along with other antiretrovirals required for treatment) with or without nevirapine. Results revealed no statistical difference in the rate of transmission: 1.4 percent with nevirapine and 1.6 percent without nevirapine. Hence, there appears to be no benefit to adding nevirapine to standard ZDV-based prophylaxis in resource-rich settings.\textsuperscript{21}

**The Role of HAART**

The introduction of protease inhibitors in the mid-1990s revolutionized treatment of HIV, and evidence soon grew that combination antiretroviral therapy had the potential to reduce the likelihood of mother-to-child transmission. The *Women and Infants* Transmission Study (WITS), a prospective natural-history study, compared the efficacy of different antiretroviral regimens in reducing perinatal transmission of HIV. Results showed that transmission was directly related to the duration and complexity of antiretroviral treatment. Transmission occurred with 20 percent of HIV-infected mothers who received no antiretroviral therapy, 10.4 percent of those receiving ZDV monotherapy, and 1.2 percent of those receiving multidrug antiretroviral therapy, also known as highly active antiretroviral therapy (HAART). This and other studies confirmed that the rate of mother-to-child transmission of HIV correlates with the maternal-serum HIV viral load at delivery: the higher the mother’s viral load, the greater the chance of HIV transmission. HAART provides the means to more effectively lower patients’ viral load and thus further reduce mother-to-child transmission of HIV.

The benefit of providing combination antiretroviral therapy (vs. ZDV monotherapy) to pregnant HIV-infected women whose viral load is undetectable (less than 400 copies/uL) is unclear. Data from WITS showed that such women already had an extremely low risk of perinatal transmission (less than 2 percent). Nevertheless, there is no definite viral-load threshold below which mother-to-child transmission of HIV will not occur. Studies show that pregnant HIV-infected women who have an undetectable viral load and who are not receiving treatment for their HIV still benefit from receiving ZDV monotherapy during pregnancy in accordance with the PACTG 076 protocol. Hence the decision whether to provide at least some form of antiretroviral prophylaxis should be made independently of the infected mother’s viral load.

**Neonatal-Only Antiretroviral Prophylaxis**

Studies have demonstrated the benefit of providing antiretroviral prophylaxis to newborns of HIV-infected mothers even in the absence of any prenatal or intrapartum care. Epidemiologic studies from New
York State support the use of a six-week course of neonatal-only ZDV to prevent the vertical transmission of HIV. In a non-breastfeeding population, the risk of transmission dropped from 27 percent to 9 percent when neonatal-only prophylaxis was started within 48 hours of delivery.22

Investigators in South Africa compared the efficacy of single-dose neonatal-only nevirapine against six weeks of neonatal-only ZDV for the prevention of vertical transmission of HIV in predominantly non-breastfeeding women. Respective transmission rates were 11.9 percent and 13.5 percent at six weeks and 14.3 percent and 18.1 percent at 12 weeks. Hence, single-dose nevirapine may be at least as effective as neonatal-only ZDV for the prevention of mother-to-child transmission of HIV.23

Finally, the NVAZ Randomized Clinical Trial studied the effect of single-dose neonatal-only nevirapine compared to single-dose neonatal-only nevirapine combined with one week of neonatal-only ZDV in a predominantly breastfeeding population in Malawi. Results showed that post-exposure prophylaxis with nevirapine and one week of ZDV was superior to nevirapine alone. Newborns receiving nevirapine alone had an infection rate of 12.1 percent, while newborns receiving the combination of nevirapine and ZDV had an infection rate of 7.7 percent, for a relative reduction of 36 percent.24

Development of Antiretroviral Resistance
A major concern with the use of antiretroviral prophylaxis for the prevention of mother-to-child transmission of HIV is the risk of causing resistance in mothers and newborns receiving the medications. Resistance is a concern because it means that these medications may not be effective if they are later used as treatment for the mothers or for babies who were infected with HIV. Several studies have attempted to elucidate this issue. A closer look at the HIVNET 012 study revealed that at six weeks, 19 percent of women receiving nevirapine had evidence of the K103N resistance mutation, and 46 percent of infants receiving the drug had evidence of the Y181C resistance mutation. After one year, most of the mutations were no longer detectable.25 Analysis of the PACTG 316 trial revealed that 15 percent of women receiving nevirapine displayed the K103N resistance mutation.26

The question of whether such peripartum mutations are clinically significant remained unanswered until recently. Investigators from the Thai Perinatal HIV Prevention Trial showed that women who had received intrapartum nevirapine were less likely to respond to later nevirapine-based antiretroviral regimens than women who had not received intrapartum nevirapine. In this study, 49 percent of women who had received intrapartum nevirapine and 68 percent of women who had not received intrapartum nevirapine had viral loads of less than 50 copies/uL after a treatment course of six months. Among women displaying resistance mutations (K103N, G190A, Y181C), effective response to treatment was 38 percent, compared to 52 percent among those without mutations.27 Thus, future investigations into the prevention of mother-to-child transmission of HIV will need to assess the clinical impact of resistance and balance it against the benefits of reducing the spread of HIV.

Use of Antiretroviral Agents in Pregnant Women
Thus far, discussion has focused on the use of antiretroviral agents for the prevention of mother-to-child transmission of HIV. Many pregnant women infected with HIV will also be candidates for treatment of their own HIV infection. All major guidelines that discuss the prevention of mother-to-child transmission of HIV recommend that appropriate antiretroviral treatment of HIV be provided to women who require it, irrespective of the decision to provide antiretroviral agents for prophylaxis. The decision to initiate antiretroviral therapy for adolescents and adults is a complex one. Guidelines to aid in the decision of when to treat are discussed in the chapter on antiretroviral
## Prevention of Mother-to-Child Transmission

### Table 2: Clinical Situations and Recommendations for the Prevention of Mother-to-Child Transmission of HIV in Resource-Limited Settings

<table>
<thead>
<tr>
<th>Clinical Situation</th>
<th>Recommendation</th>
</tr>
</thead>
</table>
| **A** HIV-infected women with indications for initiating ARV treatment who may become pregnant | • First-line regimens: ZDV + 3TC + nevirapine or d4T + 3TC + nevirapine  
• Efavirenz should be avoided in women of childbearing age unless effective contraception can be ensured.  
• Exclude pregnancy before starting treatment for HIV. |
| **B** HIV-infected women receiving ARV treatment who become pregnant | Women  
• Continue the current ARV regimen unless it contains efavirenz, in which case substitution with nevirapine 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.  
Infants  
• Infants born to women receiving either first- or second-line ARV treatment regimen: ZDV for one week or single-dose nevirapine or single-dose nevirapine plus ZDV for one week |
| **C** HIV-infected pregnant women with indications for ARV treatment | Women  
• Follow the treatment guidelines as for non-pregnant adults except that efavirenz should not be given in the first trimester. First-line regimens: ZDV + 3TC + nevirapine or d4T + 3TC + nevirapine.  
• Consider delaying ARV treatment until after the first trimester, although for severely ill women the benefits of initiating treatment early clearly outweigh the risks.  
Infants  
• ZDV for one week or single-dose nevirapine or single-dose nevirapine plus ZDV for one week |
| **D** HIV-infected pregnant women without indications for ARV treatment | Women  
• ZDV starting at 28 weeks or as soon as feasible thereafter; continue ZDV during labor; plus single-dose nevirapine at the onset of labor  
• ZDV starting at 28 weeks or as soon as feasible thereafter; continue during labor and for one week postpartum  
Infants  
• Single-dose nevirapine plus ZDV for one week  
• Regimens listed in clinical situation D’s other alternatives (no order of preference)  
• ZDV + 3TC for one week |
| **E** HIV-infected pregnant women who have indications for starting ARV treatment, but treatment is not yet available | Women  
• ZDV + 3TC starting at 36 weeks or as soon as feasible thereafter; continue during labor and for one week postpartum  
Infants  
• ZDV + 3TC for one week |
| **F** HIV-infected pregnant women with active tuberculosis | Women  
• If ARV treatment is initiated, consider: ZDV + 3TC + saquinavir/r or d4T + 3TC + saquinavir/r  
• If treatment is initiated in the third trimester, ZDV + 3TC + efavirenz or d4T + 3TC + efavirenz can be considered.  
• If ARV treatment is not initiated, follow the recommendations in clinical situation D.  
Infants  
• Exclude pregnancy before starting treatment for HIV. |
| **G** Pregnant women of unknown HIV status at the time of labor and women in labor known to be HIV-infected who have not received ARV drugs before labor | Women  
• If there is time, offer HIV testing and counseling to women of unknown status; if positive, initiate intrapartum ARV prophylaxis. If there is insufficient time for HIV testing and counseling during labor, offer testing and counseling as soon as possible postpartum and follow the recommendations in clinical situation H.  
Recommended regimens (no order of preference)  
Infants  
• ZDV + 3TC in labor and ZDV + 3TC for one week postpartum  
• ZDV + 3TC for one week |
| **H** Infants born to HIV-infected women who have not received any ARV drugs | Infants  
• Single-dose nevirapine as soon as possible after birth plus ZDV for one week. If the regimen is started more than two days after birth, it is unlikely to be effective. |

Adapted from WHO guidelines for prevention of mother-to-child transmission of HIV in resource-limited settings.

1. WHO recommendations for initiating ARV treatment in HIV-infected adolescents and adults: If CD4+ testing is available, it is recommended to offer ARV treatment to patients with WHO Stage IV disease irrespective of CD4+ cell count; WHO Stage III disease with consideration of using CD4+ cell counts less than 350 cells/μL; WHO Stage I and II disease in the presence of a CD4+ cell count less than 200 cells/μL. If CD4+ testing is unavailable, it is recommended to offer ARV treatment to patients with WHO Stage III and IV disease irrespective of total lymphocyte count or WHO Stage II disease with a total lymphocyte count less than 1200 cells/μL.

2. Conduct clinical and laboratory monitoring as outlined in the 2003 revised WHO treatment guidelines.

3. Continuing the infant on ZDV for four to six weeks can be considered if the woman received antepartum ARV drugs for less than four weeks.

4. Abacavir can be used in place of saquinavir/r; however, experience with ABC during pregnancy is limited. In the rifampicin-free continuation phase of tuberculosis treatment, a nevirapine-containing ARV regimen can be initiated.
medications. For patients who are eligible for antiretroviral treatment, most guidelines recommend a combination of agents usually consisting of two nucleoside reverse transcriptase inhibitors (NRTIs) and either a protease inhibitor (PI) or a non-nucleoside reverse transcriptase inhibitor (NNRTI). When a health care provider and a pregnant patient have decided to initiate therapy, careful thought must be given to the choice of antiretroviral agents to avoid adverse events in the developing fetus. Numerous studies have assessed the safety of using antiretroviral agents during pregnancy. A discussion of the relevant data is provided below.

**NRTIs:** ZDV and 3TC are the preferred NRTIs for use during pregnancy. Extensive experience in clinical trials indicates that they are both safe and efficacious. When ZDV or 3TC is unavailable, alternative agents include ddI, ABC, d4T, and emtricitabine. The combination of d4T and ddI should be avoided during pregnancy because of a potential increased risk of lactic acidosis attributed to this combination of agents. In addition, the combination of ZDV and d4T should always be avoided because of the potential for drug antagonism. Tenofovir should be used with extreme caution in pregnant women because of concern about its capacity to cause fetal bone

### Table 3: Clinical Situations and Recommendations for the Prevention of Mother-to-Child Transmission in Resource-Rich Settings

<table>
<thead>
<tr>
<th>SCENARIO #1</th>
<th>HIV-infected pregnant women who have not received prior antiretroviral therapy.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Pregnant women with HIV infection must receive standard clinical, immunologic, and virologic evaluation. Recommendations for initiation and choice of antiretroviral therapy should be based on the same parameters used for persons who are not pregnant, although the known and unknown risks and benefits of such therapy during pregnancy must be considered and discussed.</td>
</tr>
<tr>
<td>2.</td>
<td>The three-part ZDV chemoprophylaxis regimen, initiated after the first trimester, should be recommended for all pregnant women with HIV infection regardless of antenatal HIV RNA copy number to reduce the risk of perinatal transmission.</td>
</tr>
<tr>
<td>3.</td>
<td>The combination of ZDV chemoprophylaxis with additional antiretroviral drugs for treatment of HIV infection is recommended for infected women whose clinical, immunologic, or virologic status requires treatment or who have HIV RNA of more than 1000 copies/mL regardless of clinical or immunologic status.</td>
</tr>
<tr>
<td>4.</td>
<td>Women who are in the first trimester of pregnancy may consider delaying initiation of therapy until after 10-12 weeks’ gestation.</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>SCENARIO #2</th>
<th>HIV-infected women receiving antiretroviral therapy during the current pregnancy.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>HIV-infected women receiving antiretroviral therapy in whom pregnancy is identified after the first trimester should continue therapy. ZDV should be a component of the antenatal antiretroviral treatment regimen after the first trimester whenever feasible.</td>
</tr>
<tr>
<td>2.</td>
<td>Women receiving antiretroviral therapy in whom pregnancy is recognized during the first trimester should be counseled regarding the benefits and potential risks of antiretroviral administration during this period, and continuation of therapy should be considered. If therapy is discontinued during the first trimester, all drugs should be stopped and reintroduced simultaneously to avoid the development of drug resistance.</td>
</tr>
<tr>
<td>3.</td>
<td>Regardless of the antepartum antiretroviral regimen, ZDV administration is recommended during the intrapartum period and for the newborn.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SCENARIO #3</th>
<th>HIV-infected women in labor who have had no prior therapy.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Intrapartum intravenous ZDV followed by six weeks of ZDV for the newborn.</td>
</tr>
<tr>
<td>2.</td>
<td>Oral ZDV + 3TC during labor, followed by one week of oral ZDV-3TC for the newborn.</td>
</tr>
<tr>
<td>3.</td>
<td>A single dose of nevirapine at the onset of labor followed by a single dose of nevirapine for the newborn at age 48 hours.</td>
</tr>
<tr>
<td>4.</td>
<td>The two-dose nevirapine regimen combined with intrapartum intravenous ZDV and six-week ZDV for the newborn. In the immediate postpartum period, the woman should have appropriate assessments (i.e. CD4+ count and HIV RNA copy number) to determine whether antiretroviral therapy is recommended for her.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SCENARIO #4</th>
<th>Infants born to mothers who received no antiretroviral therapy during pregnancy or intrapartum.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>The six-week neonatal ZDV component of the ZDV chemoprophylactic regimen should be discussed with the mother and offered for the newborn.</td>
</tr>
<tr>
<td>2.</td>
<td>ZDV should be initiated as soon as possible after delivery, preferably within 6-12 hours of birth.</td>
</tr>
<tr>
<td>3.</td>
<td>Some clinicians may choose to use ZDV in combination with other antiretroviral drugs, particularly if the mother is known or suspected to have ZDV-resistant virus. However, the efficacy of this approach for prevention of transmission has not been proven in clinical trials, and appropriate dosing regimens for neonates are incompletely defined for many drugs.</td>
</tr>
<tr>
<td>4.</td>
<td>In the immediate postpartum period, the woman should undergo appropriate assessments (i.e. CD4+ count and HIV RNA copy number) to determine if antiretroviral therapy is required for her own health. The infant should undergo early diagnostic testing so that if HIV-infected, treatment can be initiated as soon as possible.</td>
</tr>
</tbody>
</table>

* U.S. Public Health Service Task Force
abnormalities, including decreased growth and reduced bone porosity. Zalcitabine (ddC) is not recommended for use in pregnancy because of its potential for teratogenicity.

**NNRTIs:** Among non-nucleoside reverse transcriptase inhibitors, nevirapine is the preferred agent. Extensive studies show that it is relatively safe for use in pregnancy. However, caution should be exercised in using this agent in women with CD4+ counts greater than 250 cells/μL, as there appears to be an increased risk of cutaneous and hepatic adverse events. Efavirenz, another NNRTI, should be avoided in the treatment of pregnant women and women of childbearing age. This agent has been linked with the development of neural-tube defects in the fetus.

**PIs:** Long-term use of protease inhibitors has been associated with certain metabolic derangements, including dyslipidemia, lipodystrophy, and hyperglycemia. Pregnancy itself is a risk factor for hyperglycemia, and pregnant patients who take PIs should be monitored closely for the development of hyperglycemia. Among the PIs, nelfinavir and saquinavir with low-dose ritonovir boosting are the preferred agents because extensive pharmacokinetic and safety data on them is available.

**Recommendations for the Use of Antiretroviral Agents for the Prevention of MTCT of HIV in Resource-Rich Settings**

*(Summary of U.S. Public Health Service Task Force Guidelines)*

**HIV-Infected Pregnant Women Who Have Not Been Receiving ARV Therapy:**

Maternal viral load >1000 copies/μL:
- Start ZDV monotherapy after the first trimester, provide intravenous ZDV during labor, then provide oral ZDV to the newborn for six weeks.
  - OR
  - Start HAART (containing ZDV) after the first trimester through delivery, provide intravenous ZDV during labor, then provide oral ZDV to the newborn for six weeks.

**HIV-Infected Pregnant Women Already on ARV Therapy:**

If pregnancy diagnosed after first trimester:
- Continue antiretroviral therapy and make effort to include ZDV as part of the regimen. Provide intrapartum intravenous ZDV and then six weeks of oral ZDV therapy to the infant.

If pregnancy diagnosed during first trimester:
- Discuss risks and benefits of continuing antiretroviral regimen. If the decision is made to continue antiretroviral therapy, make effort to include ZDV as part of the regimen; if the decision is to withhold therapy during first trimester, stop all antiretrovirals at same time, then restart regimen after first trimester. Provide intrapartum intravenous ZDV and then six weeks of oral ZDV therapy to the infant.

**HIV-Infected Mothers Who Have Not Received Antepartum Prophylactic Therapy:**

(Choose one of the four options depending on available resources.)

1. Intrapartum intravenous ZDV followed by six weeks of oral neonatal ZDV
2. Oral ZDV + 3TC during labor, then one week of oral ZDV + 3TC for the neonate
3. One dose of nevirapine for the mother during labor and one dose of nevirapine for the neonate at 48 hours
4. Combination of regimens #1 and #3
Infants Born to HIV-Infected Mothers
Who Received Prophylactic Therapy
Neither During Pregnancy Nor During Labor:
• Provide six weeks of oral ZDV to the infant starting within six to 12 hours of birth.
  Initiation of prophylaxis two or more days after birth is unlikely to prevent transmission of HIV.

Recommendations for Prevention of MTCT of HIV in Resource-Limited Settings

Below are the WHO Guidelines for the Prevention of HIV Infection in Infants in Resource-Constrained Settings.28

1. Women who need antiretroviral treatment for their own health should receive it in accordance with the WHO guidelines on antiretroviral treatment. The use of antiretroviral treatment, when indicated, during pregnancy substantially benefits the health of the woman and decreases the risk of HIV transmission to the infant.

2. HIV-infected pregnant women who do not have indications for antiretroviral treatment or who do not have access to treatment should be offered antiretroviral prophylaxis to prevent mother-to-child transmission. Such prophylaxis should employ one of several antiretroviral regimens known to be safe and effective:
   a. ZDV from 28 weeks of pregnancy plus single-dose nevirapine during labor and single-dose nevirapine and one-week ZDV for the infant. This regimen is highly efficacious, as is initiating ZDV later in pregnancy (as shown in the Thai Perinatal HIV Prevention Trial).
   b. Regimens based on ZDV alone, short-course ZDV + 3TC, or single-dose nevirapine alone are also recommended.

3. Although expanding access to programs to prevent mother-to-child transmission presents many challenges and single-dose maternal and infant nevirapine is the simplest regimen to deliver, programs should consider introducing more complex antiretroviral regimens where possible. The expansion of programs to prevent mother-to-child transmission using single-dose nevirapine should not be hindered while necessary improvements in health systems are taking place to enable more complex antiretroviral regimens to be delivered.

Non-Antiretroviral Interventions to Reduce Perinatal Transmission of HIV

In addition to the interventions described above, several non-antiretroviral interventions are known to be effective. Other non-antiretroviral interventions have been tried and shown to be ineffective. Data is presented below on the following non-antiretroviral interventions: reduction in breastfeeding, Caesarean section, nutritional supplementation, vaginal cleansing, and prophylaxis and treatment of other infections, including malaria, chorioamnionitis, and other sexually transmitted diseases.

Reduction in Breastfeeding

Studies show that breastfeeding is associated with about a doubling of mother-to-child HIV transmission risk.1 The proportions of transmissions occurring during early breastfeeding and late breastfeeding are not well-defined. The risk of early transmission through breast milk is not easy to quantify, because it is difficult to distinguish between transmissions in the uterus and early postnatal transmissions through breast milk. The risk of early transmission through breast milk may be increased by the immature immune system of the infant, as well as by higher cellular content of early breast milk. Late transmission may also be significant, because the volume of milk ingested by the infant is considerably larger, and occasional gastrointestinal infections could make the infant’s gut more susceptible.
to HIV infection. Breast infections such as mastitis, cracked nipples, and other lesions can also increase the risk of mother-to-child transmission of HIV related to breastfeeding.

A study from Durban, South Africa, suggests that in areas where exclusive formula-feeding is not possible or is not reliably practiced for cultural reasons, exclusive breastfeeding is preferable to mixed feeding (some breastfeeding and some alternative feeding). Among 549 mother-infant pairs evaluated in this study, the HIV infection rate at 3 months of age was significantly lower among infants who breastfed (14.6 percent) than among infants who received mixed feeding (24.1 percent). Breast milk contains growth factors that may help the infant’s gut mature, thus maintaining its integrity and hindering infection by the virus. Because alternative feeding (often involving giving the baby water or weak teas and cereals) may involve unhygienic food-preparation practices, bacteria and other contaminants may be introduced into the baby’s gut and cause inflammation and damage to the mucosa, providing a portal of entry for HIV.

A study in Nairobi, Kenya, compared formula-feeding by cup to breastfeeding, examining mother-to-child transmission as well as maternal and child mortality in both feeding groups. Results showed that formula-feeding by cup reduced postnatal transmission by 44 percent compared to breastfeeding. Overall, 36.7 percent of breastfed infants and 20.5 percent of formula-fed infants were infected with HIV by the age of 24 months. This study also suggested that in a majority of cases of postnatal HIV transmission through breast milk, the transmission occurs relatively early. Seventy-five percent of breast-milk transmission occurred during the first six months of life, although some transmission occurred throughout the exposure. Although mortality was not increased in the formula-fed group, mortality was quite high in both groups (20 percent and 24 percent of formula- and breastfed infants, respectively).

A final important finding of this study is that HIV-infected mothers who breast-fed their infants had an increased risk of mortality within 24 months postpartum: 10.5 percent of breastfeeding mothers died within two years of giving birth, compared to 3.8 percent of formula-feeding women. This may be because breastfeeding drains nutritional resources from the mother. However, other studies have not shown the same increase in mortality among women who breastfeed.
Some experts strongly believe in the benefits of exclusively breastfeeding infants born to HIV-infected mothers. Others remain wary of the dangers of HIV transmission through breast milk and recommend formula-feeding HIV-exposed children. There is no one “correct” answer. Breastfeeding recommendations are entirely setting-dependent. The WHO suggests the following guidelines for breastfeeding:

- When replacement feeding is affordable, feasible, acceptable, sustainable, and safe, avoidance of all breastfeeding by HIV-infected mothers is recommended.
- When replacement feeding is not possible, then exclusive breastfeeding is recommended.
- To minimize HIV transmission risk, breastfeeding should be discontinued as soon as feasible, taking into account the local circumstances, the individual woman’s situation, and the risks of replacement feeding (including infections other than HIV and malnutrition).

**Caesarean Section**

Intrapartum factors play an important role in vertical HIV transmission. HIV viral particles and infected cells have been found in cervical and vaginal secretions of HIV-infected women. The presence and quantity of virus in the genital tract could influence the risk of HIV transmission during the birthing process. One way to reduce intrapartum transmission is through Caesarean delivery. A meta-analysis of the mode of delivery was conducted using 15 prospective cohort studies representing 8533 mother-infant pairs. The results of this analysis suggest that elective Caesarean section reduces the risk of transmission of HIV from mother to infant independently of the effects of treatment with ZDV. Among women who had a Caesarean section and no ZDV, the risk of transmission was 10.4 percent. Among women who received ZDV but had a vaginal delivery, the risk of transmission was 7.3 percent. Among women who had an elective Caesarean section and received ZDV, the risk of transmission was 2 percent.

Several studies have looked at whether HIV-infected women have an increased risk of post-operative complications after Caesarean sections. In one early study, HIV-infected women appeared to be at increased risk. In a later study involving a much larger sample, complication rates for HIV-infected women overall were within the range of complication rates reported for HIV-negative women. However women with CD4+ lymphocyte counts of more than 200 cells/μL (in other words, women with AIDS) did have an increased rate of complications. In summary, for most HIV-infected women, Caesarean section is probably about as safe as it is for HIV-negative women, but for women with advanced disease or AIDS, Caesarean section carries a higher risk.

**Vitamin Supplementation**

Maternal nutritional factors may play a role in mother-to-child transmission. Several studies have evaluated the contribution of maternal micronutrient levels, particularly vitamin A, to transmission risk. Vitamin A plays a critical role in maintaining the surface integrity of the mucosa, and Vitamin A deficiency is associated with immunologic alterations, including diminished CD4+ cell number and function. A study in Durban, South Africa, examined whether vitamin A supplementation was associated with reduced mother-to-child transmission. Women were randomized to receive either vitamin A supplements (n=368) or a placebo (n=360). The two groups showed no difference in the risk of HIV infection by 3 months of age. There was also no difference in overall fetal mortality. However, there were significantly fewer preterm births in the vitamin A group compared to the group that received the placebo. Also, among the women who had preterm deliveries, those assigned to the vitamin A group were less likely to transmit HIV than those assigned to the placebo group.

Two other studies from Africa, looking at either vitamin A or multivitamin supplementation, have confirmed these findings. None of the three studies showed that vitamin supplementation was
effective in reducing overall mother-to-child transmission. However, all three showed that vitamin supplementation reduced adverse pregnancy outcomes. Multivitamin supplements are inexpensive and easy to administer and are recommended for HIV-infected pregnant women.

**Vaginal Cleansing**

Another intrapartum factor that has been studied for the reduction of perinatal HIV transmission is vaginal cleansing. A clinical trial in Malawi evaluated the effectiveness of manual vaginal swabbing with chlorhexidine-soaked cotton every four hours during labor and cleansing of the infant immediately after birth to doing neither of those things. Chlorhexidine is well-tolerated by both the mother and the infant and has been successfully used to reduce the risk of neonatal group B streptococcal infection. In addition, chlorhexidine is known to kill HIV in a test tube. However, no overall benefit of vaginal cleansing was observed in this study. Transmission rates were similar in the intervention and non-intervention groups (27 percent and 28 percent, respectively), although in a subgroup of women who had rupture of membranes for more than four hours, lower transmission rates were observed with cleansing (25 percent vs. 39 percent). Because this intervention is simple, inexpensive, and well-tolerated, and it did appear effective for a subgroup of women, a similar study is being performed in Soweto, South Africa, using a higher concentration solution of chlorhexidine.

**Prophylaxis and Treatment of Other Infections**

Malaria can increase the risk of mother-to-child transmission of HIV. Possible mechanisms might include disruption of placental integrity and increased risk of preterm delivery and low birth weight. A study to evaluate malaria prophylaxis during pregnancy as a preventive strategy to reduce perinatal transmission is being discussed.

Some studies have suggested that sexually transmitted infections (STIs) may facilitate both heterosexual and perinatal HIV transmission. As a result, it has been hypothesized that treatment of STIs might provide an effective intervention to decrease both sexual and perinatal HIV transmission. A randomized, controlled, community-based trial of mass STI treatment was conducted in Rakai, Uganda, to address this hypothesis. Although this study showed overall reductions in maternal and infant morbidity, there were no overall decreases documented for sexually or perinatally transmitted HIV infection.

**Summary**

Despite recent advances in understanding the factors that influence perinatal HIV transmission, researchers and health care providers still face a number of challenges. First, although proven strategies to reduce perinatal transmission exist, we must continue to develop more effective, less expensive, and logistically more feasible interventions. The HIVNET 012 study is clearly a major advance toward this goal. A second, more complicated challenge is to develop methods to ensure that these strategies are implemented on a global scale, leaving behind no woman or child who could potentially benefit from them. Unfortunately, doctors and public health specialists have been only modestly successful in implementing these strategies around the world, and reductions in perinatal transmission have been achieved only in the developed nations of North America and Western Europe. As the virus continues to spread and the rate of new infections among young women continues to rise, there has never been a greater imperative to confront this implementation problem to ensure that the benefit that can be derived from these strategies is quickly achieved.
**Review Questions**

1. How are most children infected with HIV?
   - make it an attractive option for prevention of perinatal HIV transmission? What is a major concern about the use of nevirapine to prevent mother-to-child transmission?

2. Name three risk factors associated with perinatal HIV transmission.

3. Describe the short-term ZDV study in Thailand and its importance for developing nations.

4. What are characteristics of nevirapine that make it an attractive option for prevention of perinatal HIV transmission? What is a major concern about the use of nevirapine to prevent mother-to-child transmission?

5. Why is mixed feeding (involving some breast milk and some alternative substances, such as water, weak tea, and cereal) a concern in some countries?

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**Exam Questions**

1. Which of the following non-antiretroviral interventions has been shown to reduce the risk of vertical HIV transmission?
   - Cervico-vaginal lavage with chlorhexidine
   - Antenatal vitamin A supplementation
   - Exclusive formula-feeding from birth
   - None of the above

2. When do most cases of perinatal transmission of HIV occur?
   - During the first trimester
   - During the second trimester
   - During the third trimester
   - Close to the time of delivery
   - Equally throughout pregnancy

3. Without any intervention, the risk of vertical transmission of HIV is estimated to be:
   - 100 percent
   - 50 percent
   - 25 percent
   - 0 percent

4. The following is true regarding the PACTG 076 regimen:
   - This regimen results in a two-thirds reduction in the risk of vertical HIV transmission
   - It employs ZDV monotherapy during the antepartum, intrapartum, and postpartum periods.
   - It reduces the transmission of HIV regardless of the mother’s viral load or CD4+ count.
   - All of the above

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Answers: 1c, 2d, 3c, 4d
Case Study #1

Ruth, a pregnant 22-year-old woman, comes to the clinic with symptoms of early labor. She appears to be near-term. She reports that before her pregnancy, she was tested for HIV and was found to be positive. She has not received any prenatal care during her pregnancy. She has experienced some symptoms of HIV in the past, including transient diarrhea and oral thrush. Currently she appears to be healthy.

**Question:** Assuming they are available in your clinic, which of the following interventions would provide the most effective and sensible method to prevent late perinatal transmission of HIV to Ruth’s baby?

- a. Oral administration of ZDV at an initial dose of 600 mg, followed by 300 mg every three hours thereafter during labor, followed by oral ZDV given to the infant at a dose of 4 mg/kg twice per day for the first seven days of life
- b. Provision of a single 200 mg oral dose of nevirapine to Ruth, followed by a single 2 mg/kg oral dose to her infant within 72 hours after birth
- c. A firm order to not breastfeed the child under any circumstances
- d. Cleansing of the infant, immediately after delivery, with a chlorhexidine-soaked cotton swab

**Answer:** Ideally, you would provide Ruth with a single 200 mg oral dose of nevirapine, followed by a single 2 mg/kg oral dose to her baby within 72 hours after birth. The HIVNET 012 study showed that this regimen was 47 percent more effective at reducing mother-to-child transmission than the regimen described in answer choice b. Because Ruth is coming to attention during delivery, it is too late to implement the ZDV regimens studied in either the ACTG 076 study or the short-course ZDV study from Thailand. Choice C is not likely to be followed if there are strong cultural expectations that a woman should breastfeed in Ruth’s community. The Malawi study of cleansing with chlorhexidine showed no reduction in mother-to-child transmission with chlorhexidine.

Case Study #2

Sarah, a woman with HIV, a CD4+ count of more than 500 and an undetectable viral load, has never required treatment for her HIV. She is recently found to be three weeks pregnant. She feels well and denies any symptoms worrisome for opportunistic infections. She is interested in receiving prenatal care and asks your advice regarding appropriate prevention of HIV to her child.

**Question:** In a resource-rich setting, which of the following preventive regimens would be considered first-line?

- a. Oral ZDV initiated at 14 weeks’ gestation, intrapartum intravenous ZDV, and neonatal ZDV for six weeks
- b. Oral 3TC initiated at 14 weeks’ gestation, intrapartum intravenous 3TC, and neonatal 3TC for six weeks
- c. Oral nevirapine initiated at 14 weeks’ gestation, intrapartum intravenous nevirapine, and neonatal nevirapine for six weeks
- d. They are all first line.

**Answer:** In resource-rich settings, all women with HIV infection who are asymptomatic with a preserved CD4+ count and undetectable viral load should receive ZDV according to the PACTG 076 protocol. Treatments using any of the other regimens have not been validated.
Question: If Sarah had not sought prenatal care and had subsequently presented to the emergency room after having delivered her baby in the car along the way, which of the following should be done for the infant (in a resource-rich setting)?
   a. Six-week course of ZDV chemoprophylaxis
   b. Four-week course of ZDV chemoprophylaxis
   c. Two-week course of ZDV chemoprophylaxis
   d. One-time dose of ZDV chemoprophylaxis

Answer: a. In resource-rich settings, the U.S. Public Health Service Task Force recommends the six-week course of ZDV based on epidemiologic data from New York State.

Suppose Sarah’s HIV was not well-controlled at the time of her initial visit; her CD4+ count was less than 200, and her viral load was greater than 10 000. You decide to start her on combination antiretroviral therapy for the duration of her pregnancy.

Question: Which of the following treatment options should you offer?
   a. Antiretroviral therapy that includes efavirenz
   b. Antiretroviral therapy that includes a combination of ddI and d4T
   c. Antiretroviral therapy that includes ZDV
   d. Antiretroviral therapy that includes ddC

Answer: c. Based on the PACTG 076 study, all women should receive antiretroviral therapy that includes ZDV. The use of efavirenz has been associated with the development of neural-tube defects in the fetus. Treatment with the combination of ddI and d4T has been linked to several cases of fatal lactic acidosis. The use of ddC has not been studied in human pregnancy, and animal studies link its use to the development of birth defects.

Case Study #3

Rachel is an HIV-infected patient of yours who is 36 weeks pregnant. She has been doing some research regarding the prevention of mother-to-child transmission of HIV and wants to know if having a Caesarean section would decrease the risk. She is currently taking HAART, and her last viral load was undetectable one week ago.

Question: As her health care provider, you can recommend that she:
   a. Have an elective Caesarean section before the onset of labor
   b. Not have a Caesarean section

Answer: b. Studies have shown that in women receiving HAART whose viral load is undetectable, the risk of mother-to-child transmission of HIV is 2 percent or less. There are no studies that indicate that a Caesarean section would reduce this risk further. Moreover, if the mother were to undergo a Caesarean section, her morbidity would be increased.

Question: You and Rachel decide that she will need a Caesarean section. The most appropriate time to perform a Caesarean section would be:
   a. At 38 weeks of gestation, prior to the onset of labor
   b. Four hours after the onset of labor
   c. It does not matter when it is performed.

Answer: a. The American College of Obstetrics and Gynecology recommends performing an elective Caesarean section at 38 weeks, prior to the rupture of membranes. Caesarean sections performed more than four hours into labor are not likely to prevent mother-to-child transmission of HIV.
References

HIV CURRICULUM FOR THE HEALTH PROFESSIONAL

(MTCT) of HIV-infection: nevirapine vs. lamivudine and zidovudine used in a randomised clinical trial (the SAINT study). *XIII International AIDS Conference*, July 9-14, 2000; Durban, South Africa. Abstract TuOrB356.


31. WHO Breastfeeding guidelines


Objectives

The purposes of this module are to:
1. Discuss the appropriate assessment of a child with HIV who has fever.
2. Describe common signs and symptoms associated with respiratory infections in children with HIV.
3. Identify the management of respiratory illnesses based on the child's age.
4. Review treatment interventions for a child with HIV who has otitis media or a sore throat.

Key Points

1. Fever may be caused by infection or malignancy but is rarely caused by HIV infection or medications used to treat HIV infection.
2. Respiratory infections may cause one or more of the following signs and symptoms: fever, cough, difficulty breathing, sore throat, runny nose, and ear pain or ear drainage.
3. Children with severe respiratory disease should be transferred to a hospital immediately.
4. Treatment of respiratory illnesses in children is dependent on the age of the child.
5. Children less than 2 months of age with pneumonia should be hospitalized.

Overview

Any sick child, regardless of HIV status, who is brought to a clinic or hospital requires a complete assessment. If the child is assessed only for the major complaint or symptom, other important signs of diseases such as pneumonia, diarrhea, malaria, measles, or malnutrition may be overlooked. If left untreated, these diseases can be very serious in young children. The first step in assessing a sick child is to ask the mother or caregiver to describe the problem(s) the child is having and to check for general danger signs.

Assessment

Assessment for general danger signs should include asking the child's caregiver:
1. Is the child unable to drink or breastfeed?
2. Does the child vomit every meal?
3. Has the child had convulsions?
4. Has the child's urine output decreased?
5. Has the child been less playful or sleeping more than usual?
6. Has the child been less interactive with the caregiver?
7. Has the child lost weight?

A child who has any of these general danger signs needs immediate urgent attention. The assessment and initial treatment, such as administering a dose of the appropriate antibiotic, should be completed as quickly as possible, and a referral should be made for further treatment at a hospital or urgent-care facility. If the child is not responsive, causes such as hypoglycemia and severe dehydration should be considered. If the child appears dehydrated,
intravenous fluids or aggressive oral rehydration should be considered.

This module reviews assessment and treatment of respiratory infections (including pneumonia), fever, otitis media, and sore throat. Other diseases, including diarrhea and neurological manifestations of HIV/AIDS, are reviewed in other modules.

Respiratory Infection

Respiratory infection may involve the upper or lower respiratory tract, including the nose, middle ear, pharynx, trachea, bronchioles, and lungs. Signs and symptoms of respiratory infection include cough, difficulty breathing, sore throat, runny nose, and ear pain or ear drainage. Fever is also common in children with respiratory infections.

Respiratory infections involving both the upper and lower respiratory tracts are common in children. Most respiratory infections are caused by viruses, such as respiratory syncytial virus (RSV). Other common causes of respiratory infection in children are group A beta-hemolytic streptococci, staphylococci, human pneumo metavirus, *Haemophilus influenzae*, *Chlamydia trachomatis*, mycoplasma, moraxella catarrhalis, and pneumococci. Younger children are more susceptible to more severe infection because of anatomic differences. Young children’s airways are narrower and more easily obstructed by edema and secretions. The eustachian tube, the tube between the nasopharynx and middle ear, is shorter in infants and young children, which leads to increased susceptibility to ear infections (otitis media).

In the early stages of HIV infection, before immune suppression develops, a child with a respiratory infection involving both the upper and lower respiratory tracts should be evaluated as an immunocompetent host. It is not until the patient develops severe immunosuppression (CD4+ count of <15 percent) that the child becomes more susceptible to opportunistic infections.

A child with a mild respiratory infection or cold may be treated symptomatically at home. A child with a more severe infection, such as pneumonia, may need to be treated in the hospital. According to the World Health Organization (WHO), upper respiratory infections are responsible for 18 percent of all deaths in developing countries. Many of these deaths occur among children who are less than 2 months of age. Early recognition and appropriate treatment of pneumonia can greatly reduce the number of deaths.

Most cases of pneumonia can be identified by checking for the two most common signs of pneumonia, fast breathing and retractions. In this module, the student will learn how to differentiate between a cold and pneumonia and how to determine which cases of pneumonia can be treated in an outpatient clinic and which require admission to a hospital.

Subjective and Objective Assessment

Assessment of a child with a respiratory infection should include both subjective data (complaints reported by the child or caregiver) and objective data (observations and measurements by the health care provider).

Subjective Data

Subjective data should include the following:

1. Which signs/symptoms are present? Does the child have a cough? Is the child having difficulty breathing? Parents may describe such breathing as “fast,” “noisy,” or “interrupted.” Does the child have a sore throat or runny nose? Is there ear pain or ear drainage? How long have they been present?
2. Does the child have fever? If yes, how high is the temperature, and how long has it been elevated?
3. Is the child complaining of chest pain? Is the pain localized or generalized, dull or sharp, deep or superficial, associated with rapid shallow respirations or grunting?
4. If the child is less than 2 months old, is he or she feeding well (i.e., tolerating at least a normal amount of breast milk or formula)?
5. If the child is older than 2 months, is he or she able to drink and interested in drinking?
6. What is the child’s activity level?
7. Has the child had convulsions?
8. Is the child abnormally sleepy or difficult to arouse?
9. When was the child’s last urine output?

**Objective Data**

Correct interpretation of objective findings will depend on the child’s age. Younger children normally have higher respiratory rates than older children. The respiratory rate should be counted for an entire minute, especially in infants, for whom variations in rate are normal. Respiration should be counted while the child is quiet.

1. The child’s respirations should be observed for rate, depth, ease, and rhythm of breathing.

<table>
<thead>
<tr>
<th>Age</th>
<th>Rapid Respiration</th>
</tr>
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<tbody>
<tr>
<td>&lt;2 months</td>
<td>&gt;60 breaths per minute</td>
</tr>
<tr>
<td>2-12 months</td>
<td>&gt;50 breaths per minute</td>
</tr>
<tr>
<td>12 months - 5 years</td>
<td>&gt;40 breaths per minute</td>
</tr>
</tbody>
</table>

**Rate** – Is the rate normal, rapid, or slow for the child?

**Depth** – Is the depth of the respiration normal, too shallow, or too deep?

**Ease** – Are the respirations effortless or labored?

Does the child need to be upright to breathe?

Are there intercostal or substernal retractions (sinking in of the chest with respiration)?

Does nasal flaring or head bobbing accompany the child’s breathing? Is the child grunting or wheezing?

**Rhythm of breathing** – Is there variation in rate and depth of respiration?

2. Is the chest movement symmetrical? Asymmetry may indicate pneumonia, pneumothorax (air in the normally closed pleural space between two membranes on the exterior of the lungs), atelectasis (collapse of a lobe of the lung), or foreign-body obstruction.

3. The lungs should be auscultated (listened to) throughout all lung fields while the child is quiet. The stethoscope should be placed directly on the child’s skin. Are any abnormal sounds present? Table 1 describes abnormal lung sounds.

4. Is there other evidence of infection, such as enlarged cervical lymph nodes, inflamed nasal mucous membranes, or discharge from the nose (rhinorrhea) or lungs (sputum)?

5. Does the child have a cough? When is the cough most frequent (e.g. morning or evening)? How frequent is the cough? Is the cough productive or nonproductive? If the cough is productive, note volume, color, viscosity, and odor of sputum. How does the cough sound – moist, dry, or croupy? Is the cough accompanied by wheezing or stridor?

6. Are there changes in skin color, such as mottling, pallor, or cyanosis? What is the distribution of the discoloration (peripheral, circumoral, central)? What is the capillary refill time? Is cyanosis

<table>
<thead>
<tr>
<th>Table 1: Description of Abnormal Lung Sounds</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sound</strong></td>
</tr>
<tr>
<td>Absent or diminished</td>
</tr>
<tr>
<td>Coarse crackle</td>
</tr>
<tr>
<td>Fine crackle</td>
</tr>
<tr>
<td>Wheeze</td>
</tr>
<tr>
<td>Rhonchi</td>
</tr>
</tbody>
</table>
associated with activity or present at rest?

7. Is clubbing present? Clubbing is an abnormal growth of tissue about the terminal phalanges (bones of the fingers and toes). Clubbing is usually associated with chronic hypoxia (decreased oxygen to body tissues).

The child’s respiratory rate needs to be adequately assessed to determine whether the child is in respiratory distress or faces impending respiratory failure. Cardinal signs of respiratory failure are restlessness, tachypnea (rapid respiration), tachycardia (rapid heart rate), and diaphoresis (profuse sweating). Early signs of respiratory failure include altered depth and pattern of respirations, shortness of breath, nasal flaring, chest-wall retractions, expiratory grunt, and wheezing and/or prolonged expiration.

Management

Most respiratory infections are mild and can be treated symptomatically. Warm or cool mist is helpful in relieving discomfort caused by inflammation of mucous membranes. Instillation of saline drops into the nares and nasal suctioning with a bulb syringe can help remove nasal secretions. This will help infants who primarily breathe through the nose to drink from the bottle or nurse without compromising the respiratory effort. Parents should be instructed to clear the infant’s nares by suctioning with the bulb syringe before feeding and before sleep. Parents should be encouraged to provide the child with plenty of rest. Good handwashing should be observed to reduce the spread of the infection to other household members. Adequate fluids should be offered to the child to prevent dehydration, especially if the child is febrile. If the child has fever, paracetamol given by mouth at a dose of 15 mg/kg/dose every 4-6 hours may be used to decrease fever. Parents should be instructed not to exceed five doses per day of paracetamol, since an overdose can cause liver failure. The child’s temperature should be rechecked 30-60 minutes after the dose to confirm the effectiveness of the medication.

Children with respiratory illnesses are treated differently depending on their age and the cause of the illness. The following discussion is based on the 2000 WHO guidelines for managing respiratory illnesses in children.

**Children Less Than 2 Months of Age**

For a child less than 2 months of age, there are three classifications of respiratory illness: severe disease, severe pneumonia, and no pneumonia (cough or cold).¹

**Severe Disease**

An infant is classified as having severe disease if any of the following danger signs are present: lethargy, decreased intake, wheezing, fever (>37.5 degrees C) or low body temperature (<35 degrees C), or severe

<table>
<thead>
<tr>
<th>Illnesses Treated</th>
<th>Medications</th>
<th>Dosing Methods</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe respiratory disease</td>
<td>Aminoglycosides (gentamicin sulfate)</td>
<td>Intravenous and intramuscular</td>
<td>Nephrotoxicity (urinalysis, BUN, creatinine) and/or ototoxicity (serum peak and trough levels should be monitored, if available); tinnitus, vertigo</td>
</tr>
<tr>
<td>Severe pneumonia</td>
<td>Penicillin</td>
<td>Intravenous and intramuscular</td>
<td>Hypersensitivity reaction</td>
</tr>
<tr>
<td>Mastoiditis</td>
<td>3rd generation cephalosporins</td>
<td>Intravenous and intramuscular</td>
<td>Hypersensitivity reaction</td>
</tr>
<tr>
<td>(ceftriaxone sodium,</td>
<td>antibiotics</td>
<td>antibiotics</td>
<td></td>
</tr>
<tr>
<td>cefazidime, cefotaxime sodium)</td>
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</tr>
<tr>
<td>Pneumonia</td>
<td>Chloramphenicol</td>
<td>Oral and intramuscular</td>
<td>Aplastic anemia; renal and liver toxicity</td>
</tr>
<tr>
<td>Otitis media</td>
<td>Penicillin</td>
<td>antibiotics</td>
<td></td>
</tr>
<tr>
<td>Any of the above illnesses</td>
<td>Penicillin, Amoxicillin</td>
<td>Oral antibiotics</td>
<td>Hypersensitivity reaction</td>
</tr>
</tbody>
</table>
malnutrition. A young infant with severe disease should be transferred immediately to a hospital. If possible, give one dose of antibiotics before the transfer.

**Severe Pneumonia**

In this age group, all pneumonia is considered severe. A child is diagnosed as having pneumonia if the respiration rate is greater than 60 breaths per minute or the infant is having chest-wall retractions. A young infant with pneumonia should be treated with intravenous antibiotics and referred to a hospital for inpatient management. The first dose of antibiotics should be given prior to the transfer of the infant.

**No Pneumonia (Cough or Cold)**

A young infant without any danger signs (lethargy, decreased intake, wheezing, fever or low body temperature, severe malnutrition) and without fast breathing, retractions, or wheezing is determined to have a cold. The infant can be cared for at home. The caregiver should be encouraged to offer frequent fluids and to clear the infant’s nose prior to feeding. The caregiver should be instructed to watch for signs of respiratory distress (e.g. nasal flaring, retractions, cyanosis, grunting) and to take the infant to the hospital immediately if any of the signs occur.

**Children 2 Months to 5 Years of Age**

There are three classifications of respiratory illness for children 2 months to 5 years of age: severe pneumonia or very severe disease, pneumonia, and no pneumonia (cough or cold). A child classified as having severe pneumonia should be transferred immediately to a hospital. If possible, give one dose of antibiotics before sending the child to the hospital.

**Pneumonia**

A majority of pneumonia cases in this age group will be characterized by rapid respiration without retractions. A child with pneumonia can be treated at home with oral antibiotics. Pneumonia can be bacterial or viral in origin. Without means to differentiate the cause, all children with pneumonia should be treated with antibiotics. The child’s caregiver should be instructed on how to administer the antibiotics; if feasible, the first dose should be given in the clinic to demonstrate proper administration. A child treated at home should return to the clinic in two days to be reassessed. The caregiver should be instructed to return to the clinic sooner if the child continues to have rapid respirations, develops retractions, continues to have fever, or does not improve on oral antibiotics. If this occurs, the child should be referred to a hospital. If the child improves on oral antibiotics, the antibiotics should be continued to complete five days or longer of treatment. If the child’s signs and symptoms have not improved and the caregiver has been giving the antibiotics correctly, a different antibiotic should be given for five to 10 days.

**No Pneumonia (Cough or Cold)**

A child without any general danger signs is determined to have a cold. This child does not require treatment with antibiotics. The child can be cared for at home. The caregiver should be instructed to watch for signs of respiratory distress (e.g. nasal flaring, abdominal or intercostal retractions, cyanosis, grunting) and to bring the child back immediately if any of these signs occur. If coughing has persisted for more than 30 days, the child should be referred to a hospital for assessment.

Caregivers should be instructed on the importance of giving antibiotics as prescribed. They should not stop
the antibiotics before instructed, even if the child appears to be better. Stopping antibiotics early facilitates the development of antibiotic resistance and relapse of the illness.

**Fever**

Fever is one of the most common parental concerns for a child with HIV. Caregivers often view fever as an illness rather than a sign or symptom. Fever is defined by the WHO as a temperature greater than 37.5 degrees Celsius (measured under the arm) continuously for more than 24 hours or intermittently for more than 24 hours in a 72-hour period.4

Fever may be caused by infection (bacterial, viral, fungal, or protozoal) or malignancy but is rarely caused by medications to treat HIV infection or by HIV infection itself. The hypothalamus causes fever in response to endogenous pyrogens (fever-producing chemicals) that are released by phagocytic leukocytes (white cells that surround and engulf foreign particles) when infection, inflammation, hypersensitivity, or trauma occurs. Fever is thought to be a protective mechanism, because many viral and bacterial organisms cannot reproduce as effectively at higher temperatures. Fever also increases leukocyte phagocytic activity, thereby fighting infection.5

In the early stages of HIV infection, before immune suppression develops, a child with fever should be evaluated as an immunocompetent host. It is not until the patient develops severe immunosuppression (CD4+ count of <15 percent) that the child becomes more susceptible to opportunistic infections. Bacterial infections, including bacteremia, pneumonia, and sinusitis, account for a majority of infectious complications in advanced HIV disease.6

Non-Hodgkin’s lymphoma, which can occur during the early stages of HIV infection, can also cause fever. Central nervous system (CNS) lymphomas, occurring more commonly in the late stages of HIV infection, are infrequently associated with fever.7

Patients in late stages of HIV infection are more susceptible to adverse drug reactions, which may manifest as fever. Adverse reactions to trimethoprim-sulfamethoxazole (TMP-SMZ) are reported at a rate of 25 percent to 50 percent, most commonly as a pruritic rash with or without fever.7

**Subjective and Objective Assessment**

Assessment of a child with fever should include both subjective and objective data.

**Subjective Data**

1. What is the child’s temperature? What is the highest it has been?
2. How long has the child had fever?
3. What is the child’s general appearance?
4. Does the child appear alert and playful or lethargic and quiet?
5. Does the child appear well-hydrated?
6. Does the child have a rash or appear pale or cyanotic (blue around the lips or face)?
7. Is the child’s respiration labored? Does the child have retractions or nasal flaring?
8. Is the child experiencing any other signs/symptoms, such as ear pain, runny nose, cough, sore throat, abdominal pain, vomiting, or diarrhea?
9. How is the child’s appetite?
10. Has the child been in contact with anyone who is ill?
11. Which treatments or medications have been given?

**Objective Data**

1. A complete physical examination is needed to locate a source for the fever. Fever in persons with HIV infection should be evaluated based on signs, symptoms, and the stage of HIV disease. The physical examination should pay particular attention to auscultation of the lungs, abdominal exam, skin, lymph nodes, and neurologic examination.7
2. If the child is less than 3 months of age and the fever is greater than 38 degrees C with no identifiable source of fever, and there is access to
laboratory tests, then a CBC, blood and urine cultures, a chest radiograph, and a lumbar puncture should be performed.8

Management
Treatment should be initiated when a source for the fever is found. The health care provider should instruct the caregiver to give the child any medicine as prescribed and to finish all medications. Fever in children should be managed symptomatically. Paracetamol can be used judiciously. Caregivers should be instructed to keep the child in a cool environment and to avoid overbundling of the child. A light blanket may be used to avoid chilling, because shivering can increase body temperature. Caregivers should be discouraged from sponging the child with alcohol, because this decreases the body temperature too quickly.

Otitis Media and Sore Throat

Otitis media, or infection of the middle ear, can be classified into four categories to help identify proper treatment: acute ear infection, chronic ear infection, mastoiditis, and no ear infection.

Acute Ear Infection
A child with an ear infection may have ear pain, ear drainage, and/or fever. On physical examination, the child will have an erythematous (abnormally red), bulging, dull, immobile eardrum and/or pus draining from the ear. If the signs and symptoms have been present for less than two weeks, the child is classified as having acute otitis media. Acute otitis media is treated with oral antibiotics at home for five days. If the child has fever for more than 48 hours on antibiotics, consider a change in the antibiotics.

Chronic Ear Infection
A child who has had ear drainage for longer than two weeks is considered to have chronic otitis media. The ear should be dried by a method known as wicking. This should be done for the first time in the clinic to demonstrate the technique to the child’s caregiver. To dry the ear, roll a clean, soft, absorbent cotton cloth into a wick. Place the wick in the child’s ear, and remove it when it is wet. Repeat these steps until the wick no longer gets wet; this indicates that the ear is dry. This should be done at home at least three times per day. Antibiotics are usually not effective in treating chronic ear infections, which are caused by different bacteria than acute ear infections.

Mastoiditis
Mastoiditis is a complication of otitis media. A child with mastoiditis will have a tender, swollen, erythematous, warm area behind the ear. Mastoiditis requires treatment with antibiotics and possible surgery. A child with mastoiditis should be referred to a hospital. The first dose of antibiotics should be given in the clinic, if feasible. The same antibiotics used to treat pneumonia are used in the treatment of mastoiditis.

Management
If antibiotics are given for an ear infection, the caregiver should be instructed to complete the full course of antibiotics and to return for follow-up as instructed. The caregiver should be instructed not to put oil or any other fluid into the child’s ear, and the child should avoid getting water into the ear. Recurrent, chronic ear infections can cause deafness.

Sore Throat
Sore throat is one of the most common symptoms of an upper respiratory infection. Most cases of sore throat are caused by viruses, can be treated symptomatically, and resolve in a few days. Occasionally a child with a sore throat will require antibiotics. Antibiotics are necessary if the sore throat is caused by a throat abscess or streptococcal infection. A child with a throat abscess will not be able to swallow secretions, fluids, or food and should be referred to a hospital for drainage of the abscess. A child with a streptococcal throat infection will have tender, enlarged lymph nodes in the front of the neck and white exudate in the posterior oropharynx and/or on the tonsils.
Management
Most children with a sore throat get better in a few days with symptomatic treatment. Caregivers should be encouraged to offer frequent liquids to keep the mucosal surface of the throat moist. Paracetamol may be given by mouth at a dose of 15 mg/kg/dose every 4-6 hours to relieve discomfort or fever. Caregivers should be instructed not to exceed five doses per day of paracetamol, since an overdose can cause liver failure. The child’s temperature should be rechecked 30-60 minutes after the dose to confirm the effectiveness of the medication. If the child has a streptococcal infection, the best treatment is a single injection of benzathine penicillin. If this is not available, the child should be treated with oral amoxicillin, ampicillin, or penicillin for 10 days. If oral antibiotics are given, the caregiver must understand the importance of completing the antibiotics to prevent complications such as rheumatic fever or a relapse of the illness.
COMMON ILLNESSES IN CHILDREN WITH HIV/AIDS

**Review Questions**

1. What are the most important questions to ask when assessing a child with HIV who has fever?
2. Name at least three causes of fever in a child with HIV.
3. What is considered a rapid respiratory rate for children less than 2 months of age?
4. Describe the treatment for respiratory illnesses in children less than 2 months of age.
5. Describe the treatment for respiratory illnesses in children 2 months to 5 years of age.
6. What is the appropriate management for children with a sore throat or otitis media?

**Exam Questions**

1. Which factor places a child with HIV/AIDS at greatest risk for an opportunistic infection?
   a. Presence of a malignancy
   b. Immune suppression
   c. Persistent high fevers
   d. Drug reaction

2. What is the most important intervention for a child less than 2 months of age with severe pneumonia?
   a. Begin oral antibiotics
   b. Hospitalize immediately
   c. Administer fluids
   d. Administer oxygen

3. Rubi, a 2-month-old, comes to your clinic with a respiration rate of 32 breaths per minute. She has had congestion for the past few days with no fever. She is drinking well. What is your assessment?
   a. Rubi has pneumonia, since she is having rapid respirations.
   b. Rubi has a normal respiratory rate.
   c. Rubi has severe respiratory disease.
   d. Rubi should be hospitalized.
A 1-month-old infant comes to clinic with a two-day history of stuffy nose, normal breastfeeding, and no fever. On physical examination, the infant’s respiratory rate is 40 breaths per minute without retractions or nasal flaring. Bilateral breath sounds are clear, and the child is afebrile.

**Question:** According to the 2000 WHO guidelines, the appropriate diagnosis for this infant is:

- a. Severe disease
- b. Severe pneumonia
- c. Pneumonia
- d. No pneumonia (cough or cold)

**Answer:** d. A young infant without any danger signs (lethargy, decreased intake, wheezing, fever or low body temperature, severe malnutrition), fast breathing, retractions, or wheezing is determined to have a cold.

**Question:** The most appropriate intervention for the above infant is:

- a. Hospitalization for intravenous antibiotics
- b. Hospitalization to monitor signs and symptoms
- c. Home with oral antibiotics
- d. Home to monitor signs and symptoms

**Answer:** d. The infant can receive care at home. The caregiver should be encouraged to offer frequent fluids and to clear the infant’s nose prior to feeding. She should be instructed to watch for signs of respiratory distress (e.g. nasal flaring, retractions, cyanosis, grunting) and to bring the infant back to the hospital immediately if any of the signs occur.

The mother brings the infant back to clinic two days later. The infant has had fever for the past 24 hours and decreased breastfeeding. On physical examination, the infant’s respiratory rate is 70 breaths per minute with retractions and nasal flaring. Bilateral breath sounds are coarse with inspiratory and expiratory wheezes.

**Question:** According to the 2000 WHO guidelines, the appropriate diagnosis for this infant is:

- a. Severe disease
- b. Severe pneumonia
- c. Pneumonia
- d. No pneumonia (cough or cold)

**Answer:** a. The infant is classified as having severe disease if any danger signs (lethargy, decreased intake, wheezing, fever or low body temperature, severe malnutrition) are present.

**Question:** The most appropriate intervention for the infant is:

- a. Hospitalization for intravenous antibiotics
- b. Hospitalization to monitor signs and symptoms
- c. Home with oral antibiotics
- d. Home to monitor signs and symptoms

**Answer:** a. A young infant with severe disease should be transferred to a hospital immediately. If possible, the first dose of antibiotics should be given before the transfer.
HEMATOLOGIC MANIFESTATIONS OF HIV/AIDS

References

Objectives

The purposes of this module are to:
1. Present an overview of normal growth and development in children.
2. Describe how HIV infection impacts growth and development in children.
3. Review the effects of highly active antiretroviral therapy (HAART) on growth and development in HIV-infected children.
4. Discuss changes in bone formation and pubertal development in HIV-positive children.

Key Points

1. Growth and development are important indicators of the health of a child.
2. Health care providers who care for children should evaluate each child’s growth and development at every visit.
3. HIV infection can lead to growth problems, developmental delays, and developmental regression.
4. When problems in growth and development are found, the health care provider should attempt to treat the underlying cause of the problem.
5. Bone problems and abnormal pubertal development are more commonly seen in HIV-infected children than in non-infected children.

Overview

Growth and development are important indicators of a child’s health. Accurate measurements of weight, height, and head circumference are essential parts of the health evaluations of growing children. Children who are unhealthy tend to grow more slowly and to be smaller than healthy children their age. Likewise, developmental delays often result from health problems.

HIV-infected children are at particular risk for problems related to growth and development. HIV and opportunistic infections often negatively influence the growth and development of young children. The lives of many HIV-infected children are complicated by a lack of nutritious food necessary for normal growth and development. When a child’s caretakers are ill or are suffering emotionally from the loss of friends and family members, they may be less available to provide appropriate developmental stimulation.

Health care providers who treat children should understand how to assess whether a child’s growth and development are appropriate for the age of the child. By evaluating growth and development at every medical visit, we can learn much about the child’s health.
Newborns: Birth-Weight Comparisons

Small size at the time of birth is not clearly associated with HIV infection in full-term newborns. A full-term newborn’s birth weight is determined by many factors, including maternal nutrition, placental function, and fetal genetics. Studies examining the role of maternal HIV infection in fetal growth have failed to show a consistent relationship. According to the European Collaborative Study and a study from Durban, South Africa, newborn height and weight of infected and uninfected children born to HIV-positive mothers are not significantly different. In contrast, a study based on a U.S. inner-city population concluded that children born to HIV-infected mothers are at increased risk of low birth weight as well as prematurity. The results of this study were adjusted for confounding factors such as tobacco, alcohol, and other drug use known to affect birth weight. Further studies are needed to clarify the reasons for the inconsistencies seen between these populations. At this time, the evidence does not clearly imply a relationship between HIV infection and infant birth weight.

While full-term newborns who are HIV-infected or HIV-exposed are not typically smaller than term unexposed infants, prematurity is more common among HIV-exposed infants. A study done prior to the implementation of prenatal prophylaxis and the routine use of HAART showed the rate of prematurity associated with HIV infection was as high as 19 percent, more than 30 percent higher than in the uninfected population. The population evaluated in the HIV-positive group was also at increased risk for smoking, alcohol use, and illicit drug use, which can contribute to a higher incidence of premature births. The use of HAART does not decrease the incidence of prematurity among children born to HIV-positive mothers. This has been demonstrated in a multicenter U.S. study of more than 3000 children born to HIV-positive women, in which the incidence of prematurity was 17 percent in the HAART-treated group and 16 percent among those not receiving HAART.

Frontal Occipital Circumference (FOC) and HIV

Head circumference is known to be correlated with brain volume. The brain is one of the primary targets of HIV infection. HIV infection in young children sometimes results in reduced brain growth. Smaller FOC at birth has been associated with developmental delays and reduced academic achievement in non-infected children. Studies have not shown a statistically significant difference in birth FOC between infected and uninfected children. The Women and Infants Transmission Study (WITS) did, however, show a trend toward smaller birth FOC in HIV-infected infants. This study also showed that infants infected with HIV had a continued decrement in brain growth as evidenced by persistent microcephaly (FOC <5th percentile for age).

The WITS group also showed an association between early HIV-positive culture and higher risk of neurologic compromise. Since microcephaly has been correlated with adverse developmental outcomes, FOC measurements may be used as a tool for the identification of infants at risk for these unfavorable outcomes. FOC may also be used as an early predictor of HIV-associated progressive encephalopathy in infants. FOC measurements are most useful during the first 2 years of life, when head circumference changes most rapidly.

Variable Onset of Growth Failure

Children’s growth is affected by many factors, including general nutrition, overall health, endocrine abnormalities, and caretaker nurturing. A child is said to be failing to thrive when his or her height and weight are less than the 5th percentile for age or he or she is crossing percentiles downward on standardized growth curves. (U.S. standardized growth charts are provided in the “Nutrition and HIV/AIDS” chapter.) Failure to thrive is a diagnosis that has
multiple etiologies, one of which is HIV infection. According to the European Collaborative Study, at 10-year follow-up, infected children were on average 7 kg lighter and 7.5 cm shorter than uninfected children.

The onset of growth failure in children with HIV has been variable. Some studies have reported growth deceleration as early as the first few months of life. Other studies have shown children with normal growth into and beyond their second year of life. Overall, studies have shown that children with HIV infection grow more slowly than uninfected children, a difference that becomes more significant with age. Asymptomatic infected children have similar growth patterns as mildly or moderately symptomatic children. However, children with severe illness tend to have poorer growth. Increased levels of postnatal viremia have been clearly associated with decreased linear growth.

**Nutrition, Growth, and HIV**

Even in patients without HIV infection, nutrition plays an important role in childhood growth. The effects of nutrition on patients with HIV have been studied with respect to CD4+ counts and growth parameters. An observational study of nutritional interventions among children with AIDS (giving adequate calories, protein, fat, and micronutrients) determined that attention to these nutritional factors may help restore intestinal absorption and improve CD4 counts. The researchers reported that providing adequate nutrition was most beneficial if started prior to the development of an AIDS-defining illness. Early nutritional interventions play an important role in helping to decrease morbidity and mortality among HIV-infected children, particularly in developing countries without access to antiretroviral therapy.

**Growth as a Predictor of Prognosis**

Children infected with HIV have been classified in three clinical groups with regard to the timing of their disease progression. Infants who develop symptoms of AIDS or who die within the first year of life are classified as “rapid progressors.” Children who suffer from an AIDS-defining illness or who die within one to five years of infection are classified as “intermediate progressors.” Those children who do not develop symptoms and who survive past 5 years of age are classified as “slow progressors.” Growth failure in children has been clearly associated with accelerated progression from asymptomatic HIV infection to AIDS. Those children who qualify for classification as “rapid progressors” have the highest incidence of growth failure.

Perinatally acquired HIV infection is sometimes associated with early and progressive decrements in weight and length. Height growth velocity (rate of growth) has been shown to predict survival independently of age, viral load, and CD4+ cell count. Studies in Thailand, Rwanda, and the U.S. have evaluated growth as a predictor of prognosis. The consensus in these studies was that growth failure is highly suggestive of rapid disease progression. Patients who failed to gain 2 kg by 4 months of age, as well as those with low CD4+ counts (maternal and infant) at time of birth and high viral loads at 2 months of age, were most likely to have rapid disease progression. In resource-limited environments, where obtaining laboratory data is sometimes not possible, growth monitoring may be the best available tool for assessing risk of disease progression.

**Effects of HAART on Growth**

Early studies demonstrated that mono or dual antiretroviral therapies containing zidovudine, didanosine, or zalcitabine led to a temporary increase in weight and linear growth rate. The transitory nature of the benefits seen with mono and dual therapy are related to the frequent occurrence of treatment failure due to drug resistance. Because HAART is less likely to lead to resistance and treatment failure, more
sustainable clinical growth responses are seen among children on HAART.\textsuperscript{16}

HAART clearly has a positive effect on height and weight in children with HIV-1 infection. According to a study performed in the Netherlands, this effect is sustained for at least 96 weeks (study duration) in patients who respond virologically to HAART. Successful application of HAART was defined as a long-term reduction in viral load of at least 1.5 log copies/ml, or viral load suppression to less than 500 copies/ml, and increased CD4+ counts. The children in this study were divided into virologic responders and virologic non-responders. Virologic responders demonstrated a significant increase in height and weight, whereas virologic non-responders did not.\textsuperscript{16}

The body mass index (BMI) has been used as a tool to evaluate nutritional status in both adults and children. The BMI is calculated by using the formula

\[
\text{BMI} = \frac{\text{weight (kg)}}{\text{height}^2 \text{ (meters)}}
\]

Unlike what has been seen in adult populations, BMIs did not vary significantly between responder and non-responder children. An increase in BMI did, however, correlate inversely with the clinical stage of HIV prior to the initiation of HAART.\textsuperscript{16} Children with worse clinical stages at the beginning of therapy had a more significant increase in BMI than children starting at better clinical stages.

Catch-up growth typically affects weight before affecting height.\textsuperscript{16} HAART’s beneficial effects on a patient’s growth likewise are first seen as increases in weight (usually by 48 weeks of therapy) and later as height improvements (usually by 96 weeks of therapy). A group from the Duke Clinical Research Institute is looking at the prediction of treatment failure using height velocity as a marker for treatment response.\textsuperscript{17} If validated internationally, this type of prediction could provide an excellent low-cost method for evaluating treatment response in resource-limited settings.

### Bone Growth: Osteopenia, Osteoporosis, and Osteonecrosis

Bone mass increases during childhood and adolescence; peak bone mass normally is achieved during the third decade of life.\textsuperscript{18} When people have low bone density for their age, they are said to have osteopenia. Those whose bone density is less than 2.5 standard deviations below the mean have the severe form of bone wasting called osteoporosis. Children who fail to form bone normally are at high risk for suffering from fractures during adulthood due to early osteoporosis. HIV-infected children accumulate bone density at a slower rate than non-infected children, and certain HAART regimens may further decrease bone density.\textsuperscript{19,20}

The mechanisms by which bone mass is decreased among HIV-positive children are complicated and incompletely understood. HIV probably affects bone development both directly and indirectly. HIV can infect bone cells directly. The virus also leads to the elevation of several cytokines (IL-1, IL-6, and TNF-alpha) that contribute to increased activity of osteoclasts (cells that break down bone).\textsuperscript{20} Vitamin D deficiency also contributes to abnormal bone metabolism and has been reported in adults with HIV.\textsuperscript{21} While increased rates of bone fractures are not commonly seen among HIV-infected children, these children are at high risk of fractures later in life due to their early development of osteopenia and osteoporosis.

Children and adults with HIV infection are also at increased risk of osteonecrosis of the hip. In children, this condition is called Legg-Calve-Perthes Disease (LCPD). A study of perinatally HIV-infected children demonstrated a prevalence of LCPD that was more than eight times that of the general population.\textsuperscript{22} LCPD is diagnosed on the basis of typical X-ray findings in a symptomatic patient. Treatments for LCPD include the use of non-steroidal anti-inflammatory and pain-control medications, temporary cessation of weight bearing, and exercises to maintain...
the range of motion. In severe cases, immobilization of the joint or surgery may be required.

Low bone density can be quantified using dual-energy X-ray absorptiometry (DEXA scans) or quantitative CT scans. The appearance of the bones on plain X-rays can also give qualitative evidence for the existence of osteopenia or osteoporosis. Weight-bearing exercises (such as jogging, dancing, and weight lifting) can help children with HIV to maximize their bone development.

Providing a diet that is rich in vitamin D, especially in areas where children have limited exposure to sunlight, will also help to ensure the best possible bone growth. Studies are currently looking at the effects of various bone-building medicines on HIV-infected children with osteopenia and osteoporosis, but no medications are currently recommended for routine use.

**Puberty**

Delay of sexual maturation is a common occurrence among children with chronic diseases. Children with HIV infection have delays both in the age of onset of puberty and in their progression through the Tanner stages. The median delay in pubertal onset is two years for girls and one year for boys. Entry into the late Tanner stages is delayed by about 2.5 years in girls and 1.5 years in boys.23 Children with increased immune-system dysfunction tend to have the most significant delays in pubertal development.24 Therefore, tracking pubertal development may help to clarify underlying disease progression.

**Developmental Assessments**

It is important that people who provide health care to children understand basic principles of developmental assessment. This is especially important for those providing care to HIV-infected children, because developmental delays are often early signs of disease progression. Many tools are available for the assessment of developmental progression. Table 1 lists some of the most commonly used tools for the screening of child development. Considering a child’s age and cultural background can help medical professionals to determine which tool is the most appropriate for each patient’s evaluation. Because some

<table>
<thead>
<tr>
<th>Table 1: Commonly Used Developmental Screening Tools</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tool</strong></td>
</tr>
<tr>
<td>Ages and Stages Questionnaire</td>
</tr>
<tr>
<td>Bayley Scales of Infant Development II</td>
</tr>
<tr>
<td>Clinical Adaptive Test/Clinical Linguistic and Auditory Milestones Test (CATT/CLAMS)</td>
</tr>
<tr>
<td>Denver Developmental Screening Test (DDII)</td>
</tr>
<tr>
<td>Kaufman Assessment Battery for Children</td>
</tr>
<tr>
<td>McCarthy Scales of Children’s Abilities</td>
</tr>
<tr>
<td>Wechsler Intelligence Scales</td>
</tr>
</tbody>
</table>
## Table 2: Developmental Milestones – The First 24 Months of Life

<table>
<thead>
<tr>
<th>Age</th>
<th>Psychosocial</th>
<th>Gross Motor</th>
<th>Fine Motor and Visual</th>
<th>Communication and Hearing</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 month</td>
<td>• Follows faces to the midline</td>
<td>• Moves all extremities equally</td>
<td>• Opens hands spontaneously</td>
<td>• Startled by loud sounds</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Lifts head when lying on stomach</td>
<td></td>
<td>• Cries</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Smiles responsively</td>
<td></td>
<td>• Quiets when fed and comforted</td>
</tr>
<tr>
<td>2 months</td>
<td>• Follows faces past the midline</td>
<td>• Lifts head up 45 degrees when</td>
<td>• Looks at own head</td>
<td>• Makes baby sounds such as cooing, squealing and gurgling</td>
</tr>
<tr>
<td></td>
<td></td>
<td>on stomach</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>• Recognizes mother</td>
<td>• Can support head for a few seconds when held upright</td>
<td>• Opens hands frequently</td>
<td>• Responds to voices</td>
</tr>
<tr>
<td></td>
<td>• Smiles responsively</td>
<td></td>
<td></td>
<td>• Laughs</td>
</tr>
<tr>
<td>4 months</td>
<td>• Follows an object with eyes for 180 degrees</td>
<td>• Bears weight on legs</td>
<td>• Brings hands together in midline (claps hands)</td>
<td>• Turns head to sound</td>
</tr>
<tr>
<td></td>
<td>• Regards own hand</td>
<td>• Good neck control when pulled to sitting position</td>
<td>• Grabs an object such as a rattle</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Anticipates food on sight</td>
<td>• Lifts chest and supports self on elbows when</td>
<td>• Reaches for objects</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>lying on stomach</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>• Reaches for familiar people</td>
<td>• Rolls from stomach to back or back to stomach</td>
<td>• Plays with hands by touching them together</td>
<td>• Responds to name</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Sits with anterior support</td>
<td>• Sees small objects such as crumbs</td>
<td>• Babbles</td>
</tr>
<tr>
<td>9 months</td>
<td>• Indicates wants</td>
<td>• Can sit without support</td>
<td>• Looks for a toy when it falls from his/her hand</td>
<td>• Responds to soft sounds such as whispers</td>
</tr>
<tr>
<td></td>
<td>• Waves “bye-bye”</td>
<td>• Creeps or crawls on hands and knees</td>
<td>• Takes a toy in each hand</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Has stranger anxiety</td>
<td></td>
<td>• Transfers a toy from one hand to the other</td>
<td></td>
</tr>
<tr>
<td>12 months</td>
<td>• Has separation anxiety</td>
<td>• Pulls self up to standing position</td>
<td>• Says at least 1 word</td>
<td>• Able to say “mama” and “dada” to respective parents (sounds to identify caretakers)</td>
</tr>
<tr>
<td></td>
<td>• Social interactions are intentional and goal-</td>
<td>• Points at objects with index finger</td>
<td>• Makes “ma-ma” or “da-da” sounds</td>
<td></td>
</tr>
<tr>
<td></td>
<td>directed</td>
<td></td>
<td>• Locates sounds by turning head</td>
<td></td>
</tr>
<tr>
<td>15 months</td>
<td>• Imitates activities</td>
<td>• Can take steps on own</td>
<td>• Can stack one cube on top of another</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Finds a nearby hidden object</td>
<td>• Can get to a sitting position from a lying</td>
<td>• Able to say “mama” and “dada” to respective parents (sounds to identify caretakers)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>position</td>
<td>• Transfers a toy from one hand to the other</td>
<td></td>
</tr>
<tr>
<td>18 months</td>
<td>• Initiates interactions by calling to adult</td>
<td>• Walks without help</td>
<td>• Says at least 3 words</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Does things to please others</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Engages in arallel (imitative) play</td>
<td>• Can take off own shoes</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Feeds self</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 years</td>
<td>• Runs without falling</td>
<td>• Looks at pictures in a book</td>
<td></td>
<td>• Combines 2 different words</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Imitates drawing a vertical line</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Table 3: Developmental Red Flags

<table>
<thead>
<tr>
<th>Age</th>
<th>Developmental Problem</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth to 3 months</td>
<td>• Failure to alert to environmental stimuli</td>
</tr>
<tr>
<td></td>
<td>• Rolling over before 2 months (indicative of hypertonia)</td>
</tr>
<tr>
<td></td>
<td>• Persistent fistig at 3 months</td>
</tr>
<tr>
<td>4-6 months</td>
<td>• Poor head control</td>
</tr>
<tr>
<td></td>
<td>• Failure to smile</td>
</tr>
<tr>
<td></td>
<td>• Failure to reach for objects by 5 months</td>
</tr>
<tr>
<td>6-12 months</td>
<td>• No baby sounds or babbling</td>
</tr>
<tr>
<td></td>
<td>• Inability to localize sounds by 10 months</td>
</tr>
<tr>
<td>12-24 months</td>
<td>• Lack of consonant production</td>
</tr>
<tr>
<td></td>
<td>• Hand dominance prior to 18 months (indicates contralateral weakness)</td>
</tr>
<tr>
<td></td>
<td>• No imitation of speech and activities by 16 months</td>
</tr>
<tr>
<td>Any age</td>
<td>• Loss of previously attained milestones</td>
</tr>
</tbody>
</table>
children may not have regular exposure to elements of the standardized screening tools, these tools may underestimate the knowledge and abilities of children in certain cultures. Cultural practices may influence the "normal" age of development of even basic motor tasks such as crawling and walking. Therefore, whenever possible, a tool that has been researched and validated for use among children of similar backgrounds should be used.

When standardized screening tools are not available, health care providers should at least keep a record of the developmental milestones that have been achieved by their pediatric patients. By identifying children who are not achieving age-appropriate milestones, providers can better recognize those patients who need more intensive evaluations and therapies. Not achieving key milestones by certain ages can be considered “red flags” that should alert medical practitioners to the need for further interventions. Tables 2 and 3 provide basic guidelines regarding normal milestone progression in young children.

Children who fail to reach age-appropriate milestones should be evaluated for conditions that lead to developmental and neurological deficits. Sustained developmental regressions (loss of the ability to perform previously acquired skills) are never normal and should prompt appropriate interventions.

**Developmental Delays in HIV-Infected Children**

HIV-infected children, especially those with other serious HIV-related symptoms, have a higher incidence of developmental delays than their non-infected peers. Uninfected children born to HIV-infected mothers, however, achieve developmental milestones at the same rate as children born to uninfected mothers. Significant cognitive and motor deficits have been shown to occur with increased frequency among HIV-infected children, beginning in infancy.25-31 These abnormalities cannot be accounted for by other biological or environmental risk factors.27-29 Children with other serious HIV-related symptomatology are at greatest risk of significant developmental impairments.25,30 It has been demonstrated among HIV-infected children in the U.S. that those children with the lowest rates of neuropsychological functioning are at highest risk of rapid HIV disease progression.26,31,32 It is not yet known whether developmental deficits would be similarly predictive of HIV disease progression in low-resource populations where factors such as poor nutrition would be expected to further complicate the clinical picture.

While HIV-infected children with the most systemically advanced HIV disease tend to have the most profound developmental delays, significant delays can also be seen in HIV-infected children with otherwise stable clinical conditions.33 The reasons for discordant control of HIV disease outside and inside the central nervous system are not yet understood. In a few case studies, improvements in functioning were seen when antiretroviral regimens were altered to include drugs with better CNS penetration.33 Further studies are needed to clarify the best interventions to optimize the care of HIV-infected children with developmental delays.
Review Questions

1. What changes in birth measurements would you expect to see in children born with HIV infection?

2. Why are developmental delays and regressions considered to be important indicators of prognosis in HIV-infected children?

3. What are some ways in which children’s development can be assessed by their health care providers?

4. What bone-related problems are seen more frequently in HIV-infected children?

5. What pubertal changes are common among HIV-infected girls and boys?

Exam Questions

1. Assessments for developmental delays in children include all of the following EXCEPT:
   a. Administering an age-appropriate standardized developmental assessment tool
   b. Evaluating the child for developmental “red flags”
   c. Tracking developmental milestones
   d. Measuring the head circumference

2. What follows is true regarding the effects of HAART on growth and development?
   a. In patients who have shown a significant viral load decrease, HAART has no effect on weight or height.
   b. Patients on HAART tend to have developmental regression secondary to drug interactions.
   c. Patients who show a virologic response to HAART usually have an increase in weight and a subsequent increase in height.
   d. HAART provides no improvement in long-term growth parameters when compared to mono-therapy.

3. Skeletal problems related to HIV infection include which of the following?
   a. Frequent fractures in young children
   b. Unusually tall stature
   c. Low bone density
   d. Osteonecrosis of the hip
   e. Both a and c
   f. Both c and d

Answers: 1d, 2c, 3f
A mother brings her 16-month-old daughter, Lupita, to clinic for evaluation. Lupita’s family is poor and frequently does not have enough nutritious food to eat. Lupita’s head circumference is at the 50th percentile for her age. Her height is at the 5th percentile for her age. Her weight is far below normal for a child her age. When you draw a line on the growth chart, you see that Lupita’s weight would be at the 50th percentile for a 9-month-old child.

**Question:** Which of the following would be appropriate to tell the child’s mother at this time?

a. Her head is too big, and tests need to be done to see why her head is growing so fast.
b. You are concerned about her weight and want to see her frequently to make sure that she is gaining weight appropriately.
c. It is important to make sure that she is getting enough nutrition to gain weight appropriately.
d. If she is sick, treating her illness will help her to gain weight.
e. b, c, and d

**Answer:** e. Children who are sick and malnourished commonly have low weight and height and relatively good head growth. Ensuring that they are getting good nutrition and treating any illnesses they have will help them to grow well. When possible, evaluating growth-delayed children more frequently than normal children will help you to ensure that the delayed children are receiving the best nutrition available to meet their needs.

You question the mother and observe the same 16-month-old child to assess her development. She first began rolling over at 5 months of age. Currently she can sit without support and can pull herself up to a standing position. Occasionally she takes a few steps without support, but she falls down frequently. She transfers toys from hand to hand and can pick up small objects such as crumbs between two fingers. Although she makes some sounds, she does not babble using consonant sounds, and she does not turn her head when her mother calls her name.

**Question:** Which of the following assessments and recommendations correspond best with the information provided regarding Lupita’s development?

a. Her development is remarkably delayed in all areas, and her parents should anticipate that she will never walk well.
b. She is meeting all age-appropriate milestones; no further evaluations are needed.
c. While her motor skills are appropriate for her age, her communication skills should be better; her hearing should be tested.
d. Her gross motor skills are delayed due to malnutrition, and intensive nutritional rehabilitation should be instituted to allow her to catch up with her peers developmentally.

**Answer:** c. This question demonstrates the importance of evaluating all aspects of a child’s development. While children who are malnourished do often have gross motor delays, Lupita does not. Her failure to respond to voices and her immature verbalization skills should alert the clinician to the likelihood of a hearing problem or other communication disorder.

**Case Study #2**

Lupita’s cousin, Maria, is also 16 months old. Maria is HIV-infected but was generally healthy during her first year of life even though antiviral therapy was not available for her. Maria’s height and weight are similar to those of her cousin. Her head circumference, however, is far below normal for a child her age. At birth, Maria’s head circumference was normal, but her
head seems to have stopped growing over the past six months.

**Question:** Which of the following is true regarding Maria’s head circumference?

a. Her poor head growth is a concerning sign and indicates that she is at high risk of poor neurodevelopmental outcomes.

b. Because her weight is also low, you can be certain that her small head circumference is due to malnutrition.

c. HIV-infected children always have small heads.

d. Because her head size was normal at birth, she must have been infected with HIV after birth.

**Answer:** a. HIV-infected children usually have normal head sizes at birth. The failure of a child’s head to continue growing at a normal rate, particularly during the first two years of life, corresponds with an increased risk of developmental delays, regressions, and other neurological problems.

At 1 year of age, Maria’s motor skills were normal. She liked to imitate sounds and was able to call her mother and father by name (Mama and Dada). She has lost the ability to do some of the things she was able to do before. She no longer can pull herself to a standing position or sit without support.

**Question:** All of the following are true regarding Maria’s development EXCEPT:

a. Developmental regressions are never normal and should always prompt additional evaluations.

b. Her development is likely to improve soon without any interventions.

c. Her poor head growth may have been an early warning sign that she was at high risk of developmental problems.

d. It is likely that her developmental problems are related to her HIV infection and will improve with the institution of HAART.

**Answer:** b. The recent poor growth and development of this HIV-infected child also indicate that she is at high risk of HIV-disease progression.

**Case Study #3**

François, a 6-year-old HIV-infected boy, is being followed in your clinic. He has had a number of opportunistic infections, including diarrheal illnesses, dermatitis, and candidiasis. For the past year his height and weight have not increased, but he is not losing weight. You are unable to check his CD4+ count or viral load and are trying to make a decision regarding whether to start this child on HAART.

**Question:** Which of the following statements provides the best support for an appropriate therapeutic decision for this patient?

a. There is no reason to start HAART until the child begins to lose weight.

b. HAART should be started because the child has had oral candida.

c. HAART should be started because the child has growth failure.

d. If his head circumference is normal, then HAART should not be started.

**Answer:** c. Growth failure is a strong predictor of early demise for HIV-infected children. Head circumference increases rapidly during the first two years of life. A child with later growth failure is not likely to have measurable deficits in head size.

**Case Study #4**

Vu, a 9-month-old boy, is brought to your clinic for the first time by his maternal grandmother. His mother died of an unknown illness. The grandmother states that the child has been doing well. When questioned further about the development of the child, she says he is unable to sit up without support and cannot roll from front to back. During your examination, you notice that the child is not reaching for toys and cannot bring his hands to the midline. He also has
poor neck control when pulled to a sitting position. The child seems to recognize his grandmother and smiles appropriately.

**Question:** Which of the following statements best represents the child’s developmental assessment?

a. The child has a significant developmental delay. Evaluations, including HIV testing, need to be started.
b. The child is at an appropriate developmental stage.
c. The child is exceeding age-appropriate milestones and needs no further workup.

**Answer:** a. According to Table 2, the patient is not meeting any of the milestones expected for a 9-month-old child. A child with a significant delay in milestones should have HIV testing as part of the evaluation, especially in areas of high disease prevalence and in cases in which the history is suggestive of exposure.

**Case Study #5**

Alexandra, a 6-month-old girl known to be HIV-infected, is brought to the clinic for a checkup. Her grandfather tells you that they have been unable to obtain any of her antiretroviral (ARV) medicines, and therefore she has not been taking them. After measuring her head circumference, weight, and height, you notice that her head is <3 percent for age, her weight is 50 percent for age, and her height is 50 percent for age. Looking at her previous growth parameters, you notice that her previous head circumferences were 25 percent and 10 percent at 2 months and 4 months respectively. Your examination shows that the child is able to roll from front to back, can sit up with support, and babbles.

**Question:** The best statement concerning the patient’s head circumference is that:

a. Alexandra’s head size is appropriate for her age, and there is no reason to be concerned about her development.
b. Alexandra’s head circumference is significantly microcephalic, and she is at higher risk of having abnormal development when compared to children with normal head circumference for age.
c. Because Alexandra’s development is adequate for a 6-month-old child, there is no further need to monitor head growth at follow-up visits.
d. Alexandra’s head circumference is significantly microcephalic, but she is at no increased risk of having abnormal development because she has reached normal developmental milestones up to this point.

**Answer:** b. Patients infected with HIV who have an abnormally small head circumference have an increased risk of developmental problems and other signs of HIV-related CNS disease. Helping the caretaker obtain the ARVs is of special importance for this patient with falling head circumference. Close monitoring of this patient’s development is necessary to ensure timely interventions.


IMMUNIZATIONS FOR CHILDREN WITH HIV/AIDS

IMMUNIZATIONS FOR CHILDREN WITH HIV/AIDS

Nancy R. Calles, B.S.N., R.N., A.C.R.N.

Objectives

The purposes of this module are to:
1. Describe the importance of immunizations for children with HIV/AIDS.
2. Review the mechanisms involved in the immune response.
3. Identify the accelerated immunization schedule for HIV-infected children.
4. Discuss the specific types of immunizations administered to HIV-infected children.
5. Understand the side effects related to the administration of immunizations to HIV-infected children.

Key Points

1. Immunizations play an important role in the prevention of childhood diseases.
2. Children infected with HIV/AIDS should receive an accelerated immunization schedule.
3. BCG is the most commonly used vaccine in the world and is the only vaccine available for Mycobacterium tuberculosis.
4. The World Health Organization (WHO) recommends the use of the oral polio vaccine (OPV) in asymptomatic and symptomatic HIV-infected children in areas of the world where the inactivated polio vaccine (IPV) is not available.
5. The measles vaccine is administered to HIV-infected children who are not severely immunocompromised.
6. The hepatitis B vaccine is recommended for HIV-infected children.
7. The yellow fever vaccine is recommended at 9 months of age and every 10 years thereafter for asymptomatic HIV-infected children living in or traveling to endemic areas of the world.

Importance of Immunizations for HIV-Infected Children

Immunization is one of the easiest ways to prevent dangerous diseases. Immunizations can also help HIV-infected children who are more likely to acquire preventable diseases because of a compromised immune system. Appropriate immunizations vary by geographic location. It is important to consider several questions regarding immunization of HIV-infected children: Should the child be immunized early before HIV has caused damage to the immune system? When should a child be immunized according to an accelerated schedule? Will an immune system that takes two to five years to fully mature benefit from a routine immunization schedule? What will be the risk to an already weakened immune system if certain vaccines accelerate HIV replication? Will this increase in viral replication hasten HIV disease progression? Should live attenuated vaccines be used in HIV-infected children?
There is limited information regarding routine immunization of HIV-infected children. However, the fact that very few adverse events have been reported leads us to believe that the benefits associated with immunization outweigh the possible risks.

**Immune Response**

Immune responses to vaccination vary, depending on the nature of the vaccine and the individual’s immune status. Adult immune systems respond when exposed to a particular antigen because of previous exposure to the antigen, either through vaccination or through acquisition of the infection. An unvaccinated child who has never been exposed to the disease-causing antigen is reacting for the first time. The immune response is usually and least expensively assessed by measurement of humoral (antibody) immunity, but this may be blunted in an HIV-infected person because of the damage HIV has done to the immune system.

**Immunization Schedule for HIV-Infected Children**

The Expanded Program on Immunizations (EPI) of the World Health Organization (WHO), in collaboration with UNICEF, recommends a narrow and accelerated immunization schedule for HIV-infected children and women of childbearing age (see Table 1). The immunization schedule may vary slightly in each country. The EPI schedule takes into consideration limited resources, barriers in the healthcare delivery system, and the urgency to better control morbidity and mortality related to infectious diseases.

**Specific Immunizations**

**Bacille Calmette-Guérin (BCG) Vaccine**

BCG is the most widely used vaccine in the world and is the only vaccine available for prevention of Mycobacterium tuberculosis. Use of the vaccine in immunocompromised children has triggered concerns of disseminated BCG infection. Many authorities believe that the possible complications of receiving the BCG vaccine, such as lymphadenitis, fistula formation at the site of injection, osteomyelitis, and disseminated disease, outweigh the benefits. Where the risk of tuberculosis is high, the WHO recommends BCG at birth or as soon as possible thereafter, in accordance with standard policies for immunization of non-HIV-infected children.

The recommended dose of BCG vaccine is 0.5ml per dose and should be administered via the intradermal route. The best sites for injection are dorsogluteal and the lateral aspect of the upper arm. Attention should be given to how high on the upper arm one should give the injection. The higher the location, the greater the tendency for a scar to form. The best location is in the lower deltoid muscle. A papule with redness appears at the site of injection within two to three weeks. This improves slowly and is followed by

**Table 1: WHO/UNICEF Recommendations for the Immunization of HIV-Infected Children and Women of Childbearing Age**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Asymptomatic HIV Infection</th>
<th>Symptomatic HIV Infection</th>
<th>Optimal Timing of Immunization</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCG</td>
<td>Yes</td>
<td>No</td>
<td>Birth</td>
</tr>
<tr>
<td>DPT</td>
<td>Yes</td>
<td>Yes</td>
<td>6, 10, 14 weeks</td>
</tr>
<tr>
<td>OPV*</td>
<td>Yes</td>
<td>Yes</td>
<td>0, 6, 10, 14 weeks</td>
</tr>
<tr>
<td>Measles</td>
<td>Yes</td>
<td>Yes</td>
<td>6 and 9 months</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Yes</td>
<td>Yes</td>
<td>Same as uninfected child: flexible 3- or 4-shot series starting at birth or 6 weeks</td>
</tr>
<tr>
<td>Yellow fever</td>
<td>Yes</td>
<td>No**</td>
<td>9 months</td>
</tr>
<tr>
<td>Tetanus toxoid</td>
<td>Yes</td>
<td>Yes</td>
<td>5 doses***</td>
</tr>
</tbody>
</table>

* IPV can be used as an alternative for children with symptomatic HIV infection

** Pending further studies

*** 5 doses of tetanus toxoid (TT) for women of childbearing age as for non-HIV-infected persons. TT: as early as possible in pregnancy; TT: 4 weeks after TT; TT: 6 months after TT; TT: 2 years after TT or during subsequent pregnancy; TT: 1 year after TT or during subsequent pregnancy.
a local lesion that may ulcerate six to eight weeks later. This lesion will heal and leave a small flat scar three to six months after vaccination. Prolonged local reactions are common after receipt of the vaccine. The reactions usually consist of localized redness and swelling, which can last a few weeks to several months. Poor injection technique, such as giving the injection too deep, can cause the formation of large pus-filled abscesses. Another short-term complication that may occur is suppurative lymphadenitis. Serious, long-term complications after vaccination are rare. The most serious adverse event related to BCG vaccination is the development of disseminated BCG infection. This can occur anywhere from four months to two years after vaccination.

**Diphtheria, Pertussis, Tetanus (DPT)**

The DPT vaccine protects against these diseases. The vaccine is not contraindicated for HIV-infected children or their close contacts. The vaccine is administered intramuscularly, usually in the anterolateral aspect of the thigh in infants and younger children and in the deltoid muscle in older children.

Mild side effects after receipt of DPT include low-grade fever, mild irritability, and tenderness at the site of the injection. These side effects are usually due to the pertussis portion of the vaccine. Severe complications that may occur include fever; high-pitched, uncontrollable crying; febrile seizures; and shock. To help minimize post-immunization fever and muscle soreness, acetaminophen or ibuprofen may be used every four to six hours for the first 24 hours after the vaccine is administered.

Parents should be instructed to return to the clinic if the child has a fever of more than 39.5 degrees C, a seizure, or difficulty breathing or cries inconsolably for more than three hours at a time.

**Polio Vaccine**

Polio has been eradicated in much of the world. The risk of an adverse event after receipt of oral polio vaccine (OPV) by HIV-infected children is low, but there have been cases of children with primary immunodeficiency syndromes (problems with which they were born) who developed vaccine-associated paralytic polio after receiving OPV. Inactivated polio vaccine (IPV) is considered the safer choice and is used for HIV-infected children and household contacts in countries where it is available. The U.S. Centers for Disease Control and Prevention (CDC) endorses the use of IPV for all children. The WHO continues to recommend OPV in asymptomatic HIV-infected children, with very few reported cases of adverse events. OPV is administered by mouth. IPV is administered via subcutaneous injection in the upper arm or thigh. There are no immediate side effects secondary to OPV administration. Vaccine-associated paralytic polio usually occurs within two months after immunization, but the risk is low, estimated at 1:7.8 million doses. Very few adverse events secondary to receiving IPV have been reported.

**Measles Vaccine**

In some developing countries, measles continues to cause serious illness and death in children under the age of 5 years. HIV-infected children have an increased risk of developing severe complications when infected with measles. A review of reported cases of measles infections in children with HIV indicates a 40 percent death rate. This risk is serious enough for the WHO to recommend immunization of HIV-infected children with measles vaccine at 6 months of age, followed by a second dose at 9 months of age.

Recommendations for HIV-infected children in the United States are to immunize against measles at 12-15 months of age, and again at 4-6 years of age, unless the youngsters have a CD4+ lymphocyte percentage of less than 15 percent or an absolute CD4+ lymphocyte count that is lower than normal for age. Children in these categories have severely impaired immune systems, and public health officials recommend that they not receive the vaccine. Because there are fewer cases of measles in the United States than in the developing world, the risk of acquiring the disease is...
lower, making this recommendation practical in this small group of children. In many other parts of the world, however, the accelerated dosage schedule is recommended, because HIV progressively does harm to the immune system, and antibody responses to the vaccine are less likely to be effective as the disease progresses. Close contacts of children with HIV infection also should be vaccinated at routine intervals unless they are HIV-infected and have severe immunosuppression.

Severely immunocompromised and symptomatic patients with HIV should receive measles serum immune globulin if exposed to measles, regardless of vaccine status. Previously immunized HIV-infected children and adolescents have developed wild type measles.

The measles vaccine is administered as a subcutaneous injection in the anterolateral region of the thigh or upper arm. Minor adverse reactions that may occur include low-grade fever one to two weeks after the injection, cough, nasal drainage, rash, redness, and swelling and tenderness at the injection site. Serious adverse events include seizures, dyspnea, and severe skin rash. Parents should be instructed to call their health care provider if the child has seizures, rash, or fever greater than 39.5 degrees C.

**Hepatitis B Vaccine**

Despite a short history of immunizing HIV-infected children with hepatitis B vaccine, the WHO recommends the immunization for children and adults infected with HIV. No adverse events associated with hepatitis vaccination of HIV-infected adults and children have been reported. However, in HIV-infected children, the antibody response mounted against hepatitis B does not appear to be long-lasting.

The hepatitis vaccine should be administered intramuscularly, avoiding the dorsogluteal muscle because of possible reduced immunological response. Anaphylaxis is a very rare but serious side effect. Anaphylaxis is a severe allergic reaction with symptoms that include swelling of the mouth, difficulty breathing, low blood pressure, and sometimes shock. But generally the vaccine is well tolerated, with very few reports of adverse events. If adverse events do occur, they are usually mild, consisting of irritability and soreness at the injection site. These symptoms usually appear within 24 hours of receiving the vaccine and resolve within one or two days.

**Yellow Fever Vaccine**

Besides mosquito control, the yellow fever vaccine is the only measure available to prevent yellow fever. Immunity occurs within one week in 95 percent of people vaccinated, and immunity lasts for at least 10 years. The EPI of the WHO recommends immunization at 9 months of age or older for asymptomatic HIV-infected children who are living in or visiting endemic areas. A booster vaccine should be administered every 10 years thereafter.

The vaccine is a live attenuated vaccine that should be administered subcutaneously in a dose of 0.5 ml. Adverse events related to immunization against yellow fever are very rare.

**Varicella or Chickenpox Vaccine**

In HIV-infected patients, chickenpox or varicella zoster virus can cause serious complications, including pneumonia and encephalitis. The CDC recommends that the varicella live attenuated vaccine be administered to HIV-infected children who are asymptomatic or mildly symptomatic in CDC Class N1 or A1 and have age-specific CD4+ lymphocyte percentages of at least 25 percent. Siblings of HIV-infected children should also be immunized with varicella vaccine.

The varicella vaccine is administered subcutaneously in the anterolateral region of the thigh or upper arm. Minor adverse events associated with varicella vaccine include fever; tenderness, redness or swelling at the injection site; and a mild maculopapular or varicelliform rash at the injection site or elsewhere on the body. Serious adverse events that may occur include severe nausea and vomiting, loss of consciousness, dyspnea, and hives.
HIV-infected children who have not received the vaccine and who are exposed to chickenpox (varicella) should receive varicella zoster immune globulin (VZIG) within the first few days after exposure. Acyclovir is beneficial in the treatment of varicella infection.

**Influenza Vaccine**

Influenza can cause severe infections and complications in HIV-infected children. Studies have shown that HIV-infected adults with influenza have a longer, more severe disease course and are more likely to suffer from lower levels of oxygen in the blood than healthy adults. In the United States, influenza vaccination is indicated for all HIV-infected children ages 6 months or older as well as their close contacts. The vaccine should be administered in the fall and repeated annually because of the vaccine’s low immunogenicity and changes in the type of influenza causing infection from year to year.

The influenza vaccine is administered as an intramuscular injection in the anterolateral upper side of the thigh in young children and the deltoid muscle in older children. A child receiving the influenza vaccine for the first time between the ages of 6 months and 8 years should receive a series of two shots separated by one month. Most adverse events are minor; they include fever, malaise, and soreness or redness at the injection site.

**Pneumococcal Vaccine**

Pneumococcus is the most common cause of bacterial invasive infections in children with HIV, causing frequent episodes of otitis media, sinusitis, and pneumonia. Preventing the disease is increasingly important, because research indicates that some forms of the bacteria are resistant to penicillin, cephalosporins, and other antibiotics, and their numbers are increasing. The pneumococcal conjugate vaccine (PCV7) and the pneumococcal polysaccharide vaccine (PPV23) are well tolerated in children with HIV. In the United States, PCV7 is recommended at 2, 4, 6, and 12-15 months of age, followed by PPV23 at 24 months of age and again three to five years later. The pneumococcal vaccine is administered as an intramuscular or subcutaneous injection in the upper anterior thigh or upper arm. Approximately 50 percent of people who receive the vaccine develop mild adverse events, such as tenderness and redness at the injection site. Only about 1 percent of pneumococcal-vaccine recipients develop fever, muscle pain, or severe local reactions.

**Immunoglobulin**

Intravenous immunoglobulin (IVIG) has been used as protection against bacterial infections, especially pneumococcal infections, for children infected with HIV. It is now no longer indicated. Studies have shown that HIV-infected children receiving *P. carinii* pneumonia prophylaxis with trimethoprim-sulfamethoxazole do not derive additional benefit from IVIG. Hyperimmune globulins are available that may be used for specific indications. The use of hyperimmune globulins is recommended for children who have been exposed to particular antigens to prevent an infection or shorten the course of the disease. For example, VZIG is recommended for children who have been exposed to varicella. Other hyperimmune products include hepatitis B immunoglobulin (HBIG), rabies immunoglobulin (RIG), tetanus immunoglobulin (TIG), cytomegalovirus intravenous immunoglobulin (CMV-IVIG), and respiratory syncytial virus intravenous immunoglobulin (RSV-IVIG).
Review Questions

1. Review the importance of immunizations for children infected with HIV/AIDS.

2. Describe the steps involved in the immune response to disease.

3. What is BCG used for, and why is it so important for vaccination in developing countries?

4. Why is measles a concern in children infected with HIV/AIDS?

5. What are the concerns related to administering OPV rather than IPV to immunocompromised children?

6. What are the side effects related to each of the immunizations given to HIV-infected children?

7. What is the accelerated immunization schedule for HIV-infected children?

Exam Questions

1. According to the EPI schedule for immunizations, which vaccines should be administered to a newborn at birth?
   a. DPT, OPV, hepatitis B
   b. BCG, OPV, hepatitis B
   c. Measles, OPV
   d. BCG, measles

2. A 6-week-old infant was immunized yesterday with his second DPT vaccination. His mother brings him back to the clinic with a high fever (>39.5 degrees C) and says he cried all night. He continues to breastfeed every three hours. What should you do?
   a. Administer hydration fluids
   b. Admit to the hospital for observation
   c. Give acetaminophen every 4 to 6 hours
   d. Discontinue breastfeeding for 24 hours

3. When should the first measles vaccine be administered to an HIV-infected child living in an area with a high prevalence of measles?
   a. At birth
   b. 6 months of age
   c. 5 years of age
   d. 2 years of age

4. You are about to administer the measles vaccine to a young child. How and where should you give the vaccine?
   a. Subcutaneous injection in the anterolateral region of the thigh
   b. Intramuscular injection in the deltoid muscle
   c. By mouth
   d. Intramuscular injection in the ventrogluteal region of the buttock

5. What concern exists for vaccination with OPV?
   a. Seizures
   b. Paralysis
   c. Bleeding
   d. Blindness
Case Study #1

A mother brings her 9-month-old asymptomatic HIV-positive son to the clinic for his first well-baby check. Which immunizations would you administer at this time?

**Question:** Which immunizations would you administer at this time?

a. DPT, OPV, hepatitis B  
b. DPT, OPV, BCG, tetanus toxoid  
d. Measles, hepatitis B.

**Answer:** c. Like children without HIV, children who are HIV-positive should receive immunizations to prevent disease. Measles continues to cause serious illness and death in young children in many developing countries. An HIV-infected child’s risk of developing complications from measles is so high that the WHO recommends measles immunization of HIV-infected children.

The child’s risk of an adverse event related to OPV is low; the WHO continues to recommend OPV for HIV-infected children.

The WHO recommends hepatitis B vaccine for people infected with HIV. There have been no reported adverse events associated with immunizing an HIV-positive person with hepatitis vaccine.

BCG and yellow fever vaccine should be administered to asymptomatic HIV-positive children in regions where M. tuberculosis and yellow fever are widespread.

**Question:** The mother brings her baby back to the clinic the next day and says he was irritable all night and had a fever. You take the baby’s temperature; it is 37 degrees C. What should you do for the mother and the baby?

a. Tell the mother her baby is having a life-threatening reaction to the immunizations and needs to be admitted to the hospital.  
b. Educate the mother about mild and serious side effects associated with administration of some immunizations.  
c. Tell the mother that her baby’s symptoms should resolve within the next 24 hours but that she should call if they persist.  
d. b and c

**Answer:** d. Caregivers should be educated at the time of immunization about the possible side effects associated with the immunizations being administered. Most mild adverse events, such as muscle soreness and low-grade fever, appear within 24 hours of receiving a vaccine and resolve within one or two days. Acetaminophen or ibuprofen may be used every four to six hours for the first 24 hours after vaccination to help minimize post-immunization fever and muscle soreness.

Case Study #2

A 25-year-old HIV-positive woman arrives in your clinic for a routine visit. You notice that she is extremely thin. She is barefoot and says she walks barefoot several kilometers daily. In assessing her immunization status, which immunization would be your highest priority?

**Question:** In assessing her immunization status, which immunization would be your highest priority?

a. Measles  
b. BCG  
c. Tetanus toxoid  
d. None. She is an adult and no longer needs immunizations.
**Answer:** c. Tetanus toxoid should be administered to women of childbearing age every 10 years. Other immunizations are not recommended at this time. This woman probably received the immunizations at a younger age or contracted the disease at some point in her life and developed antibodies, allowing her immune system to respond from memory when exposed to a particular antigen.

**References**

OPPORTUNISTIC INFECTIONS

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Objectives

The purposes of this module are to:
1. Define opportunistic infections in people with HIV/AIDS.
2. Describe primary prophylaxis to prevent opportunistic infections in people with HIV/AIDS.
3. Evaluate the clinical manifestations of bacterial, viral, parasitic, and fungal opportunistic infections in people with HIV/AIDS.
4. Describe the treatment for bacterial, viral, parasitic, and fungal opportunistic infections in people with HIV/AIDS.
5. Review specific interventions that can decrease the development of opportunistic infections in people with HIV/AIDS.

Key Points

1. An opportunistic infection is caused by organisms that would not produce significant disease in a person with a well-functioning immune system.
2. People with HIV/AIDS are susceptible to opportunistic infections because their immune systems have been suppressed and are not capable of fighting disease.
3. People with HIV/AIDS may have opportunistic infections at diagnosis.
4. Primary prophylaxis or preventive treatment is used to prevent opportunistic infections in people with HIV/AIDS.
5. Viral infections found in people with HIV/AIDS include cytomegalovirus, varicella zoster (shingles), herpes simplex, hepatitis, and Epstein-Barr virus.
6. Pneumocystis jiroveci can cause severe pneumonia in people with HIV/AIDS.
7. Prophylaxis for Pneumocystis jiroveci is recommended for people with HIV/AIDS.
8. Candida albicans is the most common fungal infection diagnosed in HIV-infected people.
9. Education regarding appropriate preparation of food and good hygiene principles is essential to prevent serious opportunistic infections.

Overview

Many people living with HIV/AIDS acquire diseases that also affect otherwise healthy people. In such cases, HIV-infected patients may have a more severe disease course than uninfected people or may develop symptoms that uninfected people do not. However, HIV-infected people are also susceptible to opportunistic infections (OIs), which are infections caused by organisms that in a normal host would not cause significant disease. Both types of infection will be discussed in this module. The most common opportunistic infections vary depending on geographic
location. This module will give a broad overview of the concepts of preventing OIs and will discuss the most commonly diagnosed diseases worldwide. The module will cover specific diseases, how to recognize them, and which medicines are recommended to treat them. Treatment recommendations are based on available information and research. Not every recommendation will be feasible in every setting. Each country and health department will need to decide which treatments are appropriate in a particular area.

People with HIV/AIDS are susceptible to opportunistic infections because of the way HIV/AIDS suppresses the immune system. Many people do not know they have HIV until the first time they have an OI. When counseling patients with HIV, it is important to emphasize ways in which they can avoid OIs. Easy ways to avoid some of these infections are through general good hygiene, including good washing of food and hands.

People with HIV need to be especially careful about how they prepare food. Meats and poultry should be cooked thoroughly. Fruits and vegetables should be washed well. Water should be taken from the cleanest source available. If clean water is not available, water should be boiled before drinking. Infections can also be passed from person to person and through contact with fecal material. Immunocompromised people should avoid contact with ill persons and human and animal feces. These measures can help prevent a person from getting a serious infection.

Primary and Secondary Prophylaxis

Oftentimes people who are known to be HIV-infected are given medicines to try to prevent them from developing an opportunistic infection. This is known as primary prophylaxis. The appropriate time to begin prophylaxis depends on the age of the patient, which infection is being prevented, and what laboratory support and medications are available in a particular area. In the United States, the patient’s CD4+ lymphocyte count helps to determine when to begin primary prophylaxis. For example, when CD4+ lymphocyte counts are less than 200 cells/ul or total lymphocyte counts are less than 1200 cells/ul, adults begin taking trimethoprim-sulfamethoxazole (TMP-SMX) to prevent *Pneumocystis jiroveci* pneumonia (PCP) as well as other diseases, such as toxoplasmosis and bacterial infections. When a person with AIDS dies, the cause of death is most often an opportunistic infection. Primary prophylaxis is a way to help patients lead longer, healthier lives.

After HIV-infected patients have been treated for an opportunistic illness, they should stay on a lower dose of the medicine for the rest of their lives to prevent them from experiencing a relapse. This is known as secondary prophylaxis. Many of the medicines used for prophylaxis have side effects. If a patient is going to be taking prophylactic medications for a long time, it is important to assess for side effects each time the patient is examined. This applies regardless of whether a patient is receiving primary or secondary prophylaxis.

Bacterial Infections

**Streptococcus Pneumoniae**

One of the most common serious bacterial infections is *Streptococcus pneumoniae*, which causes pneumonia, otitis media, septicemia, and other invasive illnesses. All patients with HIV who are more than 2 years old should be given the 23-valent-polysaccharide vaccine for pneumococcus. A new heptavalent conjugate vaccine for pneumococcus is recommended for children as young as 2 months of age.

**Syphilis**

*Treponema pallidum* is the anaerobic bacterium responsible for syphilis. Syphilis is not an opportunistic infection in a strict sense, but HIV and syphilis co-infection is common. In the United States, a meta-analysis showed that the median HIV seroprevalence among persons infected with syphilis was 15.7 percent.\(^1\) There also are indications that HIV-1 appears to alter the diagnosis, natural history,
management, and outcome of syphilis infections. *Treponema pallidum* can be transmitted from mother to child at any stage of pregnancy or delivery.

*Primary syphilis* ordinarily presents as a single painless nodule at the site of inoculation or contact that ulcerates into a chancre. Such ulcerations might facilitate transmission of HIV infection between partners. In an HIV-infected person, multiple or atypical chancres can occur, and primary lesions may be absent or missed. Asymptomatic primary syphilis occurs at a higher rate in HIV-infected patients.1

*Secondary syphilis* occurs two to eight weeks after primary inoculation. Manifestations involve all organ systems. Skin lesions (macular, maculopapular, pustular, or condyloma lata in moist or intertriginous areas) usually begin on the trunk and spread peripherally. Characteristically they are found on the palms and soles and are accompanied by generalized lymphadenopathy and constitutional symptoms (fever, malaise, anorexia, arthralgias, headache). Secondary syphilis can be difficult to distinguish from primary HIV infection. HIV infection can cause more rapid progression of syphilis.2

*Late syphilis* includes neurosyphilis, cardiovascular syphilis, and gummatous syphilis. Neurosyphilis can have a more rapid progression in HIV-infected patients. Although in general neurosyphilis manifests similarly in HIV-infected and HIV-uninfected individuals, some studies have shown that concomitant uveitis and meningitis may be more common in HIV-infected persons with syphilis.3

*Congenital syphilis* has been found in 60 percent to 100 percent of infants born to mothers who are untreated or inadequately treated for primary or secondary syphilis. Infants born to HIV-infected women have a higher rate of congenital syphilis than the general population.1 Co-infection may also increase the rate of perinatal HIV transmission. Clinical manifestations may be asymptomatic. Other manifestations are classified as either early or late manifestations. Early manifestations include hepatosplenomegaly, jaundice, mucocutaneous lesions, skin rash, nasal discharge (“snuffles”), pseudoparalysis of an extremity, anemia, thrombocytopenia, and osteochondritis. Late manifestations are defined as occurring after 2 years of age and may involve the central nervous system (CNS), bones, teeth, eyes, and skin.1

The diagnosis of syphilis is generally made either with tests that detect the organism directly (e.g., darkfield microscopy or direct fluorescent antibody to *Treponema pallidum* (DFA-TP)) or with serology that detects serum antibodies against the organism (e.g., FTA-ABS and TP-TA) or non-treponemal antibodies generated during infection (e.g., VDRL and RPR). However, there is a potential for false-negative serology.

Treatment of syphilis is the same for patients infected or uninfected with HIV, i.e., a penicillin-based regimen with adequate coverage for neurosyphilis. A pregnant woman infected with syphilis must be treated 30 or more days before delivery in order to effectively prevent perinatal transmission. Careful follow-up is required in all cases, because relapse is more likely in HIV-positive patients.2

**Tuberculosis (TB)**

*Mycobacterium tuberculosis* is not an opportunistic infection, but it is the most common cause of death of HIV-infected people worldwide. HIV attacks T lymphocyte cells, the body’s main defense against TB. Hence patients with HIV are more susceptible to TB infection. As the HIV epidemic grows, transmission of TB becomes harder to control. Please refer to the chapter on tuberculosis for details regarding the diagnosis and management of HIV and TB co-infections.

**Preventive Therapy:** Preventive therapy against TB includes one or more anti-TB drugs given to HIV-infected patients who have a latent infection with *M. tuberculosis* to prevent progression to active disease. Before a patient is considered for preventive therapy, active disease must be excluded. In 1998, the World Health Organization (WHO) and UNAIDS developed...
recommendations for preventive therapy. Preventive therapy is recommended in areas that have established HIV-care and TB-control programs. In addition, the resources must be available to:

- Distinguish active from latent tuberculosis.
- Ensure appropriate monitoring and follow-up.
- Ensure a consistent supply of medication.

**Figure 1. CMV Retinitis**

Fundoscopic examination of a 16-year-old girl with HIV infection and cytomegalovirus retinitis. There are extensive areas of hemorrhage, with white retinal exudates. Children with CMV retinitis usually present with painless visual impairment. (Image courtesy of Dr. David Coats, Houston, Texas)

Preventive therapy is recommended for HIV-infected patients with a positive Mantoux skin test who do not have active TB (i.e., have a normal chest radiograph).

In areas where skin testing is not feasible, preventive therapy should be considered for the following high-risk patients if they have HIV:

- Persons living in populations with a high prevalence (more than 30 percent) of TB infection
- Health care workers
- Household contacts of TB patients
- Prisoners
- Miners

Preventive therapy with isoniazid (INH) is recommended. The dose should be 5 mg/kg (maximum 300 mg) by mouth daily for at least six months, with clinical monitoring for adverse effects and active TB.

**Mycobacterium Avium Complex (MAC)**

*Mycobacterium avium* complex is found all over the world. Symptoms of disseminated MAC are non-

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<th>Age</th>
<th>Treatment</th>
<th>Prophylaxis</th>
<th>Alternative Prophylaxis</th>
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<tbody>
<tr>
<td>Children (0-12 years)</td>
<td>Clarithromycin (7.5 mg/kg/dose twice daily) or Azithromycin (5-20 mg/kg/dose once daily) plus Ethambutal (15 mg/kg/day)</td>
<td>Clarithromycin 7.5 mg/kg twice daily</td>
<td>Azithromycin 20 mg/kg by mouth weekly or rifabutin (&gt;6 y/o) 300 mg daily</td>
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<tr>
<td>Adolescents and adults (&gt;12 years)</td>
<td>Clarithromycin (500 mg twice daily) or Azithromycin (600 mg twice daily) plus Ethambutal (15 mg/kg/day) for at least 12 months</td>
<td>Clarithromycin 500 mg twice daily</td>
<td>Azithromycin 1.2 g by mouth weekly or rifabutin 300 mg daily</td>
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*Dosage for medications given by mouth*

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<th>Age</th>
<th>Treatment</th>
<th>Prophylaxis</th>
<th>Alternative Prophylaxis</th>
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<tr>
<td>Children (0-12 years)</td>
<td>Ganciclovir 5 mg/kg IV twice daily for 14 days</td>
<td>Ganciclovir 5 mg/kg IV once daily</td>
<td>Ganciclovir 6 mg/kg IV once daily for 5 days per week</td>
</tr>
<tr>
<td>Adolescents and adults (&gt;12 years)</td>
<td>Ganciclovir 5 mg/kg IV twice daily OR Valganciclovir 900 mg orally twice daily for 21 days</td>
<td>Ganciclovir 5 mg/kg IV once daily</td>
<td>Ganciclovir 1000 mg orally 3 times daily or Valganciclovir 900 mg orally once daily</td>
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specific and include weight loss or failure to thrive (in children), fever, abdominal pain, diarrhea, and lymphadenopathy. MAC can be grown in culture, but it grows slowly. Acid-fast staining, if available, will be positive. Treatment for MAC requires at minimum a two-drug regimen of clarithromycin and ethambutol.

The age and CD4+ lymphocyte count of the patient are used as indicators to start primary prophylaxis. In adults, prophylaxis is recommended once the CD4+ lymphocyte count is less than 100 cells/ul. In children, CD4+ lymphocyte cell counts vary with age, but if the counts are below 15 percent for the child’s age group, prophylaxis is recommended.

Recent studies suggest that once patients receive highly active antiretroviral therapy (HAART) and their CD4+ lymphocyte cell counts increase to more than 100 cells/uL for three months, primary prophylaxis may be stopped.1,2 Secondary prophylaxis should be stopped only if the patient has completed at least 12 months of therapy and has maintained a CD4+ lymphocyte cell count of more than 100 cells/uL for six months. These recommendations apply only to adults and adolescents, not to children. See Table 1 for treatment and prophylaxis guidelines.

**Viral Infections**

**Cytomegalovirus (CMV)**

Cytomegalovirus is a common viral infection worldwide. Most people with CMV develop few or no symptoms. However, a fetus exposed to CMV can suffer severe consequences, including mental retardation and even death. In patients with HIV/AIDS, the most common complication of CMV is retinitis (see Figure 1). CMV can also cause hepatitis, diarrhea and encephalitis. CMV retinitis is most commonly seen in patients with CD4+ lymphocyte counts of less than 50 cells/uL. This can lead to blindness if untreated. Patients should be advised to report to the clinic if they notice changes in their vision, including blurry vision or “floaters.” Many patients are asymptomatic. If possible, patients should have regular fundoscopic examinations (visualizing the deep structures of the eye) to check for changes and if necessary should be referred to an eye specialist. Ganciclovir is the antiviral medication recommended for treating CMV. Oral Valganciclovir has recently been approved for treatment of CMV retinitis as well. See Table 2 for the dosing schedule for treatment and post-treatment prophylaxis (also referred to as maintenance therapy). The main side effect of Ganciclovir is neutropenia. Other side effects include anemia, thrombocytopenia, and occasionally renal insufficiency.

Recent studies in adults and adolescents suggest that CMV secondary prophylaxis can be discontinued in patients who have maintained a CD4+ lymphocyte cell count of more than 100-150 cells/uL in response to HAART for at least six months. If prophylaxis is discontinued, regular ophthalmologic examinations should be maintained.

**Varicella Zoster**

Varicella zoster is the virus that causes chickenpox and shingles in children and adults. Infection with this virus can be much more serious in a person with HIV/AIDS. Primary varicella is spread by aerosolized viral particles. A person is contagious for 24-48 hours before a vesicular rash (raised, fluid-filled lesions) is observed and remains contagious until all of the lesions are crusted over.

A vaccine is available to protect patients against this virus. In May 1999, the U.S. Centers for Disease Control and Prevention (CDC) updated its varicella vaccine recommendations for HIV-infected children. The new recommendations state that if an HIV-infected child has an age-specific CD4+ lymphocyte percentage greater than 25 percent, the vaccine may be administered. HIV-infected children require two doses of the varicella vaccine, separated by at least three months. If an immunocompromised person comes into contact with someone with varicella, he or she can be protected with varicella zoster immune globulin. Acyclovir, an antiviral medication, decreases the duration of disease. In children, acyclovir can be
given intravenously or orally. The pediatric oral dose is 20mg/kg/dose every six hours for five days. The adult dose is 800 mg four times a day for five to seven days. Acyclovir can cause pancytopenia (a decrease in all forms of blood cells), particularly when given in conjunction with ZDV (AZT/Zidovudine). It is important to increase the intake of fluids while on acyclovir to avoid crystalluria (the presence of crystals in the urine as a symptom of irritation) and possible acute renal failure.

Reactivation can cause painful grouped vesicles usually isolated to a single dermatome months or years after primary infection. This is referred to as zoster or shingles. Treatment with acyclovir can lessen the severity.

**Herpes Simplex Virus (HSV)**

HSV 1 and HSV 2 infections also can be severe in patients with HIV/AIDS. HSV can cause ulcers around the mouth, known as cold sores. HSV can cause encephalitis as well. Acute disease usually resolves spontaneously, but treatment for pain associated with the lesions may help the patient feel more comfortable. Genital herpes is a sexually transmitted disease (STD). Using condoms can decrease a patient’s risk of contracting HSV. Oral or genital herpes can be treated with acyclovir in severe cases. Patients with HSV and HIV/AIDS often have severe recurrent attacks. For these patients, prophylaxis with daily acyclovir can help. The pediatric prophylactic dose is 10 mg/kg/dose twice daily orally. The adult prophylactic dose is 200 mg three times a day or 400 mg twice a day orally.

**Epstein-Barr Virus (EBV)**

EBV usually causes minor symptoms, much like the common cold or “strep” throat. However, EBV infection of HIV-infected children can be associated with a pulmonary disease known as lymphoid interstitial pneumonia (LIP). LIP occurs in 20 percent to 30 percent of HIV-infected children. It usually occurs in children over 2 years of age. The diagnosis of LIP is usually made based on clinical criteria, as definitive diagnosis requires lung biopsy.

Patients with LIP may initially be asymptomatic. As the disease progresses, they may present with generalized lymphadenopathy, hepatomegaly, and/or digital clubbing. Children may also have non-tender, bilateral enlargement of the parotid glands. Respiratory difficulties may become evident because of secondary bacterial infections. In areas where tuberculosis is endemic, TB must be ruled out prior to a diagnosis of LIP. The chest radiograph associated with LIP will show bilateral diffuse reticulo-nodular infiltrations and mediastinal lymphadenopathy, which may be confused with TB. Patients often respond well to steroid therapy. In addition, antiretroviral treatment can decrease the complications associated with LIP.

EBV also has been associated with Burkett’s lymphoma.

**Viral Associated Malignancies**

**Kaposi’s Sarcoma**

Kaposi’s sarcoma is primarily a skin malignancy, but it can also involve internal organs such as lungs, liver, and spleen. It is associated with the human herpes virus 8 (HHV-8). Although Kaposi’s sarcoma has been observed in immunocompetent children in Africa, it is more common in children and adults with HIV/AIDS. In HIV-infected children, the median age of onset of Kaposi’s sarcoma is 33 months. Kaposi’s sarcoma associated with HIV/AIDS can present in two forms, mucocutaneous and lymphadenopathic. The mucocutaneous form may be an early type of the lymphadenopathic form. Cutaneous lesions characterizing Kaposi’s sarcoma can be flat, raised, or nodular and usually are purple or brown. They can occur anywhere on the body, including the palms of the hands, as well as inside the mouth. The most effective treatment for Kaposi’s sarcoma is antiretroviral therapy. Chemotherapy is often used, particularly when viscera are involved. Limited research also shows that ganciclovir may be associated with reduced disease progression or with lesion regression. Prognosis for Kaposi’s sarcoma seems to be related to the patient’s overall immune status and the organ systems that are involved.
HHV-8 can be transmitted through sexual intercourse, blood via needle sharing and possibly deep kissing. HIV-infected patients should be counseled to use condoms, not to share needles, and to avoid deep kissing with people infected with HHV-8 or at high risk of infection.

**Human Papilloma Virus (HPV)**
HPV infects cutaneous and mucosal squamous epithelium. It can cause general, anal, conjunctival, nasal, oral, and laryngeal warts. In young children, general warts may be a sign of sexual abuse. Men who have sex with men (MSM) have a high prevalence of anal HPV infection.

HPV infection is commonly associated with cervical cancer. Women who are immunocompromised have a higher rate of cervical cancer, as well as a higher rate of recurrence of cervical cancer after treatment. Use of condoms can reduce the risk of transmission of STDs and may reduce the risk of transmitting HPV. Women with HIV should have a Papanicolaou (Pap) smear every six months for the first year after diagnosis of HIV. If these smears are negative, women with no other risk factors for cervical cancer should have a Pap smear once a year.

Multiple treatments for HPV-associated skin and external lesions are available. Specific treatments must be catered to the circumstances of the patient.

**JC Virus**
JC virus is the virus believed to be associated with progressive multifocal leukoencephalopathy, a disease characterized by altered mental status, limb weakness, or both. Patients may also exhibit personality changes with frequent emotional outbursts. This disease has a variable course. It is rarely seen in children. Definitive diagnosis is confirmed by brain biopsy. On an image from computerized tomography (CT), one can see diminished density or demyelination (deterioration of the covering of the nerve). There is no treatment for this illness, but strong antiretroviral medications can sometimes improve the symptoms.

**Parasitic Infections**

**Pneumocystis Jiroveci**
*Pneumocystis jiroveci* (formerly *pneumocystis carinii*) is an organism that does not cause illness in immunocompetent hosts. However, it can cause very severe pneumonia in patients with HIV/AIDS. This infection is prevalent worldwide. *Pneumocystis jiroveci* pneumonia (PCP) should be suspected in patients with tachypnea (increased rate of respiration), cough, and shortness of breath. Lung auscultation (sounds) may be normal, as rales and rhonchi may develop late in the clinical course. It is common for a patient to be hypoxic with a normal chest radiograph. The chest
radiograph may show bilateral interstitial infiltrates (Figures 2 and 3). Children can be very ill with this disease, and it is often the first AIDS-defining illness in a child. Definitive diagnosis requires identifying the organism, usually from a bronchoalveolar lavage (a washing that can retrieve cells or tissue from the lungs and the alveoli in them) or an induced sputum sample. PCP is best treated with trimethoprim-sulfamethoxazole (TMP-SMX).

Adult patients who have a CD4+ lymphocyte cell count below 200/uL or a total lymphocyte cell count below 1200 cells/uL or who have had oropharyngeal candidiasis (a fungal infection of the mouth and pharynx) should be started on preventive treatment. Children should receive prophylaxis if they 1) have an age-specific CD4+ lymphocyte cell percentage of less than 15 percent or 2) have ever had PCP or 3) have chronic oral candidiasis (thrush). Infants who are born to mothers known to be HIV-infected should begin PCP prophylaxis when they are 4-6 weeks of age and should remain on prophylaxis until they are 12 months old or until it can be determined definitively whether they are HIV-infected. If they are HIV-infected, their treatment should follow the guidelines for HIV-infected children.

Primary treatment of PCP includes TMP-SMX 15-20 mg TMP/kg/day divided every six to eight hours for 21 days, plus steroid therapy. Supplemental oxygen should be given if needed. The prophylaxis dose (see Table 3) for adults is TMP 160mg and SMX 800mg once a day orally for three consecutive days a week. As in adults, this may be given to children every day to protect against toxoplasmosis. If patients are unable to tolerate TMP-SMX, have G6PD deficiency (an enzyme disorder affecting red blood cells), are allergic to sulfa drugs, or experience side effects, dapsone may be used. The main side effect of TMP-SMX is rash. As with all sulfonamides, TMP-SMX can on rare occasions cause agranulocytosis (destruction of certain white blood cells), aplastic anemia (loss of bone-marrow production), other blood disorders, Stevens-Johnson syndrome (a severe allergic reaction characterized by breakdown of mucous membranes), and hepatic necrosis (death of liver cells). The dose of dapsone for adults is 100mg once a day every day. For children, the recommended dose is 2mg/kg daily, with a maximum dose of 100 mg/day.

Both primary and secondary prophylaxis can be discontinued in adults and adolescents who have maintained a CD4+ lymphocyte cell count of more than 200 cells/uL for at least three months. The discontinuation of prophylaxis in children has not been studied extensively but may be considered on a case-by-case basis.

**Cryptosporidium**

Cryptosporidium is a parasite that causes persistent diarrhea and cholecystitis (gall bladder inflammation) in immunocompromised patients. Cryptosporidium is

<table>
<thead>
<tr>
<th>Weight</th>
<th>Suspension: 40 mg TMP + 200mg SMX/5ml</th>
<th>Tablets (SS): 80 mg TMP/400mg SMX</th>
<th>Tablets (SS): 160 mg TMP/800mg SMX</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-4 kg</td>
<td>2.5 ml</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>5-8 kg</td>
<td>5 ml</td>
<td>1/2 tab</td>
<td>-</td>
</tr>
<tr>
<td>9-16 kg</td>
<td>10 ml</td>
<td>1 tab</td>
<td>1/2 tab</td>
</tr>
<tr>
<td>17-50 kg</td>
<td>20 ml</td>
<td>2 tabs</td>
<td>1 tab</td>
</tr>
<tr>
<td>&gt; 50 kg</td>
<td>20 ml</td>
<td>2 tabs</td>
<td>1 tab</td>
</tr>
</tbody>
</table>
spread by direct contact with infected adults, children in diapers or of the age to be in diapers, and infected animals. Food and water contaminated with feces can spread infection as well. People with HIV/AIDS should be very careful when coming in contact with human feces (e.g. changing diapers) or animal feces, as well as when working with the soil. Good handwashing and boiling water when advised are important for preventing infection.

Patients with cryptosporidiosis will have frequent, watery, voluminous stools. They also may experience abdominal cramping. If the biliary system (gall bladder and biliary ducts) is involved, they also may have nausea and right-upper-quadrant abdominal pain. Cryptosporidia in stool can be seen under a microscope with a modified acid-fast staining method. Nitazoxanide has been shown to be effective in the treatment of cryptosporidiosis in immunocompetent patients. Dosing for adults is 500mg by mouth twice daily for three days. Children ages 12-47 months should receive 100 mg by mouth twice daily for three days; children 4-11 years old should receive 200 mg by mouth twice daily for three days; and those ages 12 years and older should receive the adult dose. Studies have found that nitazoxanide was ineffective in HIV-infected children. Metronidazole and azithromycin have been used in the treatment of cryptosporidium with variable success.

Isospora Belli

*Isospora belli* spreads by the same routes of transmission as cryptosporidium and has the same symptoms. Isospora can be diagnosed on acid-fast stain of stool. TMP-SMX can be used to treat *Isospora*, but there is a 50 percent relapse rate among adults. Prophylaxis with TMP-SMX may be needed to prevent relapses. The dosing and side effects of TMP-SMX for *Isospora belli* are the same as for *Pneumocystis jiroveci* (see Table 3).

Malaria

Malaria is a disease caused by several species of *Plasmodium*, a parasite transmitted via mosquito bites. It is primarily found in tropical regions of the world. About 90 percent of malaria cases occur in sub-Saharan Africa. This poses significant problems, since HIV prevalence in the region is also very high; the two infections can have several harmful interactions.

Pregnant women with HIV infection are at increased risk of malaria. HIV increases the chances of placental malaria, which is associated with a greater risk of HIV transmission to the infant, low birth weight, and mortality. Some studies indicate that patients suffering from AIDS are at increased risk of symptomatic malaria. A study in Malawi suggests that malaria infection might increase HIV viral load.

Prevention is the mainstay of malaria reduction in many areas. One of the most effective prevention strategies is the use of insecticide-treated nets (ITN) over the bed. ITN use has been shown to decrease pediatric morbidity and mortality from malaria. Most nets need to be retreated with insecticide every six months. Wearing long sleeves and long pants can also prevent infection. So can remaining indoors at dawn and dusk, the times of highest transmission risk. Intermittent prophylaxis with medication for pregnant women and children is being studied. Finally, community efforts to eliminate or cover standing water can prevent mosquito breeding.

Proper treatment of malaria is imperative to minimize morbidity and mortality. It is important to realize that different regions of the world have different types of malaria, some of which can be drug-resistant. Treatment regimens for a particular setting depend on national guidelines. Examples of drugs used to treat malaria are chloroquine, quinine, primaquine, mefloquine, pyrimethamine-sulfadoxine, and atovaquone plus proguanil.

Toxoplasma Gondii

*Toxoplasma gondii* (*T. gondii*) is transmitted via raw or undercooked meat, particularly pork, lamb, and venison. It also can be transmitted via cat feces. Meat should be thoroughly cooked, and immunosuppressed
individuals should avoid contact with stray cats and cat feces. Good handwashing can prevent infection.

Toxoplasmosis in the immunocompromised host usually causes CNS disease, specifically brain abscesses. It is not uncommon for toxoplasmosis to become reactivated, causing repeated infections. Patients have focal neurologic deficits, including seizures, hemiparesis, hemiplegia, cerebellar tremor, cranial nerve palsies (e.g. unilateral facial droop), hemisensory loss, visual problems or blindness, personality changes, and cognitive disorders. Severe localized headache that does not respond to analgesics may be present. *T. gondii* infection is classically seen as multiple-ring enhancing lesions on a CT scan. Antibodies often can be detected in the blood or other body fluids (cerebral spinal fluid). This disease is much more common in adults than in children.

Toxoplasmosis is treated with pyrimethamine and sulfadiazine. Treatment for toxoplasmosis should continue for a minimum of four weeks after complete resolution of disease. See Table 4 for treatment and secondary prophylaxis guidelines. Folinic acid is usually also given during treatment because pyrimethamine inhibits folate metabolism. Primary prophylaxis is recommended with TMP-SMX daily for severely immuno-compromised patients (see Table 3 for dosing guidelines).

Patients who have experienced an increase in CD4+ lymphocyte cell count secondary to HAART to more than 200 cells/μL for three months may stop primary prophylaxis for toxoplasmosis. Secondary prophylaxis may be discontinued if a patient maintains a CD4+ cell count of more than 200 cells/μL for at least six months. These recommendations have not been extensively studied in children.

**Fungal Infections**

*Candida albicans*

*Candida albicans* is the most common fungal infection diagnosed in HIV-infected patients. Oral candidiasis (also called thrush) is particularly common. It is often one of the presenting signs of HIV infection in patients who do not have other reasons (e.g. recent antibiotic use) to have fungal disease. Patients have white or yellow plaques on the oropharyngeal mucosa and on the tongue. If esophageal infection is also present, the patient may complain of inability to swallow or retrosternal chest pain when swallowing. Infants may begin to feed and then stop after the first few swallows, arching their backs and turning their heads because of difficulty in swallowing. Patients who are critically ill, have been treated with long-term systemic antibiotics, or have an indwelling catheter (e.g. central venous access device) may develop systemic candidiasis or candidemia. Oral

<table>
<thead>
<tr>
<th>Age</th>
<th>Treatment</th>
<th>Secondary Prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Children (0-12 years)</strong></td>
<td>Pyrimethamine: 1-2 mg/kg/day orally for 2 days, then 1 mg/kg/day orally for 2 months, then 1 mg/kg/day orally 3 days/wk (maximum 50 mg) AND Sulfadiazine: 100 mg/kg oral loading dose, then 50 mg/kg twice daily by mouth AND Folinic acid: 5-10 mg orally or intramuscularly 3 times a week</td>
<td>Pyrimethamine: 1 mg/kg orally daily (maximum 25 mg) AND Sulfadiazine: 40 mg/kg/day orally 3 times a day AND Folinic acid: 5 mg orally every 3 days</td>
</tr>
<tr>
<td><strong>Adolescents and adults (&gt;12 years)</strong></td>
<td>Pyrimethamine: 200 mg orally in divided doses, then 50 mg orally daily AND Sulfadiazine: 2000 mg orally 3 times daily AND Folinic acid: 15 mg orally daily</td>
<td>Pyrimethamine: 25 mg orally daily AND Sulfadiazine: 1000 mg orally 3 times a day AND Folinic acid: 15 mg orally daily</td>
</tr>
</tbody>
</table>
Cryptococcosis

Cryptococcosis usually occurs in HIV-infected patients with severe immune suppression and most commonly causes cryptococcal meningitis. Mortality during the first six weeks after diagnosis can be as high as 20 percent. Clinical signs and symptoms of this infection can be very subtle. The most common clinical manifestation is indolent fever. Patients may have headache and altered mental status. These symptoms usually evolve over weeks or months. Meningismus (irritation of the brain and spinal cord without inflammation) as well as signs and symptoms of increased intracranial pressure may be present.

Diagnosis is made by India ink preparation of spinal fluid or by testing spinal fluid and/or serum for cryptococcal antigen. Cryptococcal meningitis is often associated with a high opening pressure on spinal tap. Treatment is usually amphotericin B plus flucytosine for two weeks, followed by fluconazole (400 mg/day for eight to 10 weeks). After initial treatment, lifelong secondary prophylaxis with fluconazole is recommended for both adults and children. The doses are the same as the maximum doses listed for candidiasis (Table 5).

Adult and adolescent patients appear to be at low risk for recurrence of cryptococcosis if they have completed primary treatment, remained asymptomatic, and been able to maintain a CD4+ lymphocyte cell count greater than 100-200 cells/μL for more than six months. Some experts would recommend a repeat evaluation of cerebral spinal fluid to document a negative culture in an asymptomatic patient prior to stopping

Table 5: Recommended Dosing for Prevention of Severe and Recurrent Candidiasis

<table>
<thead>
<tr>
<th>Age</th>
<th>Nystatin dose</th>
<th>Fluconazole dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonates (&lt;1 month)</td>
<td>100 000 units 4 times daily by mouth</td>
<td>3-6 mg/kg by mouth every 72 hours (if ≥14 days old, use infant dose)</td>
</tr>
<tr>
<td>Infants (1-12 months)</td>
<td>200 000 units 4 times daily by mouth</td>
<td>3-6 mg/kg by mouth daily</td>
</tr>
<tr>
<td>Children (1-12 years)</td>
<td>400 000 units 4 times daily by mouth</td>
<td>3-6 mg/kg by mouth daily</td>
</tr>
<tr>
<td>Adults (&gt;12 years)</td>
<td>400 000-600 000 units 4 times daily by mouth</td>
<td>100-200 mg by mouth daily</td>
</tr>
</tbody>
</table>
prophylaxis. These recommendations have not been extensively studied in children and apply to adults and adolescents only.

**Histoplasmosis**

*Histoplasma capsulatum (H. capsulatum)* is a fungus endemic in certain parts of the United States, Latin America, and other parts of the world. In endemic areas, more than 25 percent of HIV-infected patients develop disseminated histoplasmosis.\(^1\) *H. capsulatum* can infect the lungs and the oropharyngeal and gastrointestinal tract as well as skin, brain, adrenal glands, and bone marrow. Patients may present with fever and weight loss, lymphadenopathy, splenomegaly, and diarrhea or abdominal pain. Some HIV-infected patients may present with intestinal ulcers. Those with pulmonary infection may be asymptomatic or may present with dyspnea. A chest radiograph will be abnormal in 70 percent of patients with histoplasmosis.\(^1\)\(^2\)

A radiograph may show diffuse interstitial or reticulonodular infiltrates.

Culture, antigen testing, or fungal stain of the tissues can be used to make the diagnosis. Depending on the site of infection, patients may present with anemia, leukopenia, elevated hepatic enzymes, or an elevated serum lactate dehydrogenase.\(^1\)\(^2\) Treatment is with amphotericin B (0.7-1 mg/kg/day) initially, followed by itraconazole 200mg once or twice daily. Itraconazole has been shown to be more effective than ketoconazole or fluconazole. Treatment may last for up to one year. In patients with CD4+ lymphocyte counts of less than 150 cells/μL, life-long maintenance therapy is recommended at the same dose of itraconazole. Itraconazole can interact with many different medications, including rifampin, so it must be monitored closely.
OPPORTUNISTIC INFECTIONS

Review Questions

1. Review the concept of primary prophylaxis for people with HIV/AIDS.
2. Describe the signs and symptoms of the major types of bacterial, viral, parasitic, and fungal infections experienced by people with HIV/AIDS.
3. Name the high-risk groups that should receive preventive therapy for tuberculosis.
4. Identify the types of treatment used to manage the most common types of opportunistic infections found in people with HIV/AIDS.
5. Discuss at least three interventions that can help reduce opportunistic infections in people with HIV/AIDS.
6. Review the situations in which it is appropriate to stop prophylaxis.

Exam Questions

1. Why do opportunistic infections occur in people with HIV/AIDS?
   a. Increased exposure to other people with infection
   b. Decreased ability of the immune system to respond
   c. Decreased ability of red blood cells to carry oxygen
   d. Decreased ability to tolerate antibiotic therapy
2. What is the definition of primary prophylaxis?
   a. Measures used to prevent transmission of HIV
   b. Medicines given to prevent an opportunistic infection
   c. Method of handwashing to prevent spread of infection
   d. Measures used to prevent HIV from spreading
3. Preventive therapy against tuberculosis involves administration of which medication?
   a. Clarithromycin
   b. Trimethoprim-sulfamethoxazole
   c. Isoniazid
   d. Ketoconazole
4. What is important for health care providers to teach when there is concern about an infection caused by Cryptosporidium?
   a. Good handwashing can prevent the spread of the organism.
   b. The organism is spread through expectorated sputum.
   c. Administering antibiotics can prevent the infection.
   d. Observe for signs of pneumonia and high fever.
5. A 3-year-old child is found to have white plaques on the oropharynx and tongue. Which medication would be given to the mother to use?
   a. Trimethoprim-sulfa capsules
   b. Gentian violet solution
   c. Isoniazid
   d. Clarithromycin

Answers: 1b, 2b, 3c, 4a, 5b
Case Study #1

Mpho is 22 years old. She is HIV-infected and lives on a farm with her family. Her responsibilities include taking care of the chickens and pigs and helping in the fields. She complains that sometimes in the middle of the day she feels very dizzy. The only water available in the field is from a small stream. Currently she has no illnesses and is maintaining her weight.

**Question:** Which of the following interventions might a nurse recommend for Mpho?
- a. She should wash her hands before eating.
- b. She should eat any pork raw.
- c. It is good to drink lots of water, so she should drink freely from the stream.
- d. She should avoid animal feces if possible.
- e. b and d
- f. a and c
- g. a and d

**Answer:** g. There are many steps this patient can take to avoid developing opportunistic infections. Washing her hands thoroughly is a very important way to avoid infection. Many infections that can be harmful to immunocompromised patients are found in animal feces, so feces should be avoided as much as possible. Water that is not clean can also carry many types of infections. She should NOT be told to drink the stream water unless it is a clean source of water. If there is a clean source near her house, she should try to bring water with her to the fields. Finally, raw pork may carry *toxoplasma gondii* and should be avoided.

**Question:** What might be causing Mpho to be dizzy? What might help her symptom?
- a. Dehydration
- b. Hunger
- c. Heat stroke
- d. All of the above
- e. None of the above

**Answer:** d. Any of these things can cause dizziness. Mpho should be advised to drink plenty of clean water and eat frequently while she is working to increase her strength. Protein-rich foods will help her have more energy. She should cover her head when working in the fields to avoid ill effects of the sun and heat.

Case Study #2

A 4-month-old infant presents at the clinic with low-grade fever, hypoxia, and a rapid respiratory rate. On auscultation, the infant’s lungs sound clear. When questioned, the mother states that last year one of her babies died at 9 months of age from a severe diarrheal illness. That child had never grown well and had always had thrush. This infant has had thrush once. Mom has never been tested for HIV.

**Question:** Which is the most likely diagnosis for this infant?
- a. PCP
- b. TB
- c. LIP
- d. *Streptococcus pneumoniae* infection

**Answer:** a. Although each of these respiratory illnesses is possible, PCP is the most likely for several reasons. Infants with TB rarely present with solely respiratory difficulties. Likewise, an infant with streptococcus pneumonia would most likely have a higher fever and have abnormalities on a lung exam (focal rales, etc). LIP is less common in infants than in older children. Hence, this constellation of symptoms is most consistent with PCP. PCP can only be definitively diagnosed with special stains done on lung fluid or biopsy. Treatment includes TMP-SMX and supportive care.

**Question:** The infant is diagnosed with PCP. What would you advise the mother to do? Practice how you might give this advice.
OPPORTUNISTIC INFECTIONS

a. To go home, because this infant is sure to die
b. To be tested for HIV
c. To start taking INH for TB herself
d. None of the above

Answer: b. *Pneumocystis jiroveci* pneumonia is one of the most common AIDS-defining illnesses in infants and children. Most likely, this infant was infected with HIV vertically (from its mother). The mother should be tested so that she knows her status and can make informed choices about care for herself, her children, and future pregnancies. The mother should receive pretest counseling. The infant can be tested, but at 4 months of age, only PCR or HIV culture tests would be definitive. A positive ELISA result would show that the infant had been exposed. This mother will most likely need lots of emotional support when faced with these issues. Discuss how you as a health care provider will help provide this support.

Case Study #3

Joe is a 30-year-old mine worker who comes to the mining clinic with several complaints. Over the past three months, he has lost 9 kg. Before that, he weighed 75 kg. For the past month, he has felt febrile every evening. Last week he had a painful red rash on one side of his chest wall. Now he complains of white patches in his mouth. He also complains that he is having trouble eating because every time he swallows, he feels a burning behind his sternum. In your physical exam, you note a thin, ill-appearing man. The rash on his chest wall does not extend over the midline of his body and is mostly crusted over. His oropharynx is covered with thrush.

Question: What organism most likely caused Joe's rash?

a. EBV
b. Varicella zoster virus
c. JC virus
d. HHV-8

Answer: b. The rash as described is classic for zoster or shingles. This rash is typically confined to one dermatome (the region of the skin innervated by one nerve), is painful and red, and crusts as it resolves. The same virus that causes chickenpox or varicella causes the rash. Recurrence of this rash is common in immunocompromised patients. EBV is associated with minor cold-like symptoms (rhinorhea, cough) and can be associated with lymphoid interstitial pneumonia. JC virus is associated with progressive multifocal leukoencephalopathy, and HHV-8 is associated with Kaposi's sarcoma. Treatment for zoster includes pain management, keeping the lesions covered until they crust to avoid spread, and in severe cases acyclovir.

Question: According to the WHO diagnostic criteria, does Joe have symptomatic HIV infection? If so, which clinical stage?

a. No, Joe does not have HIV by symptomatic criteria.
b. Not enough information is given to determine Joe's HIV status.
c. Yes, Joe has HIV by WHO criteria, and he is Stage 4.
d. Yes, Joe has HIV by WHO criteria, and he is Stage 2.

Answer: c. According to the WHO symptomatic criteria for HIV, an adult must have two major and two minor symptoms. Joe's major symptoms are his weight loss (more than 10 percent) and unexplained fever for more than one month. His minor symptoms are zoster (shingles) and thrush. Joe's weight loss and fever combined define HIV wasting syndrome, which makes him Stage 4.

Question: What would be the most effective treatment for Joe's presumed candidiasis?

a. Gentian violet solution
b. Trimethoprim-sulfamethoxazole
c. Acyclovir
d. Fluconazole

Answer: d. Joe describes retrosternal pain with swallowing. Coupled with the finding of oral candidiasis on physical exam, this suggests esophageal
candidiasis. Although gentian violet is good first-line therapy for oral thrush, it is not appropriate if esophageal candidiasis is suspected. Hence, fluconazole would be the treatment of choice. TMP-SMX and acyclovir are not accepted treatments for fungal disease.

**Case Study #4**

Gloria is 21 years old and pregnant for the first time. As part of her prenatal care, she is tested for HIV and found to be positive. Her CD4+ cell count is 125 cells/uL. She is started on TMP-SMX as well as antiretroviral medications. After delivering her child, Gloria is re-evaluated. Her CD4+ count is now 250 cells/uL.

**Question:** Should her TMP-SMX be discontinued?

- a. Yes
- b. No
- c. Maybe

**Answer:** c. Gloria’s TMP-SMX should be stopped only if her CD4+ cell count has been more than 200 cells/uL for at least three months.

**Question:** Why was TMP-SMX started?

- a. To prevent *pneumocystis carinii* pneumonia
- b. To prevent oral thrush
- c. It should not have been started
- d. None of the above

**Answer:** a. TMP-SMX is recommended for all adults with a CD4+ cell count of less than 200 cells/uL to prevent *pneumocystis carinii* pneumonia.

**Question:** Two years later, Gloria has stopped taking her antiretroviral medications. Her CD4+ cell count is 90 cells/uL. Should her TMP-SMX be restarted?

- a. Yes
- b. No

**Answer:** a. For patients whose CD4+ cell counts again fall below 200 cells/uL, appropriate prophylaxis should be restarted.

**References**


Objectives

1. Describe the epidemiology of tuberculosis (TB).
2. Describe the clinical manifestations and the diagnosis of TB.
3. Describe the treatment of TB.
4. Describe the interaction between anti-TB and antiretroviral drugs.
5. Describe preventive therapy for TB.

Epidemiology of Tuberculosis

*Mycobacterium tuberculosis* infection occurs commonly worldwide. Primary pulmonary infection often is silent, with no obvious signs, symptoms, or radiographic abnormalities. The likelihood of symptom development is age-dependent, being greatest in infants and the elderly. The risk of active tuberculosis (TB) in individuals with latent infection is increased 100-fold by HIV co-infection. TB is the most common cause of death among HIV-infected people worldwide.

HIV produces progressive loss of CD4+ lymphocytes (T-cells), cells critical to the body’s defense against *M. tuberculosis*. HIV promotes the occurrence of TB at any stage of HIV disease, but clinical features of TB do vary by CD4+ lymphocyte count. Adults with HIV and CD4+ lymphocyte counts of more than 350 cells/μL typically manifest pulmonary disease alone, with predominantly upper-lobe infiltrates and/or cavitations. Extrapulmonary TB (including pleuritis, pericarditis, meningitis, and disseminated disease) often is observed among HIV-infected adults with CD4+ lymphocyte counts of less than 50 cells/μL. Chest radiographs often show lower- and middle-lobe infiltrates, often miliary and typically without cavitation. The occurrence of TB is associated with higher HIV virus load and more rapid progression of HIV disease.

A review of the natural history of pulmonary tuberculosis in childhood indicates that 50 percent to 75 percent of children develop radiographically visible hilar adenopathy after primary infection with *M. tuberculosis*, but more than 90 percent of these do not progress. Children with the highest risk of disease progression are those less than 2 years of age. Younger children tend to develop non-cavitary, segmental lung lesions, whereas older children can have reactivation pulmonary TB that resembles adult disease.

Diagnosis

TB can be diagnosed in several ways. The standard test for pulmonary TB consists of three morning expectorated sputum samples for acid-fast bacillus (AFB) smear and culture. If there is no sputum production, induced sputum or bronchoscopy can be used. The sensitivity of expectorated sputum samples for diagnosis of TB in adults with or without HIV is about 50 percent. This figure is comparable to that
of induced sputum or bronchoscopy. Several DNA probe and nucleic acid amplification methods have been evaluated in the diagnosis of TB. The best of these may have sensitivity greater than that of AFB smear and culture. Such tests also are highly specific for *M. tuberculosis*, and their use hastens bacterial identification, but cost is prohibitive in many settings (U.S. $50-$100 per test). Where available, these newer tests can be helpful in confirming the diagnosis of TB in moderate- or high-risk patients where other clinical and laboratory findings present a confusing picture.

Diagnosis of TB in young children (less than 5-6 years of age) is made more difficult by their inability to expectorate sputum suitable for AFB smear and culture. The best specimen for diagnosis of pulmonary TB in a young child is an early-morning gastric aspirate, obtained with a nasogastric tube on awakening the child and before the child ambulates or eats. Three such specimens typically should be collected on separate days. Gastric aspirate specimens should be cultured for *M. tuberculosis*; AFB smears are not useful.

Because *M. tuberculosis* is slow-growing, culture confirmation prior to initiation of therapy is not always practical. A presumed diagnosis of TB can be made based on a history of contact with an individual with TB, appropriate clinical signs and symptoms, a positive Mantoux tuberculin skin test, and typical chest radiographic features. Classic signs and symptoms include chronic cough, hemoptysis (blood-stained or bloody sputum), night sweats, fever, and weight loss. Common chest radiographic findings include hilar adenopathy, pleural effusion, focal infiltrates in the upper and hilar regions, and cavitations.

Mantoux tuberculin skin testing using purified protein derivative (PPD) is performed in many settings to screen for infection with *M. tuberculosis*. However, HIV-infected individuals often are anergic (non-reactive) to PPD as a consequence of HIV-related impairment of cell-mediated (T-cell) immunity. In addition, interpretation of the Mantoux test in patients who have received Calmette-Guerin bacillus (BCG) vaccine can be complicated. In general, the Mantoux test should be interpreted irrespective of whether the patient has received BCG vaccine. In HIV-infected patients, a Mantoux test measuring 5 mm or greater in diameter is considered positive. A negative Mantoux test does not exclude TB.

HIV-infected individuals may develop extrapulmonary TB. One form appears as diffuse lymphadenopathy. Biopsy or fine-needle aspirate will reveal necrotizing and non-necrotizing granulomas. Young children with TB are at increased risk of disseminated disease with meningitis, pleural or pericardial effusion, or involvement of the spine.

**Figure 1: Right Middle Lobe Lung Infiltrate in a Child With Pulmonary TB**
Management and Treatment

Ideally, patients newly diagnosed with TB should be managed in coordination with public health professionals (e.g., the local TB-control program) who are well versed in contact investigation, local factors influencing treatment choices (e.g., local prevalence of drug resistance), and available local resources. Treatment choices generally are dictated by relevant national protocols. Adults with HIV and TB can be treated with standard regimens, with the total duration of therapy extended to nine months, or six months after sputum smears and cultures become negative, whichever is longer. Children with HIV and drug-susceptible TB often are treated for nine to 12 months. In both adults and children, a commonly prescribed regimen for drug-susceptible TB is isoniazid, rifampicin, and pyrazinamide for one or two months, followed by isoniazid and rifampicin alone. Rifabutin can be substituted for rifampicin. In settings where directly observed therapy for TB is available, twice-weekly treatment with isoniazid and rifampicin often is given after an initial one- or two-month period of daily three- or four-drug treatment. Response to TB treatment is largely unaffected by HIV status.

Patients with TB should be monitored carefully to help ensure medication adherence, identify drug toxicity, and gauge treatment response. Liver enzymes must be monitored closely in patients concomitantly receiving antiretroviral and TB medications. Pyridoxine (10 mg by mouth daily) is recommended for all HIV-infected adults and children receiving isoniazid to help prevent drug-associated peripheral neuropathy. Signs and symptoms of peripheral neuropathy include numbness, tingling or prickling sensations in the hands and feet, absent deep-tendon reflexes, and foot drop.

Interactions Between Anti-TB and Antiretroviral Drugs

Many of the medications used to treat TB interact with medications used to treat HIV. Of particular note is the interaction between rifampicin and either non-nucleoside reverse transcriptase inhibitors (NNRTIs) or protease inhibitors (PIs). In addition, anti-TB and antiretroviral drugs have overlapping toxicities; the large number of drugs involved in treating the two diseases concomitantly poses significant adherence challenges; and paradoxical reactions due to immune reactivation or reconstitution after initiation of antiretroviral therapy may occur in 7 percent to 36 percent of patients. Because of these considerations, simultaneous initiation of treatment for both TB and HIV usually is not recommended.

A diagnosis of TB in and of itself generally is not considered an indication for antiretroviral treatment of an HIV-infected patient. Ideally, HIV treatment can be delayed until the patient has completed anti-TB treatment. The exception is a patient with advanced HIV-related immune suppression in whom prolonged delay of antiretroviral therapy may not be advisable. World Health Organization (WHO) guidelines are as follows:

1. **CD4+ count <200 cells/μL**: Start antiretroviral therapy two to eight weeks after initiating anti-TB treatment with efavirenz-based highly active antiretroviral therapy (HAART); alternative third drugs are saquinavir plus ritonavir, abacavir, or nevirapine.

2. **CD4+ count 200-350/μL**: Consider antiretroviral therapy.

3. **CD4+ count >350/μL**: Defer antiretroviral therapy.

If a patient already is receiving antiretroviral medications at the time TB is diagnosed, these medications should not be discontinued. If possible, anti-TB medications that have fewer interactions with antiretroviral medications should be utilized (e.g., substitution of rifabutin for rifampicin). Alternatively, one may consider using an antiretroviral regimen with fewer interactions with the anti-TB medications.

Interaction between rifampicin and many antiretroviral drugs occur largely because these antiretroviral drugs are metabolized by the cytochrome P450 system of...
enzymes that is induced by rifampicin. The affected antiretroviral drugs are broken down at an accelerated rate, thus lowering their blood levels. Nucleoside reverse transcriptase inhibitor drugs (NRTIs) are not metabolized by cytochrome P450 and are unaffected by rifampicin.

Pharmacological studies with small numbers of patients indicate that serum levels of the NNRTIs (nevirapine and efavirenz) and PIs are reduced in patients who are simultaneously treated with rifampicin. Blood levels of antiretroviral drugs are affected by co-administration of rifampicin as shown below:

- Nevirapine: Reduced by 37 percent
- Efavirenz: Reduced by 25 percent
- Indinavir: Reduced by 89 percent
- Ritonavir: Reduced by 35 percent
- Saquinavir: Reduced by 84 percent
- Nelfinavir: Reduced by 82 percent
- Lopinavir/r: AUC reduced by 75 percent

It is not known whether this type of interaction is serious enough to compromise the antiretroviral efficacy of NNRTIs, as there are few clinical outcomes data from controlled studies. Further, it is not known whether there are racial differences in these drug interactions. However, some recent data indicate that rifampicin can be used for treatment of active TB in patients whose antiretroviral regimen includes the NNRTI efavirenz and two NRTIs. U.S. Centers for Disease Control and Prevention (CDC) guidelines suggest that rifampicin may also be used in antiretroviral regimens that include the NNRTI nevirapine.

The interaction between rifampicin and the PI class of drugs is problematic, as there is strong evidence to indicate that rifampicin-induced reductions in the blood level of PIs may cause failure of antiretroviral treatment. In industrialized countries, rifabutin often is substituted for rifampicin. However, rifabutin is not part of TB treatment guidelines in most developing

| Table 1: Co-Administration of Antiretroviral Drugs With Rifampicin |
|-----------------|------------------|------------------|---------------|
| **Single PIs**   | **Recommended Adult Dose When Combined With Rifampicin** | **Comments** |
| Ritonavir        | 600 mg 12-hourly | Ritonavir is poorly tolerated in adults because of gastrointestinal side effects and is therefore not commonly used as a single PI. |
| Amprenavir       | Rifampicin should not be used together with these single PIs. |
| Indinavir        |                   | Change the regimen to make it compatible with rifampicin, taking the patient's previous antiretroviral therapy into account (do not use a drug that the patient has previously failed). |
| Nelfinavir       |                   | |
| Saquinavir       |                   | |
| **Boosted PI Combinations** |                  |               |
| Saquinavir/Ritonavir | Saquinavir 400 mg + ritonavir 400 mg 12-hourly | Limited clinical experience |
| Lopinavir/Ritonavir | Lopinavir/ritonavir (Kaletra) 400 mg/100 mg + ritonavir 300 mg 12-hourly | Limited clinical experience |
| **Non-Nucleoside Reverse Transcriptase Inhibitors** |                  |               |
| Efavirenz        | 600 mg/d          | CDC guidelines recommend 800mg, but efavirenz metabolism is slower in African-Americans, and increased central nervous system side effects may occur with the 800 mg dose. |
| Nevirapine       | 200 mg twice daily | Possible increased risk of hepatotoxicity, particularly during the first 2 months of nevirapine-containing antiretroviral therapy |
countries; it is expensive, and problems have been reported in obtaining sufficient supplies due to a world shortage of the drug. One way to overcome the difficulty of low PI serum levels is to give ritonavir concomitantly with the PI. Because ritonavir is the preferred substrate of the cytochrome P450 system, the system metabolizes ritonavir while allowing the concentration of the other PI to rise to levels similar to those that would be achieved in the absence of rifampicin. This is the principle that underpins protease inhibitor boosting.

**TB Preventive Therapy**

Preventive therapy against TB includes giving one or more anti-TB drugs to individuals with latent *M. tuberculosis* infection to prevent progression to active disease. Before a person is considered for TB preventive therapy, active TB should be excluded. In 1998, the WHO and UNAIDS developed recommendations for preventive therapy. Preventive therapy is recommended in countries that have established HIV-care and TB-control programs. In addition, resources must be available to:

- Distinguish active from latent TB
- Ensure appropriate monitoring and follow-up
- Ensure consistent supply of medications
- Link preventive therapy against TB to voluntary counseling and testing for HIV

Preventive TB therapy is recommended for HIV-infected individuals with a positive Mantoux skin test who do not have evidence of active TB (i.e. who have a normal chest radiograph and no suggestive clinical symptoms). In areas where Mantoux testing is not feasible, preventive therapy should be considered for the following high-risk individuals if they are infected with HIV:

- Persons living in populations with a high prevalence of TB (more than 30 percent)
- Health care workers
- Household contacts of TB patients
- Prisoners
- Miners

Preventive therapy with isoniazid in adults is recommended at the dose of 5 mg/kg (maximum 300 mg) by mouth daily for six months with clinical monitoring for adverse effects and active TB.

Until recently, isoniazid preventive therapy had not been studied in HIV-infected children. In a recent placebo-controlled randomized trial, isoniazid dosed at 10 mg/kg orally once daily or three times weekly was associated with a 53 percent reduction in mortality. The survival benefit occurred early (within 50 days) and was apparent in all CDC HIV categories of disease. Although these results are preliminary and the population studied lived in the Western Cape Province of South Africa, a region with one of the highest incidence rates of TB worldwide (4.1 percent annualized risk for children), they make a strong case for offering isoniazid preventive therapy to HIV-infected children living in other countries with high TB prevalence.
References

1. MMWR. 2003; 52RR-10-1.

11. Updated guidelines for the use of rifabutin or rifampicin for the treatment and prevention of tuberculosis among HIV-infected patients taking protease inhibitors or non-nucleoside reverse transcriptase inhibitors. MMWR 2000;49(09):185-9
Objectives

The purposes of this module are to:
1. Review the most common cutaneous manifestations of HIV infection.
2. Describe the types of treatment for each cutaneous lesion.

Key Points

1. Cutaneous lesions are often the first manifestation of HIV noted by patients and health professionals.
2. Cutaneous lesions occur frequently in both adults and children infected with HIV.

Overview

Many people with HIV infection develop cutaneous lesions. The risk of developing cutaneous manifestations increases with disease progression. If recognized with other signs and symptoms of HIV infection, these lesions may lead to early diagnosis of AIDS (Table 1).

This module focuses on many of the most common cutaneous manifestations of HIV. However, several cutaneous manifestations are covered in depth in other sections. To avoid duplication, they will only be mentioned briefly in this section.

### Table 1: Cutaneous Manifestations of HIV

<table>
<thead>
<tr>
<th>Cause</th>
<th>Manifestations</th>
</tr>
</thead>
</table>
| Neoplasia | • Kaposi’s sarcoma  
| | • Lymphoma  
| | • Squamous and basal cell carcinoma |
| Infections | • Zoster  
| | • Herpes virus infections  
| | • Superficial fungal infections  
| | • Angular cheilitis  
| | • Chancroid  
| | • Cryptococcosis  
| | • Histoplasmosis  
| | • Human papillomavirus  
| | • Impetigo  
| | • Lymphogranuloma venereum  
| | • Molluscum contagiosum  
| | • Mycobacterial infection  
| | • Syphilis  
| | • Furunculosis  
| | • Folliculitis  
| | • Pyomyositis  
| | • Verucca planus |
| Others | • Pruritic papular eruption  
| | • Seborrhoeic dermatitis  
| | • Drug eruptions  
| | • Vasculitis  
| | • Xeroderma  
| | • Psoriasis  
| | • Granuloma annulare  
| | • Thrombocytopenic purpura  
| | • Telangiectasis  
| | • Hyperpigmentation  
| | • Dry atrophic skin  
| | • Hair changes |

Adapted from AIDS in Africa

Kaposi’s Sarcoma

Kaposi sarcoma is commonly seen in adults and children infected with HIV worldwide. Kaposi’s sarcoma is more prevalent in East and Central Africa.
and less common in West and South Africa. It is a vascular neoplasm associated with infection with human herpes virus 8 (HHV-8). Kaposi's sarcoma lesions often present as red or brown-violaceous lesions. They can be macular, papular, or nodular and can be seen on the skin as well as mucous membranes (Figure 1). Chest lesions may mimic those of tuberculosis (TB). Please see the chapter on opportunistic infections for a more detailed description of Kaposi’s sarcoma.

**Cutaneous Infection With HSV**

In adults, a relationship has been observed between decreased CD4+ lymphocyte counts and an increased incidence of cutaneous herpes simplex virus (HSV). Although herpes stomatitis is more common in children, cutaneous lesions can be found at other body sites (Figure 2). The lesions are small and blister-like, and diagnosis is confirmed by viral culture, if available. Treatment with acyclovir 10-20 mg/kg/dose four times per day for five to seven days for children and 400 mg/dose five times per day for five to seven days for adults. Adults have been treated with both valacyclovir (1 g three times a day) and famciclovir (500mg twice a day) for seven days. However, neither has been studied in controlled trials with immunocompromised patients. Patients taking acyclovir need to be instructed to drink plenty of fluids to maintain adequate hydration.

**Chickenpox (Primary Varicella Zoster Virus Disease) and Herpes Zoster**

Chickenpox (primary VZV disease) can occur in children with HIV infection. Complications include hemorrhagic skin lesions, hepatitis, pneumonia, encephalitis, bacterial complications, and death. An HIV-infected child who is exposed to chickenpox should receive varicella zoster immune globulin (VZIG) within 96 hours of exposure. Uncomplicated

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**Figure 1: Kaposi’s Sarcoma**

Photo courtesy of David Bowman, M.D.

**Figure 2: Herpes Simplex**

Herpes simplex virus infection in an HIV-infected girl. Chronic or progressive herpetic skin lesions are observed occasionally in HIV-infected children.
culture can be used to diagnose VZV. The treatment of choice for herpes zoster is acyclovir 20 mg/kg/dose by mouth, administered four times per day for seven days; the maximum dose is 800 mg administered four times daily. Children who have severe disease or who are unable to take liquids should be treated with acyclovir 10 mg/kg/dose intravenously every eight hours for seven days.

**Molluscum Contagiosum**

Molluscum contagiosum is commonly found in persons with advanced HIV infection. In adults, it occurs more commonly with CD4+ lymphocyte counts of less than 200 cells/mm³. Adults with CD4+ lymphocyte counts of less than 50 cells/mm³ are more prone to numerous lesions and to giant lesions greater than 1 cm in size. Molluscum contagiosum lesions are pearly or flesh-colored, dome-shaped papules 3-5 mm in size with a central core. Giant lesions often occur on...
the face, and they can be disfiguring (Figure 5).² Treatment includes pricking each lesion with a needle or sharpened orange stick and dabbing the lesion with phenol.³ Other treatment options include tretinoin, imiquimod, trichloroacetic acid, and/or sursica remaral.³ Despite treatment, the recurrence rate is high. Highly active antiretroviral treatment (HAART) coupled with increasing CD4+ lymphocyte cell counts lessen the

<table>
<thead>
<tr>
<th>Bacterial Skin Infection</th>
<th>Causative Organism</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Folliculitis (pimple)</td>
<td>Staphylococcus</td>
<td>Inflammation, infection of hair follicle</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>Streptococcus, Staphylococcus, Haemophilus influenzae</td>
<td>Inflammation of skin and subcutaneous tissues, characterized by edema, erythema, and pain</td>
</tr>
<tr>
<td>Skin abscess</td>
<td>Streptococcus, Staphylococcus, Haemophilus influenzae</td>
<td>Localized collection of pus in a cavity formed by disintegration of tissue; may be a complication of untreated cellulitis</td>
</tr>
<tr>
<td>Impetigo</td>
<td>Staphylococcus</td>
<td>Vesicles or bullae that become pustular, rupture, and form yellow crusts</td>
</tr>
<tr>
<td>Furunculosis (boil)</td>
<td>Staphylococcus, Streptococcus</td>
<td>Inflammation, infection of the skin and subcutaneous tissue surrounding a hair follicle; larger than folliculitis</td>
</tr>
<tr>
<td>Paronychia</td>
<td>Staphylococcus</td>
<td>Inflammation, infection involving the folds of tissue surrounding the fingernail or toenail.</td>
</tr>
</tbody>
</table>

Figure 5: Molluscum Contagiosum

Severe molluscum contagiosum in an HIV-infected boy

Figure 6: Staphylococcus Aureus

An HIV-infected girl with granulocytopenia and Staphylococcus aureus bacteremia. Note the presence of multiple necrotic skin lesions. The left calf is erythematous, swollen, and indurated secondary to cellulitis and myositis.
severity of disease, although lesions may be present up to eight months after starting HAART.

**Bacterial Skin Infections**

Bacterial skin infections can include folliculitis, cellulitis (Figure 6), skin abscesses, impetigo, furunculosis, and paronychia (Table 2). *Staphylococcus aureus* is the cause in most bacterial skin infections. Treatment for bacterial skin infections includes keeping the lesions clean with soap and water. Parents should be instructed in good handwashing to prevent the spread of lesions. *Staphylococcus aureus* often colonizes the nails of patients. Antibacterial creams such as mupiricin should be applied to the nails twice daily for three to four weeks to prevent spread within a household. More severe cases of bacterial skin infections can be treated with an oral penicillinase-resistant penicillin such as dicloxacillin. In areas where methicillin-resistant *Staphylococcus aureus* (MRSA) is prevalent, empiric antibiotic coverage of skin infections should include coverage of this organism. Appropriate coverage will change depending on the setting, but often MRSA acquired in the community is sensitive to either clindamycin or trimethoprim-sulfate.

**Fungal Skin Infections**

Fungal skin infections among people with HIV/AIDS include candidiasis and dermatophytosis. Cutaneous candidiasis is found most commonly in the diaper area and skin folds. It appears as a vivid, erythematous (red) rash with well-demarcated borders and satellite lesions. Cutaneous candidiasis is treated topically with 1 percent aqueous solution of gentian violet applied to lesions three times per day for three days, or nystatin ointment applied to lesions three times per day until the rash resolves. If there is no response to topical treatment, systemic treatment with ketoconazole 3.3-6.6 mg/kg/day given by mouth, once a day for two to four weeks may be used, or fluconazole 3-6 mg/kg/day (maximum 100-200mg) once daily for 14 days. Ketoconazole interacts with many antiretroviral medications, so a thorough drug history should be taken prior to initiating therapy. Patients should be instructed to take ketoconazole with food to prevent stomach upset.

Dermatophytosis usually occurs as tinea corporis or tinea capitis. It is characterized by flat, scaling lesions with raised borders (Figure 7). The lesions are very extensive and refractory to treatment in HIV-infected persons. Dermatophytosis is treated with a topical broad-spectrum antifungal, such as clotrimazole 1 percent cream applied to lesions twice a day until the rash resolves. More severe cases can be treated with systemic medications such as griseofulvin microsize tablets, 20 mg/kg per day given once daily by mouth. Duration of therapy depends on the location of infection. Tinea corporis should be treated for two to four weeks; tinea capitis should be treated for four to six weeks. Itraconazole may also be used. Patients should be instructed to take griseofulvin with a meal that is high in fat to enhance absorption. Monitor CBC, electrolytes, blood urea nitrogen, creatinine, and liver function test after four weeks of receiving griseofulvin, when available.

**Scabies**

Scabies infection in adults and children is characterized by pruritic papular lesions found most commonly in the webs of the fingers and toes, folds of the wrist, antecubital area, and axilla. Infants may also have lesions on the palms and soles of the feet (Figure 8). Scrapings observed under a microscope may reveal...
the mite, eggs, or feces. Treatment consists of an application of topical benzyl benzoate lotion, 25 percent, which is left on the skin to dry and repeated the next day. HIV-infected patients with advanced disease can experience a variant of scabies called Norwegian scabies. This type of scabies is characterized by generalized scaling and enlarged, crusted plaques (Figure 9). After a patient is treated for scabies, the family should be advised to wash all clothing and bedclothes in hot water and iron them to kill mites that may live in the cloth.

**Drug Eruptions**

Drug eruptions can occur in patients receiving treatment for HIV infection. Common medications that cause drug eruptions include sulfa drugs, penicillin, cephalosporins, and dapsone. Drug eruptions usually appear as pink to erythematous papules that run together and create a blotchy appearance but may include elevated patches (hives), mucous-membrane ulceration, scaling, and light sensitivity. Most drug eruptions are mild and resolve after the causative medication is discontinued. Non-nucleoside reverse transcriptase inhibitors (nevirapine and efavirenz), a class of antiretroviral medications, have been associated with pruritic, maculopapular eruptions. Most eruptions are mild, and the medication can be continued with eventual spontaneous resolution of the eruption. To promote comfort, the patient can be given oral antihistamine such as diphenhydramine hydrochloride 1 mg/kg every six hours. In more severe cases, the eruptions resolve when the medication is discontinued.

**Seborrheic Dermatitis**

Seborrheic dermatitis occurs in up to 85 percent of adults and children with HIV infection. Seborrheic dermatitis may be an early sign of HIV. Seborrheic dermatitis is characterized by thick, yellow scales occurring on the scalp but may also be seen on the face or in the diaper area. Older children may also have involvement of the nasolabial folds, the skin behind the ears, and the eyebrows. Treatment consists of selenium sulfide or ketoconazole shampoo, topical coal tar, UVB light therapy, or salicylic acid. To decrease inflammation, 1 percent hydrocortisone cream can be applied to the affected area (exclusive of the face) three times per day. Parents should be
instructed to use 1 percent hydrocortisone cream sparingly in the diaper area.

**Pruritic Papular Eruption**

Pruritic papular eruption (PPE) is a chronic eruption of papular lesions on the skin whose etiology is unclear (Figure 10). Patients with PPE show evidence of increased immunoglobulin E (IgE) and eosinophilia. Some studies suggest that PPE may represent an over-exuberant reaction to insect bites. As the name suggests, PPE is very pruritic. The rash is usually evenly distributed on the trunk and extremities. Between 11 percent and 45 percent of HIV-infected patients will present with PPE. PPE is believed to be a marker of worsening immunosuppression and is more commonly associated with a CD4+ lymphocyte count of less than 50 cells/mm³. PPE can contribute to high morbidity in children with slow-progressing disease, as well as in adults. It may cause distress to the patient and quite often becomes superinfected with *Staphylococcus aureus* and *Streptococcus* organisms. In many areas, the characteristic PPE rash has become associated with HIV and may be stigmatizing. Treatment of PPE is difficult and usually requires antihistamines and local steroids with or without antibiotics. UVB light may assist with symptomatic treatment.

**Clinical Considerations**

Patients should be encouraged to complete all medication as prescribed and to report any lesions that get worse or do not heal. Patients should be instructed to monitor for the development of bacterial superinfection of lesions. Superinfection or secondary infection occurs when a primary lesion becomes infected with a secondary organism, such as a varicella lesion that becomes infected with *Staphylococcus aureus*. Patients should be instructed on how to maintain hygiene without producing dry skin. They should be instructed to avoid deodorant soaps and to use tepid water when bathing. Skin should be patted dry without rubbing, and moisturizer should be applied to the skin immediately after bathing. Bedridden patients should be turned every two hours to avoid skin breakdown. Patients should keep their nails short and smooth and be discouraged from scratching lesions. Scratching can lead to open lesions and secondary infections. If open lesions are present, patients should be instructed to avoid contact with other areas of the skin to prevent spread of the infection.

![Figure 10: Pruritic Papular Eruption](Photo courtesy of Dr. Ikeo)
Review Questions

1. Describe the most common types of cutaneous lesions found in children with HIV/AIDS.

2. List the treatment for each type of skin manifestation.

Exam Questions

1. Approximately what percentage of children who have had varicella have a recurrence of disease within 24 months?
   - a. 15 percent
   - b. 20 percent
   - c. 50 percent
   - d. 25 percent

2. Lesions on which part of the body can help distinguish a rash caused by scabies from other types of rashes?
   - a. Back of the neck
   - b. Behind the knees
   - c. Webs of fingers/toes
   - d. Behind the ears

3. Lesions associated with Kaposi’s sarcoma can be seen on which areas of the body?
   - a. Hard palate (mouth)
   - b. Skin of the extremities (arms/legs)
   - c. Skin of the chest
   - d. None of the above
   - e. a, b, and c

4. Seborrheic dermatitis is seen in what percentage of HIV-infected persons?
   - a. 15 percent
   - b. 40 percent
   - c. 60 percent
   - d. 85 percent

Answers: 1c, 2c, 3e, 4d
A 4-year-old HIV-infected child presents to your clinic. The caregiver states that the child has a rash that started on the head/face about four days ago. It has continued to spread down the body, and the child is scratching a great deal. The lesions start out as vesicles (small fluid-filled lesions), but the earliest ones have crusted over. The caregiver states that her next-door neighbor’s child had a similar rash the week before and the two children had been left together. Currently the child has no fever, is eating and drinking well, but is uncomfortable because the rash itches so much.

**Question:** What is the most likely diagnosis?  
- a. Scabies  
- b. Kaposi’s sarcoma  
- c. Varicella zoster  
- d. Impetigo

**Answer:**  c. The description given is a classic presentation of primary varicella: vesicles presenting over time, starting from the head, then ulcerating and ultimately developing a crust.

**Question:** What treatment would you recommend for this child?  
- a. Symptomatic treatment only  
- b. Varicella zoster immune globulin  
- c. Acyclovir  
- d. All of the above  
- e. A and C only

**Answer:**  a. If the child had presented to clinic within 96 hours (four days) of her initial exposure to the disease, varicella zoster immune globulin (VZIG) would have been an appropriate treatment. However, at this time it will be of little benefit. Acyclovir given early in the course of infection can often decrease the severity, but this child has had lesions for four days. It is unlikely that acyclovir will change the course of illness, although it can be given.

**Question:** What would you advise the caregiver to watch for in the next several days?  
- a. Fever  
- b. Change in the rash, especially a new redder appearance  
- c. Difficulty breathing  
- d. Abdominal pain  
- e. All of the above

**Answer:**  e. All of these signs/symptoms can be related to complications of varicella. Secondary bacterial infections often occur, especially if scratching has excoriated the lesions. Fever and a change in the appearance of the lesions can signal a secondary bacterial infection. Pneumonia and hepatitis can also present as complications of varicella and should be monitored for. HIV-infected children may often have a prolonged course of varicella zoster and are more likely to experience recurrences, so they should be monitored closely.
References

Objectives

The purposes of this module are to:
1. Discuss the importance of oral and dental care for patients with HIV infection.
2. Review the classification of orofacial lesions associated with HIV infection in adults and children.
3. Describe the clinical presentation and management of the most common oral manifestations of HIV infection.

Key Points

1. Oral health care is an important part of HIV primary care.
2. Oral manifestations are common clinical findings in children and adults with HIV infection.
3. Early diagnosis and management of oral manifestations is important to prevent complications.

Importance of Oral Manifestations of HIV Infection

Since HIV infection was first described in 1981, a variety of oral conditions associated with HIV disease have been documented. Studies have shown that 70 percent to 90 percent of people infected with HIV will develop at least one oral manifestation during the course of the disease. A review of the dental literature shows that HIV-associated orofacial lesions have been considered:
- clinical indicators of HIV infection in otherwise healthy, undiagnosed individuals.
- early clinical features of HIV infection.
- clinical markers for the classification and staging of HIV disease.
- predictors of HIV disease progression.

In developed countries, HIV disease progression is monitored by two key laboratory markers: CD4+ lymphocyte count and HIV viral load. Unfortunately, these tests are not readily available in many developing countries. There, other important clinical findings guide clinicians in the evaluation and treatment of HIV disease. Since the oral cavity is easily accessible to clinical examination, orofacial lesions associated with HIV infection may be used as clinical markers of HIV disease progression.

The advent of highly active antiretroviral therapy (HAART) in 1996 has led to a large reduction in the mortality and morbidity of HIV-infected patients who have access to treatment. The incidence rates of many opportunistic infections associated with HIV disease have decreased, including that of HIV-associated orofacial lesions.

Evaluation of oral health status is an important part of routine health care. A thorough oral examination...
is important at every stage in the management of HIV disease. It is also desirable to encourage close collaboration among general medical practitioners, infectious-disease doctors, general and pediatric dentists, and oral pathologists to provide the best care possible for HIV-positive patients.

**Classification of Orofacial Lesions Associated With HIV**

There are two main classification systems of oral lesions associated with HIV infection. The first is based on the etiology of the oral lesions. According to this system, orofacial lesions are classified as bacterial, viral, or fungal infections or neoplastic lesions or other conditions. The second, more widely used system, recommended by the EC Clearinghouse on Oral Problems Related to HIV Infection and WHO Collaborating Centre on Oral Manifestations of the Human Immunodeficiency Virus, classifies orofacial lesions into three groups according to the degree of their association with HIV infection. Table 1 and Table 2 show this classification of orofacial lesions associated with HIV/AIDS in adults and children, respectively.

**Clinical Presentation and Management**

**Oral Candidiasis**
Oral candidiasis is the most common orofacial manifestation of HIV infection. Its prevalence may depend on study population, diagnostic criteria, study design, and availability of antiretroviral therapy. Reported prevalence rates have varied widely, up to 72 percent in children and 94 percent in adults. Oral candidiasis has also been shown to be a significant predictor of HIV disease progression in both adults and children. The median time of survival from its clinical diagnosis to death has been

<table>
<thead>
<tr>
<th>Table 1: Orofacial Lesions Associated With HIV/AIDS in Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lesions strongly associated with HIV infection</strong></td>
</tr>
<tr>
<td>• Candidiasis</td>
</tr>
<tr>
<td>Erythematous</td>
</tr>
<tr>
<td>Pseudomembranous</td>
</tr>
<tr>
<td>• Hairy leukoplakia</td>
</tr>
<tr>
<td>• Kaposi’s sarcoma</td>
</tr>
<tr>
<td>• Non-Hodgkin’s lymphoma</td>
</tr>
<tr>
<td>• Periodontal disease</td>
</tr>
<tr>
<td>Linear gingival erythema</td>
</tr>
<tr>
<td>Necrotizing (ulcerative) gingivitis</td>
</tr>
<tr>
<td>Necrotizing (ulcerative) periodontitis</td>
</tr>
<tr>
<td><strong>Lesions less commonly associated with HIV infection</strong></td>
</tr>
<tr>
<td>• Bacterial infections</td>
</tr>
<tr>
<td>Mycobacterium avium-intracellulare</td>
</tr>
<tr>
<td>Mycobacterium tuberculosis</td>
</tr>
<tr>
<td>• Malignant hyperplasia</td>
</tr>
<tr>
<td>Necrotizing (ulcerative) stomatitis</td>
</tr>
<tr>
<td>• Salivary gland disease</td>
</tr>
<tr>
<td>Dry mouth due to decreased salivary flow rate</td>
</tr>
<tr>
<td>Unilateral or bilateral swelling of the major salivary</td>
</tr>
<tr>
<td>glands</td>
</tr>
<tr>
<td>• Thrombocytopenic purpura</td>
</tr>
<tr>
<td>• Ulceration NOS (not otherwise specified)</td>
</tr>
<tr>
<td>• Viral infections</td>
</tr>
<tr>
<td>Herpes simplex virus</td>
</tr>
<tr>
<td>Human papillomavirus (wart-like lesions)</td>
</tr>
<tr>
<td>Condyloma acuminatum</td>
</tr>
<tr>
<td>Focal epithelial hyperplasia</td>
</tr>
<tr>
<td>Verruca vulgaris</td>
</tr>
<tr>
<td>Varicella zoster virus</td>
</tr>
<tr>
<td>Herpes zoster</td>
</tr>
<tr>
<td>Varicella</td>
</tr>
<tr>
<td><strong>Lesions seen in HIV infection</strong></td>
</tr>
<tr>
<td>• Bacterial infections</td>
</tr>
<tr>
<td>Actinomyces israel</td>
</tr>
<tr>
<td>Escherichia coli</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
</tr>
<tr>
<td>• Cat-scratch disease</td>
</tr>
<tr>
<td>• Drug reactions (ulcerative, erythema multiforme,</td>
</tr>
<tr>
<td>lichenoid, toxic epidermolyisis</td>
</tr>
<tr>
<td>• Epithelioid (bacillary) angiomatosis</td>
</tr>
<tr>
<td>• Neurologic disturbances</td>
</tr>
<tr>
<td>Facial palsy</td>
</tr>
<tr>
<td>Trigeminal neuralgia</td>
</tr>
<tr>
<td>• Fungal infection other than candidiasis</td>
</tr>
<tr>
<td>Cryptococcus neoformans</td>
</tr>
<tr>
<td>Geotrichum candidum</td>
</tr>
<tr>
<td>Histoplasma capsulatum</td>
</tr>
<tr>
<td>Mucoraceae (mucormycosis/ zygomycosis)</td>
</tr>
<tr>
<td>Aspergillus flavus</td>
</tr>
<tr>
<td>• Recurrent aphthous stomatitis</td>
</tr>
<tr>
<td>• Viral infections</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
</tr>
<tr>
<td>Molluscum contagiosum</td>
</tr>
</tbody>
</table>
reported as 3.4 years among HIV-infected children. The main etiologic factor of oral candidiasis is Candida albicans, although other species of Candida may be involved.

**Clinical appearance:** Oral candidiasis is frequently observed in one of the following four clinical forms: erythematous (atrophic) candidiasis, pseudomembranous candidiasis, hyperplastic candidiasis, and angular cheilitis. Erythematous (atrophic) candidiasis appears clinically as multiple small or large patches, most often localized on the tongue and/or palate (Figure 1). Pseudomembranous candidiasis (oral thrush) is characterized by the presence of multiple superficial, creamy white plaques that can be easily wiped off, revealing an erythematous base (Figure 2). They are usually located on the buccal mucosa, oropharynx, and/or dorsal face of the tongue. In hyperplastic candidiasis, the lesions appear white and hyperplastic and cannot be removed by scraping. This form of oral candidiasis is rare in HIV-infected persons. Angular cheilitis is characterized by the presence of erythematous fissures at the corners of the mouth. It is usually accompanied by another form of intra-oral candidiasis.

**Treatment:** Treatment with topical and systemic antifungal agents is recommended (Table 3).

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**Table 2: Orofacial Lesions Associated With Pediatric HIV Infection**

<table>
<thead>
<tr>
<th>Lesions commonly associated with pediatric HIV infection</th>
<th>Lesions less commonly associated with pediatric HIV infection</th>
<th>Lesions strongly associated with HIV infection but rare in children</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Oral candidiasis</td>
<td>• Parotid enlargement (swelling of the major salivary glands)</td>
<td>• Neoplasms</td>
</tr>
<tr>
<td>Pseudomembranous</td>
<td>• Recurrent aphthous ulcers</td>
<td>Kaposi's sarcoma and non-Hodgkin's lymphoma</td>
</tr>
<tr>
<td>Erythematous</td>
<td>Minor</td>
<td>Oral hairy leukoplakia</td>
</tr>
<tr>
<td>Angular cheilitis</td>
<td>Major</td>
<td>Tuberculosis-related ulcers</td>
</tr>
<tr>
<td>Herpes simplex virus infection</td>
<td>Herpeticform</td>
<td></td>
</tr>
<tr>
<td>Linear gingival erythema</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Bacterial infections of oral tissues</td>
<td>• Viral infections</td>
<td></td>
</tr>
<tr>
<td>Periodontal diseases</td>
<td>Cytomegalovirus</td>
<td></td>
</tr>
<tr>
<td>Necrotizing ulcerative gingivitis</td>
<td>Human papillomavirus</td>
<td></td>
</tr>
<tr>
<td>Necrotizing ulcerative periodontitis</td>
<td>Molluscum contagiosum</td>
<td></td>
</tr>
<tr>
<td>Necrotizing stomatitis</td>
<td>Varicella zoster virus</td>
<td></td>
</tr>
<tr>
<td>Xerostomia</td>
<td>Herpes zoster</td>
<td></td>
</tr>
<tr>
<td>Seborrheic dermatitis</td>
<td>Varicella</td>
<td></td>
</tr>
</tbody>
</table>

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**Figure 1:** Erythematous Candidiasis in an HIV-Infected Child

**Figure 2:** Pseudomembranous Candidiasis in an HIV-Infected Child
Oral Hairy Leukoplakia
Oral hairy leukoplakia (OHL) is more common among HIV-infected adults than among HIV-infected children. The reported prevalence of OHL in adults is about 20-25 percent, increasing as the CD4+ lymphocyte count decreases, whereas in children the prevalence is about 2-3 percent. The presence of OHL is a sign of severe immuno-suppression. OHL has been described as a significant predictor of HIV disease progression in adults. Although its etiology is not clear, OHL seems to be caused by Epstein-Barr virus (EBV) infection.

Clinical appearance: OHL presents as white, thick patches that do not wipe away and that may exhibit vertical corrugations with a “hair-like” appearance (Figure 3). The lesions usually start on the lateral margins of the tongue and sometimes inside the cheeks and lower lip. They may be unilateral or bilateral, and they are asymptomatic. OHL is often associated with oral candidiasis.

Treatment: OHL usually does not require any treatment, but in severe cases systemic antivirals are recommended (Table 3). When OHL is associated with oral candidiasis, therapeutic management of oral candidiasis is required.

HIV-Associated Periodontal Disease
Periodontal (gum) disease is common among HIV-infected patients. It is characterized by bleeding gums, bad breath, pain/discomfort, mobile teeth, and sometimes sores. Its reported prevalence ranges widely, between 0 and 50 percent. Left untreated, HIV-associated periodontal disease may progress to life-threatening infections, such as Ludwig’s angina and noma (Cancrum oris).

Clinical appearance: Four forms of HIV-associated periodontal disease have been described: linear gingival erythema, necrotizing ulcerative gingivitis, necrotizing ulcerative periodontitis, and necrotizing stomatitis. Linear gingival erythema (LGE) is characterized by the presence of a 2-3 mm red band along the marginal gingiva, associated with diffuse erythema on the attached gingiva and oral mucosa (Figure 4). The degree of erythema is disproportionately intense compared to the amount of plaque present on the teeth.

Necrotizing ulcerative gingivitis (NUG) is more common in adults than in children. It is characterized by the presence of ulceration, sloughing, and necrosis of one or more interdental papillae, accompanied by pain, bleeding, and fetid halitosis. Necrotizing ulcerative periodontitis (NUP) is characterized by the extensive and rapid loss of soft tissue and teeth. Necrotizing stomatitis is thought to be a consequence of severe, untreated NUP. It is characterized by acute and painful ulceronecrotic lesions on the oral mucosa that expose underlying alveolar bone.
**Treatment:** Management and control of HIV-associated periodontal disease begin with good daily oral hygiene. In addition to brushing, flossing and use of oral rinses are effective ways to prevent and control periodontal disease. Table 3 presents various therapeutic options.

*Noma*, also known as *Cancrum oris*, is a gangrenous condition that primarily affects children. Noma has been reported mainly in developing countries in West Africa, but cases have also been described in other parts of the world.\(^{29,30}\) It is a multifactorial disease. The most important risk factors are poverty, chronic malnutrition, poor oral hygiene, and severe immunosuppression. Though considered a preventable disease, noma has a case-fatality rate of 70-90 percent if left untreated.\(^{29,30}\)

**Herpes Simplex Virus (HSV) Infection**

Herpes simplex virus (HSV) infection may either be primary (herpetic gingivo-stomatitis) or secondary (herpes labialis). The prevalence of oral HSV infection varies between 10 and 35 percent in adults and children with HIV infection.\(^{2,4,21-25}\) The presence of HSV infection for more than one month constitutes an AIDS-defining condition.

**Clinical appearance:** HSV infection appears as a crop of vesicles usually localized on the keratinized mucosa (hard palate, gingiva) and/or vermilion borders of the lips and perioral skin (Figure 5). The vesicles rupture and form irregular painful ulcers. They may interfere with mastication and swallowing, resulting in decreased oral intake and dehydration.

**Treatment:** Systemic therapy with antiviral agents is recommended (Table 3). The treatment is more effective if it is instituted in the prodromal stage of infection.

**Recurrent Aphthous Ulcers (RAUs)**

Recurrent aphthous ulcers occur in about 1-7 percent of HIV-infected patients.\(^{2,4,21-25}\) They are painful ulcers on the nonkeratinized oral mucosa, such as labial and buccal mucosa, soft palate, and ventral aspect of the tongue. Severe recurrent aphthous lesions usually occur when the CD4+ lymphocyte count is less than 100 cells/mm\(^3\). This may be suggestive of HIV disease progression. The etiology of RAUs is not well known.

**Clinical appearance:** RAUs may present as minor, major, or herpetiform aphthae. *Minor aphthous ulcers* are ulcers less than 5 mm in diameter covered by pseudomembrane and surrounded by an erythematous halo. They usually heal spontaneously without scarring (Figure 6). *Major aphthous ulcers* resemble minor aphthous ulcers, but they are fewer and larger in diameter (1-3 cm), are more painful, and may persist longer. Their presence interferes with mastication, swallowing, and speaking. Healing occurs over two to six weeks. Scarring is very common. *Herpetiform aphthous ulcers* occur as a crop of numerous small...
### Table 3: Therapeutic Options for the Most Common HIV-Associated Oral Manifestations

<table>
<thead>
<tr>
<th>Oral Lesion</th>
<th>Treatment for Adults</th>
<th>Treatment for Children</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral Candidiasis (Erythematous, Pseudomembranous, and Hyperplastic)</td>
<td><strong>Topical</strong>&lt;br&gt;- Nystatin (Mycostatin)&lt;br&gt;- Oral gel: apply gel q8h or q6h, for 10-14 days&lt;br&gt;- Cream: Apply q12h, for 10-14 days &lt;br&gt;- <strong>Systemic</strong>&lt;br&gt;- Nystatin (Mycostatin) 400,000-600,000 U q6h, for 14 days&lt;br&gt;- Ketoconazole (Nizoral) 200-400 mg PO qd.&lt;br&gt;- Fluconazole (Diflucan) 50-100 mg PO qd.&lt;br&gt;- Itraconazole (Sporanox) (Capsules or solution) 200 mg PO qd for 7 days&lt;br&gt;- Amphotericin B10 mg IVq6h, for 10 days</td>
<td><strong>Topical</strong>&lt;br&gt;- Nystatin suspension 200,000-400,000 U/day divided in 4-6 doses, for 14 days&lt;br&gt;- Clotrimazole troches 10 mg q8h or q6h, for 4 weeks&lt;br&gt;- Gentian violet 1% aqueous solution painted in the affected areas q8h</td>
<td>• Different forms of oral candidiasis may occur simultaneously.&lt;br&gt;• Hyperplastic candidiasis requires systemic treatment.&lt;br&gt;• Ketoconazole may interact with Lopinavir-Ritonavir (Kaletra) at doses &gt;200 mg/day.&lt;br&gt;• Topical fluoride should be used if antifungal agents are administered for long periods to counteract high sugar content of some antifungal medications.&lt;br&gt;• Amphotericin B may be used in azole-resistant infections.&lt;br&gt;• Amphotericin B may also be available as a topical preparation.&lt;br&gt;• Dentures should be removed when medication is applied.</td>
</tr>
<tr>
<td>Angular Cheilitis</td>
<td><strong>Topical</strong>&lt;br&gt;- Nystatin-triamcinolone (Mycolog II) ointment applied on the affected areas after meals and at bedtime&lt;br&gt;- Clotrimazole 1% (Mycelex) cream&lt;br&gt;- Miconazole 2% cream applied q12h on the affected areas, for 1-2 weeks</td>
<td><strong>Topical</strong>&lt;br&gt;- Nystatin-triamcinolone (Mycolog II) ointment applied on the affected areas after meals and at bedtime&lt;br&gt;- Clotrimazole 1% (Mycelex) cream&lt;br&gt;- Miconazole 2% cream applied q12h on the affected areas, for 1-2 weeks</td>
<td>• Lesions tend to heal slowly because of the repeated opening of the mouth.</td>
</tr>
<tr>
<td>Herpes Simplex Virus (HSV) Infection</td>
<td><strong>Systemic</strong>&lt;br&gt;- Acyclovir (Zovirax) 800 mg PO q4h, for 10 days&lt;br&gt;- Foscarnet 24-40 mg/kg PO q8h, for resistant herpetic lesions</td>
<td><strong>Systemic</strong>&lt;br&gt;- Acyclovir 10 mg/kg PO q6h or q8h&lt;br&gt;- Foscarnet 24-40 mg/kg PO q8h, for resistant herpetic lesions</td>
<td>• Ganciclovir, Valacyclovir and Famciclovir are probably effective.&lt;br&gt;• Foscarnet is the drug of choice for Acyclovir-resistant cases.&lt;br&gt;• Patients taking Acyclovir should be instructed to drink plenty of fluids.&lt;br&gt;• Topical antiviral medications may be used for labial and perioral herpetic lesions.</td>
</tr>
<tr>
<td>Linear Gingival Erythema (LGE)</td>
<td><strong>Local</strong>&lt;br&gt;- Scaling and root planing&lt;br&gt;- 0.12% Chlorhexidine gluconate (Periogard, Periex) 0.5 oz q12h rinse, for 30 sec. and spit</td>
<td><strong>Local</strong>&lt;br&gt;- Scaling and root planing&lt;br&gt;- 0.12% Chlorhexidine gluconate (Periogard, Periex) 0.5 oz q12h rinse, for 30 sec. and spit</td>
<td>• Prophylaxis is recommended: brushing, flossing, and use of mouth rinses.&lt;br&gt;• Antifungal agents may be useful in the treatment of LGE.</td>
</tr>
<tr>
<td>Xerostomia</td>
<td><strong>Topical</strong>&lt;br&gt;- Chewing or sucking sugarless candy&lt;br&gt;- Frequent sips of water&lt;br&gt;- Commercial artificial saliva substitutes&lt;br&gt;- Topical fluoride products&lt;br&gt;- Pilocarpine (Salagen) 5 mg PO q8h before meals; it may increase to 7.5 mg PO q8h</td>
<td><strong>Topical</strong>&lt;br&gt;- Chewing or sucking sugarless candy&lt;br&gt;- Frequent sips of water&lt;br&gt;- Commercial artificial saliva substitutes&lt;br&gt;- Topical fluoride products</td>
<td>• Good oral hygiene measures and diet control (control of sugar and sugary foods) are recommended to prevent dental caries.&lt;br&gt;• Mouth rinses with high alcohol content should be avoided due to drying effect.</td>
</tr>
<tr>
<td>Parotid Enlargement (of major salivary glands)</td>
<td><strong>Systemic</strong>&lt;br&gt;- Non-steroidal anti-inflammatories&lt;br&gt;- Analgesics&lt;br&gt;- Antibiotics&lt;br&gt;- Steroids</td>
<td><strong>Systemic</strong>&lt;br&gt;- Non-steroidal anti-inflammatories&lt;br&gt;- Analgesics&lt;br&gt;- Antibiotics&lt;br&gt;- Steroids</td>
<td>• Surgical removal of the parotid gland may be necessary for esthetic reasons.</td>
</tr>
</tbody>
</table>
### Table 3 Continued: Therapeutic Options for the Most Common HIV-Associated Oral Manifestations

<table>
<thead>
<tr>
<th>Oral Lesion</th>
<th>Treatment for Adults</th>
<th>Treatment for Children</th>
<th>Comments</th>
</tr>
</thead>
</table>
| **Oral Hairy Leukoplakia (OHL)** | • Podophyllin resin 25% 1-2 applications on the affected areas, at 1 week apart  
• Retinoic acid (Tretinoin)  
• Surgical excision  
**Systemic**  
• Acyclovir (Zovirax) 800 mg PO q4h or q6h, for 14 days  
• Famciclovir 500 mg PO q8h, for 5-10 days  
• Valacyclovir 1000 mg PO q8h, for 5-10 days | **Local**  
• Podophyllin resin 25% 1-2 applications on the affected areas, at 1 week apart  
• Retinoic acid (Tretinoin)  
• Surgical excision  
**Systemic**  
• Acyclovir (Zovirax) 800 mg PO q4h or q6h, for 14 days  
• Famciclovir 500 mg PO q8h, for 5-10 days  
• Valacyclovir 1000 mg PO q8h, for 5-10 days | • Recurrence often occurs after the treatment is discontinued.  
• OHL is rare in children. Symptomatic and extensive lesions may require topical treatment.  
• OHL has been shown to disappear in patients receiving zidovudine (AZT). |
| **Necrotizing Ulcerative Gingivitis (NUG), Necrotizing Ulcerative Periodontitis (NUP), Necrotizing Stomatitis (NS)** | **Local**  
• Debridement of affected areas  
• Irrigation with povidon-iodine (10% Betadine)  
• 0.12% chlorhexidine gluconate (Periex, Periogard) mouth rinse q12h  
**Systemic**  
• Metronidazole (Flagyl) 250 mg PO q6h or 500 mg q12h, for 7-10 days  
• Clindamycin (Cleocin) 150 mg PO q6h or 500 mg PO q8h, for 7 days  
• Amoxicillin clavulanate (Augmentin) 250 mg PO q12h, for 7 days | **Local**  
• Debridement of affected areas  
• Irrigation with povidon-iodine (10% Betadine)  
• 0.12% chlorhexidine gluconate (Periex, Periogard) mouth rinse q12h  
**Systemic**  
• Metronidazole (Flagyl) 15-35 mg/kg PO q8h, for 7-10 days  
• Clindamycin (Cleocin) 20–30 mg/kg PO q6h, for 7 days  
• Amoxicillin clavulanate (Augmentin) 40 mg/kg PO q8h, for 7 days | • Prolonged use of chlorhexidine may cause staining of teeth, tongue, and restorations; taste alteration; and mucosal desquamation and irritation.  
• Metronidazole should not be given to patients taking didanosine (ddI) or zalcitabine (ddC), because it may potentiate peripheral neuropathy. |
| **Oral Ulcers (Recurrent Aphthous Ulcers)** | **Topical**  
• Triamcinolone in Carboxymethylcellulose 0.1% paste  
• Betamethasone phosphate:  
• 0.5 mg tablet dissolved in 10 ml mouthwash and rinse q4h  
• spray on ulcer (1 spray = 100 µg) up to 800 µg  
• Fluocinonide (Lidex) 0.05% ointment applied on ulcer q4h  
• Dexamethasone elixir (0.5 mg/5ml) rinse and expectorate  
**Systemic**  
• Prednisone starting at 30-40 mg PO daily with taper over 1 month for severe disease resistant to topical agents  
• Thalidomide 200 mg PO daily | **Topical**  
• Triamcinolone in Carboxymethylcellulose 0.1% paste applied in a thin layer q6h daily  
• Betamethasone phosphate:  
• 0.5 mg tablet dissolved in 10 ml mouthwash and rinse q4h  
• spray on ulcer (1 spray = 100 µg) up to 800 µg  
• Fluocinonide (Lidex) 0.05% ointment q4h  
• Dexamethasone elixir (0.5 mg/5ml) rinse and expectorate  
**Systemic**  
• Prednisone 2 mg/kg q6h, for 5–7 days with gradual tapering | • Major aphthous ulcers usually require systemic steroids.  
• Aphthous ulcers may be exacerbated by stress.  
• Iron, vitamin B12, and folate deficiencies should be ruled out.  
• Dexamethasone elixir should be used for multiple ulcers or ulcers not accessible for topical application.  
• Thalidomide is indicated only when recurrences are severe and frequent.  
• The treatment with Thalidomide should be monitored thoroughly due to its teratogenicity. Birth control measures are required. |
| **Oral Warts** | **Topical**  
• Podophyllin resin 25% applications q6h for long period  
• Surgical excision  
• Laser ablation  
• Cryotherapy  
**Systemic**  
• Cimetidine (Tagamet) 600 mg PO q6h, for long period (months)  
• Interferon alfa–n3 SC/IM 3,000,000 U (1 ml) qwk, for several weeks | **Topical**  
• Podophyllin resin 25% applications q6h for long period  
• Surgical excision  
• Laser ablation  
• Cryotherapy | • The recurrence rate is high.  
• Concurrent therapeutic approaches should be considered. |

**Abbreviations used in Table 3:**  
PO = per os (by mouth); IV = intravenous; qd = every day; qwk = every week; q2h = every two hours; q4h = every four hours; q6h = every six hours; q8h = every 8 hours; q12h = every 12 hours.
lesions (1-2 mm) disseminated on the soft palate, tonsils, tongue, and/or buccal mucosa.

**Treatment:** The first line of management of RAUs is pain control and prevention of superinfection. Depending on the severity of the ulcers, topical and/or systemic steroid agents are recommended (Table 3).

**Parotid Enlargement and Xerostomia**
Parotid enlargement is commonly associated with HIV infection in children (10-30 percent), and less commonly in adults. It has been shown to occur in the late course of HIV infection and to be associated with a slower rate of HIV disease progression. The median time from its diagnosis to death has been reported to be 5.4 years among HIV-infected children. Lymphocytic infiltration of the salivary glands may be an etiologic factor.

**Clinical appearance:** Parotid enlargement occurs as unilateral or bilateral swelling of the parotid glands. It is usually asymptomatic and may be accompanied by decreased salivary flow (xerostomia or dry mouth). Problems with dry mouth in HIV-infected patients are often caused by medications that interfere with salivary secretion, such as antihistamines, anti-anxiety medications, antidepressants, and some antiretroviral drugs (didanosine and zalcitabine).

**Treatment:** Treatment is required only in severe cases and may consist of systemic analgesics, anti-inflammatory agents, antibiotics, and/or steroids (Table 3).

**Human Papillomavirus (HPV) Infection (Oral Warts)**
The incidence of oral warts due to human papillomavirus (HPV) infection has increased dramatically since the advent of HAART. The lesions are more prevalent in adults (1-4 percent of cases) than in children.

**Clinical appearance:** Oral warts may appear cauliflower-like, spiked, or raised with a flat surface. They are asymptomatic. The most common location is the labial and buccal mucosa. The most common clinical presentation is multifocal flat lesions resembling focal epithelial hyperplasia (Heck’s disease).

**Treatment:** Treatment may be required for patients with multiple lesions. Topical and systemic agents and various surgical approaches are available (Table 3).

**General Management Considerations**
To prevent the need for expensive dental services, it is imperative to treat the oral manifestations of HIV infection at all levels of care. Personal oral-hygiene practices, such as tooth brushing and use of interdental cleaning aids, are the most effective ways of maintaining good oral health.

At the primary level of oral care, prevention of oral diseases takes priority. This involves improving oral-hygiene awareness through health education at the individual and community levels. Oral-health education messages should be made visible in all community forums. Home-based care providers should undergo training in basic oral hygiene practices so that they can impart these to patients under their care. Use of simple materials such as warm salty mouth rinse or commercial mouthwash (chlorhexidine) can improve basic oral hygiene cost-effectively. Patients whose manual dexterity is intact should be taught appropriate brushing techniques. Other adjuvant oral-hygiene methods, such as flossing and use of interdental toothbrushes, will depend on the availability and affordability of supplies.

The secondary level of oral care involves visits to clinical-care facilities. Depending on local resources, the health cadre available at this level may range from nursing staff at a health center to primary-care physicians. In some countries, health centers may have no oral-health personnel or may offer only relief of pain with analgesics and extractions. Health care workers at this level should be trained to recognize suspicious lesions that may be oral manifestations of
HIV infection, and they should know when and where to refer patients to a higher level of oral care. At the tertiary level of oral care, a dentist should be available to make definitive diagnoses of oral lesions and provide professional oral services such as prophylaxis, restorations, biopsies, and the prescription of appropriate medication.

Acknowledgment
We would like to thank Professor Sudeshi Naidoo, Department of Community Dentistry, Faculty of Dentistry and WHO Collaborating Centre, University of the Western Cape, South Africa, for providing the pictures of oral lesions used in this chapter.

Case Studies

Case Study #1
A 36-year-old HIV-infected woman comes to the clinic complaining of constant oral pain for almost two months. She is unable to eat and drink and has lost 10 pounds (4.5 kg). Her CD4+ cell count is 85 cells/mm³. The oral exam shows a large ulcer (1.5 cm in diameter) on the soft palate, with an erythematous halo and covered by pseudomembranes.

Question: The most likely diagnosis is:
   a. Pseudomembranous candidiasis
   b. Major aphthous ulcer
   c. Herpes simplex virus infection
   d. Oral hairy leukoplakia

Answer: a. Major aphthous ulcers are 1-3 cm in diameter, covered by pseudomembranes, and localized on the soft palate, labial and buccal mucosa, and/or ventral aspect of the tongue. Pseudomembranous candidiasis presents as white plaques on the palate, dorsum of the tongue, and/or buccal mucosa. Herpes simplex virus infection appears as irregular, painful ulcerations localized on the hard palate and gingiva. Oral hairy leukoplakia is characterized by the presence of white or gray non-removable patches on the lateral margins of the tongue.

Case Study #2
A 28-year-old graduate student complains to his doctor that he has been experiencing bleeding gums, pain, and bad breath for two weeks. An oral examination reveals numerous mobile teeth and extensive gingival tissue loss. He has not been on HIV medications since his diagnosis three years earlier.

Question: The most likely diagnosis is:
   a. Noma
   b. Necrotizing ulcerative gingivitis (NUG)
   c. Necrotizing ulcerative periodontitis (NUP)
   d. Oral hairy leukoplakia

Answer: c. NUP is characterized by extensive and rapid soft tissue loss and loss of teeth. NUG presents as ulcerations, sloughing, and necrosis of interdental papillae and is confined to the gingival tissue. Noma is a gangrenous condition that involves soft and hard tissues of the mouth and may be a consequence of NUG. Oral hairy leukoplakia presents as white or gray thick patches that do not wipe away, usually along the lateral margins of the tongue.
Review Questions

1. Describe the most common oral manifestations of HIV infection in adults.

2. Describe the most common oral manifestations of HIV infection in children.

3. Briefly describe the clinical significance of the presence of oral lesions in HIV infection.

Exam Questions

1. Which of the following is not used for treatment of oral candidiasis in both adults and children?
   a. Acyclovir
   b. Clotrimazole 1% ointment
   c. Ketoconazole
   d. Fluconazole

2. Clinically, oral hairy leukoplakia appears as:
   a. Irregular ulcers localized on the keratinized mucosa (hard palate, gingiva)
   b. Erythematous fissures at the corners of the mouth
   c. White, thick, non-removable patches on the lateral margins of the tongue
   d. Bilateral swelling of the parotid glands

3. Which of the following is a clinical presentation of oral candidiasis in HIV-infected patients?
   a. Pseudomembranous
   b. Erythematous
   c. Angular cheilitis
   d. Hyperplastic
   e. All of the above

4. Which of the following is not true of pseudomembranous candidiasis?
   a. It is commonly referred to as oral thrush.
   b. It is the most common type of oral lesion seen in HIV infection.
   c. The most common site is the lips.
   d. It is easily wiped off.

5. Which of the following is not true of oral manifestations of HIV infection?
   a. They are signs of HIV infection.
   b. They are symptoms of HIV infection.
   c. They are not predictors of HIV disease progression.
   d. They are used in the classification and staging of HIV disease.

Answers: 1a, 2c, 3e, 4c, 5c
Case Study #3

A 6-year-old vertically HIV-infected child presents at the clinic with a white extensive lesion on the dorsum of the tongue and buccal mucosa that is accompanied by a burning sensation. He has not been very compliant with HAART. His last CD4+ cell count (two months earlier) was 352 cells/mm³. On clinical examination, the lesion is easily wiped off, revealing a raw surface.

Question: **What is the most likely diagnosis?**

- a. Oral hairy leukoplakia
- b. Herpes simplex virus infection
- c. Pseudomembranous candidiasis
- d. Necrotizing stomatitis

**Answer:** c. Pseudomembranous candidiasis appears as creamy white plaques that can be easily wiped off, revealing a raw erythematous surface. Oral hairy leukoplakia is characterized by white thick patches that do not wipe away, on the lateral margins of the tongue. Herpes simplex virus infection presents as a crop of vesicles on the keratinized mucosa. Necrotizing stomatitis appears as an extensive ulceronecrotic lesion on the oral mucosa that exposes the underlying alveolar bone.

Question: **What is the first line of treatment of this oral lesion?**

- a. Topical antifungal treatment only
- b. Systemic antifungal treatment only
- c. Both topical and systemic antifungal treatment

**Answer:** c. Taking into account the general status of the child and the clinical presentation of the oral lesion, concurrent topical and systemic antifungal treatment is recommended for 10-14 days.

References


Objective

The purposes of this module are to:
1. Describe the types of malignancies commonly found in children and adolescents with HIV/AIDS.

Key Points

1. Children with HIV are at increased risk of developing certain malignancies.
2. The most common malignancy found in U.S. children with HIV/AIDS is non-Hodgkin's lymphoma.
3. Regional variations in the prevalence of HIV-associated malignancies exist.
4. Treatment for HIV-associated malignancies may be complicated by HIV-associated organ dysfunction, infectious complications, and drug interactions between chemotherapy treatments and antiretroviral drugs.

Overview

Evidence of the relationship between HIV and cancer became evident early in the HIV/AIDS epidemic. In 1981, the U.S. Centers for Disease Control and Prevention (CDC) described a clustering of cases of Kaposi's sarcoma, until then a rare form of cancer, among homosexual men in New York and California. The following year, CDC reported a clustering of cases of gay men in San Francisco with diffuse, undifferentiated non-Hodgkin's lymphoma (NHL), another rare cancer. In time, it became apparent that these unusual forms of cancer were appearing as a result of infection with HIV. However, this association would not be limited to these two forms of malignancy. Numerous other neoplastic disorders, most notably primary central nervous system (CNS) lymphoma, leiomyosarcoma, and cervical cancer, have also been linked to HIV infection.

This module will discuss the relationship between HIV and malignancy, with special attention to the tumors most commonly seen in the pediatric and adolescent populations. An overview of the epidemiology of HIV-related malignancy will be followed by discussions of the pathogenesis, clinical manifestations, and treatment of each of these tumors.

Epidemiology and Pathogenesis

Numerous studies have shown that malignancy occurs much more commonly in HIV-infected children than in uninfected children. HIV-infected children are at about 40 times higher risk of developing malignancy than the general population. Among HIV-infected children in the United States, the incidence of
malignancy is about 1 case per 1000 children per year. In contrast, the incidence of cancer among all U.S. children is about 1-2 cases per 10,000 per year.

Children with HIV also have a predilection for developing very rare tumors. In the general U.S. pediatric population, leukemia and brain tumors make up the vast majority of new cases of malignancy each year. However, among U.S. children infected with HIV, NHL is the most common type of cancer, followed by Kaposi's sarcoma and leiomyosarcoma.1-4

In response to this epidemiologic data, the CDC has added NHL, primary CNS lymphoma, and Kaposi's sarcoma to the list of Category C symptoms (or AIDS-defining illnesses) for children and has added leiomyosarcoma to the list of Category B symptoms. (See the chapter “HIV/AIDS Diagnostic Criteria” for a discussion of the CDC clinical categories.)

In addition, studies show that invasive cervical cancer occurs much more commonly in female HIV-infected adolescents (and adults) than in the general population. As a result, the CDC has included invasive cervical cancer as a Category C symptom (or AIDS-defining illness) for HIV-infected adolescents (and adults) and has added cervical dysplasia (moderate to severe) and non-invasive cervical carcinoma to the list of Category B symptoms for adolescents (and adults).

Though not listed in the CDC revised classification system, cancers such as Hodgkin's disease, anal cancer, lung cancer, lip cancer, and testicular cancer are also more common in the setting of HIV infection.1,5-7

The incidence of cancer is lower among children with HIV than among adults with HIV (0.1 percent per year versus 4 percent per year). Furthermore, the relative incidence of specific cancers differs between children and adults. For example, in the United States, Kaposi's sarcoma is the most common HIV-associated cancer in adults with HIV, whereas it is much less common in children with HIV. In contrast, leiomyosarcoma is found more commonly among children than among adults with HIV.7

Regional variations in the prevalence of pediatric HIV-related malignancy exist. While NHL has been found to be the most common pediatric HIV-related malignancy in the United States, studies have shown that Kaposi's sarcoma remains the most common pediatric HIV-related malignancy in sub-Saharan Africa. Why these differences exist is not entirely clear. However, some data shows that the prevalence of human herpes virus 8 (HHV-8), the virus necessary for the development of Kaposi's sarcoma, is much higher in central Africa than in the United States.

The pathogenesis of HIV-related malignancy is related to a number of factors. HIV weakens the immune system, thus diminishing the body's innate tumor-surveillance capacity, much in the way that immunosuppressive agents put transplant patients at risk of malignancy. Furthermore, viruses such as the Epstein-Barr virus (EBV), human papilloma virus (HPV), and HHV-8 interact with HIV to create an environment that enhances tumor growth. The relationship between HIV-related malignancy and certain viruses is well-established. For example, nearly every case of Kaposi's sarcoma is linked with the presence of HHV-8, and nearly every case of HIV-

### Table 1: Site-Dependent Symptoms of Non-Hodgkin’s Lymphoma

<table>
<thead>
<tr>
<th>Mediastinal or Pharyngeal Tumor</th>
<th>Abdominal Tumor</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Tachypnea</td>
<td>• Abdominal distention</td>
</tr>
<tr>
<td>• Nasal flaring</td>
<td>• Ascites</td>
</tr>
<tr>
<td>• Retractions</td>
<td>• Palpable abdominal mass</td>
</tr>
<tr>
<td>• Decreased breath sounds</td>
<td>• Jaundice</td>
</tr>
<tr>
<td>• Cough</td>
<td>• Pain</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Central Nervous System Disease</td>
<td>Maxillofacial Tumor</td>
</tr>
<tr>
<td></td>
<td>• Jaw mass</td>
</tr>
<tr>
<td>• Headache</td>
<td>• Numbness of the chin (peripheral facial nerve compression)</td>
</tr>
<tr>
<td>• Vomiting</td>
<td>• Asymmetric facial expression</td>
</tr>
<tr>
<td>• Visual disturbances</td>
<td></td>
</tr>
<tr>
<td>• Gait instability</td>
<td></td>
</tr>
<tr>
<td>• Developmental delay</td>
<td></td>
</tr>
<tr>
<td>• Cranial nerve palsies</td>
<td></td>
</tr>
<tr>
<td>• Hemiparesis</td>
<td></td>
</tr>
<tr>
<td>• Seizures</td>
<td></td>
</tr>
</tbody>
</table>
related primary CNS lymphoma is linked with the presence of EBV infection. Additionally, EBV is frequently isolated from HIV-related leiomyosarcoma, systemic NHL, and Hodgkin’s disease.\textsuperscript{1-3}

Common Types of Cancers Diagnosed in Children and Adolescents With HIV Infection

Non-Hodgkin’s Lymphoma (NHL)\textsuperscript{4-10}

NHL accounts for about 7 percent of cancers among all U.S. children less than 20 years of age. In contrast, NHL is one of the most common types of malignancy among HIV-infected children, accounting for more than 80 percent of HIV-related cancers. HIV-infected children most commonly develop Burkitt’s (small non-cleaved cell) lymphoma and immunoblastic (large cell) lymphoma.

Clinical Presentation: HIV-infected children who are diagnosed with NHL often have extra-nodal disease (disease spread outside the lymph nodes) at the time of presentation. At diagnosis, the cancer will likely have already metastasized to such places as the brain, bone marrow, and gastrointestinal tract.

Symptoms of cancer can be indistinguishable from symptoms of chronic HIV infection, and NHL is no exception. Symptoms such as fever, fatigue, weight loss, night sweats, anorexia, hepatosplenomegaly, and lymphadenopathy may reflect underlying HIV infection, but they may also reflect the presence of lymphoma. Organ-specific symptoms are numerous (see Table 1).

Diagnosis and Staging: Diagnosis of NHL is made through biopsy of affected tissue. Staging involves the use of CT scans (particularly of the head, abdomen, and pelvis), bone-marrow biopsy, and cerebrospinal fluid (CSF) analysis.

Studies show that prognosis is better in patients with CD4+ counts greater than 100 per mm\textsuperscript{3}, a near-normal serum lactate dehydrogenase (LDH) level, no history of opportunistic infections, and a good performance status (i.e. the ability to function in a near-normal capacity during daily activities).\textsuperscript{5}

Treatment: Current first-line treatment for NHL consists of CHOP, a chemotherapy regimen that combines cyclophosphamide, hydroxydaunomycin (also known as doxorubacin), oncovin (also known as vincristine), and prednisone (a type of steroid). Because HIV-related NHL frequently has already spread to the brain, treatment often includes CNS prophylaxis with intrathecal (chemotherapy placed within the spinal fluid) methotrexate or cytarabine (see Table 2).

Primary CNS Lymphoma

Primary CNS lymphoma (PCNSL) is a subtype of NHL that is limited to the brain tissue. PCNSL is much more common in HIV-infected children than in uninfected children. The differential diagnosis of CNS lymphoma includes opportunistic infections such as toxoplasmosis or cryptococcosis. Unlike adults with
HIV, where toxoplasmosis is the most common cause of a brain mass, PCNSL is the most common cause of an isolated brain mass in HIV-infected children. PCNSL should be suspected in any HIV-infected child with neurologic abnormalities accompanied by mass lesions on a CT scan or MRI of the brain. While about 30 percent to 50 percent of HIV-related systemic lymphomas are associated with EBV, HIV-related PCNSL appears to have a near 100 percent association with EBV.

**Diagnosis:** Diagnosis of PCNSL often begins with cytological assessment of the CSF for malignant cells. These cells are present in up to 23 percent of patients. Analysis of CSF for the presence of EBV DNA using PCR is also very useful in suggesting the presence of PCNSL. Definitive diagnosis of PCNSL requires a brain biopsy. Assessment of serum for toxoplasma IgG can help in determining the likelihood of CNS infection with toxoplasmosis. Negative titers make toxoplasmosis an unlikely diagnosis.

**Treatment:** Treatment for PCNSL involves either the use of whole-brain radiation or high-dose methotrexate. Unfortunately, prognosis remains poor for this tumor. Without treatment, survival is less than one month; with treatment, survival is two to four months.

**Lymphoproliferative Disorders**
Studies show that children with HIV are at high risk of developing lymphoproliferative disorders. Examples include lymphoid interstitial pneumonitis (LIP), pulmonary lymphoid hyperplasia (PLH), diffuse interstitial lymphocytosis syndrome (DILS), and mucosa-associated lymphoid tumors (MALTs).

**Smooth-Muscle Tumors**
Leiomyomas/leiomyosarcomas occur very rarely in children without HIV infection. The incidence of leiomyosarcoma is estimated to be only two cases per 10 million children annually. However, with the onset of the AIDS epidemic, increased numbers of leiomyomas/leiomyosarcomas have been reported in HIV-infected children. One large case series of HIV-infected children with cancer reported that 17 percent of their patients had leiomyomas/leiomyosarcomas. This increased incidence in HIV-infected children has

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**Table 2: Chemotherapy Agents Used in the Treatment of NHL**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Cyclophosphamide</th>
<th>Vincristine</th>
<th>Doxorubicin</th>
<th>Methotrexate</th>
<th>Cytarabine</th>
<th>Prednisone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class</td>
<td>Alkalating agent</td>
<td>Plant alkaloid</td>
<td>Anthracycline antibiotic</td>
<td>Antimetabolite; folic acid antagonist</td>
<td>Antimetabolite</td>
<td>Corticosteroid</td>
</tr>
<tr>
<td>Action</td>
<td>• Prevents DNA synthesis and cell division</td>
<td>• Disrupts mitosis; Cell cycle phase specific for M phase and active in S phase</td>
<td>• Inhibits DNA, DNA-dependent RNA, and protein synthesis</td>
<td>• Inhibits conversion of folic acid to tetrahydrofolic acid, which inhibits DNA synthesis</td>
<td>• Slows DNA synthesis</td>
<td>• Causes lysis of lymphoid cells</td>
</tr>
<tr>
<td></td>
<td>• Cell cycle phase nonspecific*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Increases likelihood that cell cycle specific agents will work better</td>
</tr>
<tr>
<td>Potential Side Effects</td>
<td>• Bone-marrow suppression</td>
<td>• Peripheral neuropathy</td>
<td>• Bone-marrow suppression</td>
<td>• Bone-marrow suppression</td>
<td>• Bone-marrow suppression</td>
<td>• Gastric irritation</td>
</tr>
<tr>
<td></td>
<td>• Hemorrhagic cystitis</td>
<td>• Constipation</td>
<td>• Cardiac dysfunction</td>
<td>• Nausea and vomiting</td>
<td>• Nausea and vomiting</td>
<td>• Hyperglycemia</td>
</tr>
<tr>
<td></td>
<td>• Nausea and vomiting</td>
<td>• Alopecia</td>
<td>• Nausea and vomiting</td>
<td></td>
<td></td>
<td>• Sodium and water retention</td>
</tr>
<tr>
<td></td>
<td>• Stomatitis</td>
<td></td>
<td>• Stomatitis</td>
<td></td>
<td></td>
<td>• Weight gain</td>
</tr>
<tr>
<td></td>
<td>• Alopecia</td>
<td></td>
<td>• Alopecia</td>
<td></td>
<td></td>
<td>• Behavioral changes (mood swings), hypertension</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Adrenal suppression</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Immune suppression</td>
</tr>
</tbody>
</table>

* Kills both resting and dividing tumor cells
led the CDC to classify leiomyosarcoma as a Category B symptom. Interestingly, there has not been a parallel rise in the incidence of leiomyosarcoma in HIV-infected adults.

The etiology of HIV-related leiomyosarcoma is unknown. However, EBV has been isolated in relatively high titers from leiomyosarcomas in pediatric patients with HIV. In addition, it has been noted that these tumors present relatively late in the course of children with AIDS, suggesting a role of chronic immune suppression in tumor pathogenesis.

**Clinical Presentation:** Leiomyosarcoma most commonly presents within the gastrointestinal tract. Children with HIV, however, may present with tumors in unusual locations, such as the lungs, spleen, adrenal glands, pleural space, or intracranially. The course of the disease is variable, with slow-growing tumors often not requiring intervention while more aggressive, disseminated tumors require multi-modal treatment with surgery and chemotherapy.

Gastrointestinal lesions may cause abdominal pain, rectal bleeding with anemia, abdominal masses, and bowel obstruction. Children with lung disease may appear cyanotic (blue around the face or lips). Respiratory insufficiency may be related to bronchial obstruction causing wheezing, or secondary to persistent respiratory infections. Chest radiography often shows multiple pulmonary nodules. Children with brain lesions often show signs of increased intracranial pressure, such as nausea, vomiting, and headaches. Other neurologic findings may also be present, such as visual disturbances, gait instability, and difficulty with coordination.

**Treatment:** Because smooth-muscle tumors are not particularly responsive to chemotherapy or radiotherapy, surgery is the treatment of choice. When surgery fails or is not an option, treatment involves chemotherapy with the VACA regimen (vincristine, adriamycin, cytoxan, and dactinomycin) alternating with ifosfamide and etoposide over the course of a year. Chemotherapy is sometimes given with radiation therapy.

**Kaposi’s Sarcoma**

From its original description in 1872 until the onset of the AIDS epidemic, Kaposi’s sarcoma was a rare illness found mainly among elderly Eastern European Jews, transplant patients, and certain populations of central Africa.

Though Kaposi’s sarcoma is well-described in children with HIV infection, it is much more common among HIV-infected adults, in particular among homosexual men. In Western nations, Kaposi’s sarcoma is rarely the first sign of HIV infection in children. In the United States, Kaposi’s sarcoma is the first AIDS-defining condition in less than 1 percent of children less than 15 years of age.

In other parts of the world, particularly central and eastern Africa, the incidence is much higher. In Uganda, for example, Kaposi’s sarcoma accounts for nearly 20 percent of all pediatric cancers. Since 1986, the incidence of Kaposi’s sarcoma in Uganda has risen by 14 percent.

**Pathogenesis:** Immunosuppression is believed to be an integral factor in the pathogenesis of Kaposi’s sarcoma. An increased incidence of Kaposi’s sarcoma is found in other immunosuppressed patients, in particular among transplant patients receiving immunosuppressive agents. Recent data has also revealed a strong link between underlying infection with HHV-8 and the development of Kaposi’s sarcoma. HHV-8 has also been implicated in the pathogenesis of other neoplastic conditions, such as primary effusion lymphoma (a rare
form of NHL also known as body cavity lymphoma) as well as multi-centric Castleman’s disease (a rare disorder of the lymph nodes).

**Clinical Presentation:** Kaposi’s sarcoma most commonly affects the skin and oral mucosa. Its lesions are often found on the tip of the nose, trunk, arms, or neck, or in the mouth. On patients with dark skin, the lesions appear as dark plaques or nodules. On lighter-skinned people, the lesions are reddish-purple or brownish. Skin lesions may first appear as erythematous macules, but over time they darken and become raised or nodular. Cutaneous lesions, specifically of the lower extremities, have been associated with peripheral edema, which can be quite debilitating. Close to 30 percent of patients with Kaposi’s sarcoma also have lesions of the oral mucosa, most commonly on the hard palate. As these lesions grow, they may interfere with eating and speaking.

The differential diagnosis for cutaneous Kaposi’s sarcoma lesions includes hemangiomomas, nevi, dermatofibromas, and bacillary angiomatosis. Distinguishing bacillary angiomatosis (BA) from Kaposi’s sarcoma is particularly important, because BA is caused by gram-negative bacteria (a Bartonella species) and thus may be readily treated with antibiotics. When necessary, performing a punch biopsy will help in making the correct diagnosis.

In addition to causing skin disease, Kaposi’s sarcoma may spread to the lymphatic system, the lungs, and the digestive tract. A physical exam may reveal lymphadenopathy (enlarged lymph nodes), which may be firm and non-tender. Lesions in the oral mucosa often correlate with the presence of other gastrointestinal lesions. These lesions may be asymptomatic (often found at autopsy) or can lead to such problems as diarrhea and rectal bleeding. Metastases to the lungs may cause shortness of breath or hemoptysis (bloody cough). Though less common, some patients may present with pulmonary or gastrointestinal Kaposi’s sarcoma with no apparent skin lesions.

**Treatment of Localized Disease:** Recent data indicates that most forms of Kaposi’s sarcoma will regress with the initiation of highly active antiretroviral therapy (HAART), with response rates of 60 percent to 80 percent. Thus, treatment with antiretrovirals should always be incorporated in the treatment of Kaposi’s sarcoma.

For patients who do not respond adequately to antiretroviral therapy alone, other forms of treatment have been shown to be effective. Isolated lesions on the skin or in the mouth can be treated with alitretinoin gel, intralesional vinblastine, liquid nitrogen, laser ablation, or radiotherapy.

Subcutaneous alpha interferon has been used in children with early disease. Though capable of inducing clinical responses in 32 percent to 40 percent of patients, interferon is often complicated by the development of flu-like symptoms, such as fever, chills, headaches, and myalgias. Nonsteroidal anti-inflammatory agents may help ameliorate some of these symptoms.

**Treatment of Diffuse Disease:** For patients with widespread cutaneous disease or organ involvement, systemic chemotherapy is often required. Currently, the treatment of choice is liposomal doxorubicin or liposomal daunorubicin. Recent studies have shown them to be more effective and less toxic than combination chemotherapy, which usually includes doxorubicin, vincristine, and bleomycin and which until recently was the standard of care. Side effects of liposomal doxorubicin and daunorubicin include myelosuppression and alopecia. Liposomal doxorubicin has also been associated with hand-foot syndrome (painful erythema and desquamation of the palms and soles).

When liposomal agents fail, paclitaxel (Taxol) is often used next. Response rates of 70 percent to 90 percent have been reported. Paclitaxel has been associated with myelosuppression, alopecia, peripheral neuropathy, and hypersensitivity reactions.

Though treatment of Kaposi’s sarcoma has evolved tremendously since the onset of the HIV epidemic,
there is no effective cure for this cancer. The goal of treatment should be the palliation of symptoms.

**Cervical Cancer**

Cervical cancer has been reported to be the second-most-common cancer in women worldwide. Furthermore, HIV-infected women develop cervical cancer more often than non-HIV-infected women. Studies show that for women with HIV, the risk of developing invasive cervical cancer is five to nine times as high as for women without HIV. Because of this increased risk in HIV-infected women, the CDC has added invasive cervical cancer to the list of AIDS-defining illnesses for adolescents (and adults) and has added moderate to severe cervical dysplasia and cervical carcinoma in situ to the list of Category B symptoms for these age groups.

**Pathogenesis:** HPV is a sexually transmitted virus that has been implicated in the development of cervical cancer. HPV is found in more than 99 percent of cervical-cancer specimens; types 16 and 18 make up more than 60 percent of these oncogenic HPV subtypes.

Compared to HIV-negative women, HIV-infected women are more likely to be infected with HPV, more likely to be infected with multiple types of HPV, and more likely to have persistent HPV infection. In addition, HIV-positive women are more likely to develop cervical dysplasia when infected with HPV than are women who are HIV-negative. Several studies comparing women with cervical dysplasia found that risk factors for dysplasia included HIV-positive serostatus, persistent HPV infection, and a low CD4+ count (<200/µL).

**Screening and Prevention:** The Papanicolaou (Pap) smear is an important screening tool for early detection of cervical cancer in all sexually active women. Most preventive health guidelines recommend that all sexually active adolescents obtain yearly Pap smears. However, because of the heightened risk of cervical cancer in HIV-positive women, both the U.S. Public Health Service and the Infectious Diseases Society of America recommend Pap smears every six months for all HIV-infected women during the first year after HIV diagnosis, with yearly Pap smears thereafter if the initial two smears are negative.

Conventional Pap smears have been found to be as sensitive and specific in women with HIV as in women without HIV. HPV DNA tests of cervical cell scrapings are not recommended as a screening tool, although they may assist in triaging women without HIV to colposcopy in the presence of low-grade squamous intraepithelial lesions (LGSIL).

While HPV is sexually transmitted, male condoms have not been found to decrease HPV transmission to women. Male condoms may offer a protective benefit to men, but study results have been conflicting and often confounded. Data on female condoms and spermicides is scant. Unlike other bacterial and viral sexually transmitted infections, including HIV, HPV also infects external genital tissue, which may account for the lack of protection via barrier methods. While barrier and microbicidal methods may theoretically decrease viral exposure, they have not been proven to have a protective effect.

The ultimate primary prevention of genital HPV may be a vaccine, one of which was in Phase III clinical trials in 2004.

**Management of Abnormal Pap-Smear Results:** Pap smears that are abnormal often require further investigation with colposcopy. This is especially true for women infected with HIV. For example, HIV-infected women are more likely (more than 10 percent) to have high-grade squamous intraepithelial lesions (HGSIL) on workup of ASCUS than are women who are HIV negative, and therefore even ASCUS should be colposcopically evaluated in HIV-positive women, regardless of HPV status. Colposcopy in this setting should be used to examine the vagina and vulva in addition to the cervix, given the increased risk of other genital-tract dysplasias and cancers in HIV-positive women.
Dysplasia, specifically LGSIL that persists for more than one or two years and HGSIL, should be treated with excision or ablation. Conical excision may be accomplished through laser, “cold-knife,” or loop electrosurgical excisional procedure (LEEP) cautery. Ablative modalities include laser and liquid nitrogen (cryotherapy). Post-excisional bleeding was significantly higher (more than 20 percent) in a small series of women with HIV.

Women with HIV are more likely to have multiple recurrences of dysplasia after therapy than women without HIV infection (62 percent and 18 percent, respectively), independent of ablational or excisional procedure type. Thus HIV-infected women require diligent gynecologic follow-up after treatment procedures. Women on HAART may have a more favorable natural history of dysplasia, although the data is inconclusive. While women on HAART may have better immune control of their HPV, they may be at increased risk of infection with multiple HPV strains.14

Treatment: Cervical cancer is managed through surgery with or without radiation and chemotherapy, depending on the extent of invasion. Recurrence or persistence of cervical cancer occurs in 35 percent of women. Patients with HIV have a higher mortality rate from cervical cancer than HIV-negative women. The data on the effect of HAART on cervical-cancer progression is limited; long-term follow-up of larger groups of women is needed.14

Post-Chemotherapy and Radiation Therapy Care and Considerations17

Supportive care for patients receiving chemotherapy is important and should include Pneumocystis carinii prophylaxis, regardless of the CD4+ count; monitoring for fevers and infections during periods of neutropenia; thrombocytopenic precautions when the patient has a decreased platelet count; and blood transfusion therapy and epoetin therapy for symptomatic anemia (see Table 3).

General side effects of radiation therapy include radiation dermatitis (skin inflammation) and myelosuppression (suppression of the bone marrow). Site-specific side effects may also occur. Children receiving radiation therapy who experience side effects will require symptom management (see Table 4).

Children receiving interferon therapy may experience flu-like symptoms (fever, chills, muscle or joint pain, headache), fatigue and malaise, anorexia (loss of appetite), diarrhea, changes in mental status (e.g. poor concentration, somnolence, depression, forgetfulness, irritability), abnormal liver-function tests, neutropenia, thrombocytopenia, and bone pain.

Use of zidovudine along with myelosuppressive (bone marrow-toxic) chemotherapy should be avoided, if possible, because the combination may heighten the potential for anemia, neutropenia, and thrombocytopenia.

Childhood cancer chemotherapy and radiation may cause a number of acute as well as late effects. Late effects found in long-term survivors may include neurocognitive deficits, neuroendocrine disturbances, gonadal dysfunction, secondary tumors, and multi-organ damage. Radiation to the brain or intrathecal chemotherapy places long-term survivors of childhood cancer at risk of cognitive deficits and developmental delay. Risk factors for therapy-induced neurocognitive damage include early age at the time of therapy, high doses of therapy, and use of intrathecal or systemic methotrexate as part of the chemotherapy regimen.

Hearing, vision, and dentition may also be affected by irradiation and some chemotherapeutics. Systemic effects may include hepatotoxicity, renal toxicity, cardiac toxicity (primarily by anthracyclines and thoracic radiation), vascular damage, lung fibrosis, endocrine dysfunction (particularly thyroid disturbance and growth effects), osteoporosis, and sterility. Second malignant neoplasms (SMNs) are 6.38 (95% CI (5.69, 7.13)) times as likely among childhood childhood cancer survivors as in the general population, with breast and bone SMNs occurring at up to 16 and 19
## Table 3: Supportive Care for Children Receiving Chemotherapy

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Definition</th>
<th>Management</th>
<th>Care Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenia</td>
<td>Absolute neutrophil count (ANC) &lt;500/mL</td>
<td>• Monitor for fever, skin ulcerations, pain, respiratory symptoms, stomatitis, perirectal fissures</td>
<td>Neutropenic precautions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Obtain blood (including central line) and urine cultures and provide antibiotic therapy for temp. &gt;38.5°C or temp. &gt;38.0°C three times in 24 hours*; detailed exam to identify source with further workup prn</td>
<td></td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>Platelet count &lt;100,000/mm³</td>
<td>• Assess for bleeding, bruising, petechiae, purpura</td>
<td>Thrombocytopenic precautions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Transfuse with platelets 1 unit (10 mL/kg to keep plt &gt;10K-20K, x)</td>
<td>• Quiet activities</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Keep plt &gt;50K if active bleeding or fever, or before LP, IM injections, and other minor procedures</td>
<td>• Avoid procedures:</td>
</tr>
<tr>
<td>Anemia</td>
<td>Hemoglobin &lt;10 gm/dl</td>
<td>• Assess for tachycardia, heart murmur, pallor, tachypnea, dyspnea, level of consciousness</td>
<td>- Avoid IM injections, lumbar puncture if possible</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Transfuse with CMV-negative, leukoreduced, irradiated PRBCs 10-15mL/kg prn when symptomatic or Hgb &lt; 7</td>
<td>- No rectal temperatures or exams</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Provide oxygen during periods of respiratory distress</td>
<td>- Avoid urinary catheterization</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Monitor for associated symptoms</td>
<td>• Give antibiotics as ordered</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Monitor temperature</td>
<td></td>
</tr>
<tr>
<td>Nausea and Vomiting</td>
<td>Stomach upset and/or forceful expulsion of stomach contents</td>
<td>• Serotonin-Receptor Antagonists: Ondansetron (4-11 years old) 4 mg PO TID, (&gt;11 yo) 8 mg PO TID; Granisetron (&gt;2 years old) 10-40 mg/kg IV; Dolasetron (&gt;2 years old) 1.8 mg/kg as single dose PO/IV. Give 0.5-1 hour before chemo for prevention of NV.</td>
<td>• Assess frequency of vomiting and monitor level of hydration</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Antiemetics: Diphenhydramine 5 mg/kg/day divided q6-8 hrs, or Hydroxyzine 2 mg/kg/day PO divided q6-8 hrs</td>
<td>• Accurate intake and output</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Phenothiazines (use with Diphenhydramine to reduce extra-pyramidal side effects: Promethazine; 0.25-1 mg/kg PO/IV q4-6h prn; Prochlorperazine (&gt;10 kg) 0.4 mg/kg/day PO/PR prn in 3-4 divided doses (max 15 mg/day); Chlorpromazine (&gt;6 months) 0.5-1 mg/kg PO/IM/IV q 6-8 hours (max dose &lt;5 years = 40 mg/day; 5-12 years = 75 mg/day)</td>
<td>• Avoid spicy foods</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Dexamethasone initial 10 mg/m2/dose IV (max 20 mg), then 5 mg/m2/dose q6 hrs prn</td>
<td>• Offer small quantities of food</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Other antiemetics: Dimenhydrinate, Lorazepam, Meclizine, Metoclopramide, Thiethylperazine, Trimebromipamide, Droperidol, Dronabinol (cannibanoid)</td>
<td>• Stir bubbles out of carbonated beverages</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Dexamethasone initial 10 mg/m2/dose IV (max 20 mg), then 5 mg/m2/dose q6 hrs prn</td>
<td>• Administer IV fluids or oral rehydration solutions as ordered</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Other antiemetics: Dimenhydrinate, Lorazepam, Meclizine, Metoclopramide, Thiethylperazine, Trimebromipamide, Droperidol, Dronabinol (cannibanoid)</td>
<td>• Give antiemetics as needed; use to prevent anticipatory NV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Assess frequency of vomiting and monitor level of hydration</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Accurate intake and output</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• Avoid spicy foods</td>
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<td></td>
<td>• Administer IV fluids or oral rehydration solutions as ordered</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Give antiemetics as needed; use to prevent anticipatory NV</td>
<td></td>
</tr>
<tr>
<td>Stomatitis</td>
<td>Breakdown of mucosa +/- secondary infection</td>
<td>• Rinse with a solution of a tablespoon of salt and a tablespoon of baking soda in a quart of water for several minutes 5-6 times a day, or perform 30-second oral rinse and spit with Chlorhexidine Gluconate 15 mL TID</td>
<td>• Frequent oral examinations for evidence of erythema ulcers, plaques</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Acetaminophen 10-15 mg/kg PO q4hrs and/or codeine 1 mg/kg PO q4hrs</td>
<td>• Meticulous oral hygiene while awake</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Benadryl/Maalox/Viscous Lidocaine 1:1:0.5 solution swish and spit q4hrs</td>
<td>• Avoid spicy foods, hot or very cold foods, acidic foods, and exposure to tobacco products or smoke</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Nystatin oral suspension (100 000 u/ml) 5 ml PO q4h</td>
<td>• Give pain medication as ordered</td>
</tr>
</tbody>
</table>

### Table 4: Symptom Management for Children Receiving Radiation Therapy

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Management</th>
<th>Care Guidelines</th>
</tr>
</thead>
</table>
| Nausea and Vomiting*           | • Serotonin-Receptor Antagonists: Ondansetron (4-11 years old) 4 mg PO TID; (>11 yo) 8 mg PO TID; Granisetron (>2 years old) 10-40 mg/kg IV; Dolasetron (>2 years old) 1.8 mg/kg as single dose PO/IV. Give 0.5-1 hour before chemo for prevention of NV.  
  • Antihistamines: Diphenhydramine 5 mg/kg/day divided q6-8 hrs, or Hydroxyzine 2 mg/kg/day PO divided q6-8 hrs  
  • Phenothiazines (use with Diphenhydramine to reduce extra-pyramidal side effects: Promethazine; 0.25-1 mg/kg PO/IV q4-6h prn; Prochlorperazine (>10 kg) 0.4mg/kg/day PO/PR prn in 3-4 divided doses (max 15 mg/day); Chlorpromazine (>6 months) 0.5-1 mg/kg PO/IM/IV q 6-8 hours (max dose <5 years = 40 mg/day; 5-12 years = 75 mg/day)  
  • Dexamethasone initial 10 mg/m2/dose IV (max 20 mg), then 5 mg/m2/dose q6 hrs prn  
  • Other antiemetics: Dimenhydrinate, Lorazepam, Meclizine, Metoclopramide, Thiethylperazine, Trimethobenzamide, Droperidol, Dronabinol (cannibinoid)  | • Assess frequency of vomiting and monitor level of hydration  
  • Accurate intake and output  
  • Avoid spicy foods  
  • Offer small quantities of food  
  • Stir bubbles out of carbonated beverages  
  • Administer IV fluids or oral rehydration solutions  
  • Give antiemetics prn |
| Stomatitis                     | • Rinse with a solution of a tablespoon of salt and a tablespoon of baking soda in a quart of water for several minutes 5-6 times a day, or perform 30-second oral rinse and spit with Chlorhexidine Gluconate 15 mL TID  
  • Acetaminophen 10-15 mg/kg PO q4hrs and/or codeine 1 mg/kg PO q4hrs  
  • Benadryl/Maalox/Viscous Lidocaine 1:1:0.5 solution swish and spit q4hrs  
  • 3-4 day rest period from RT  | • Frequent oral exams for evidence of erythema ulcers, plaques, bleeding  
  • Meticulous oral hygiene while awake  
  • Avoid spicy foods, hot or very cold foods, acidic foods, and exposure to tobacco products or smoke  
  • Give medications as ordered  
  • Assess for pain and provide pain medications prn |
| Skin Toxicity                  | • Aloe vera lotion 4-6 times a day  
  • Benadryl (1mg/kg/dose PO; max 5 doses/day) prn itching  
  • Hydrocortisone 1% for itching or moderate erythema  
  • Silvadene cream 1-2 times/day for moist desquamation  | • Frequent skin assessment for erythema, erosions, ulcers, blisters  
  • Avoid heat and cold, sun, and perfumed ointments  
  • Use gentle soap on the radiated surface; rinse off and pat dry  
  • Avoid placing adhesive tape or perfumed lotions in the radiation field  
  • Do not scrub skin when removing ink marking RT field  
  • Apply topical preparations prn, and give systemic medications prn  
  • Assess for pain and provide pain medications prn |
| Enteritis                      | • Loperamide: children 2-5 years 1 mg PO TID; 6-8 years 2 mg PO BID; 8-12 years 2 mg PO TID  
  • 3-4 day rest period from RT if dehydration occurs  | • Assess frequency of diarrhea, and monitor level of hydration  
  • Restrict roughage or residue in diet; if not successful, restrict dietary fat  
  • Restrict dietary lactose  
  • Provide an elemental diet (absorbed in the upper small bowel) to relieve symptoms  
  • Accurate intake and output  
  • Administer IV fluids or oral rehydration solutions  
  • Obtain daily weight  
  • Give anti-diarrheal medications prn |


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sometimes the expected incidence rates, respectively. In a childhood cancer survivor study, SMNs of any type were reported to be independently and significantly associated with younger age of the child at primary cancer diagnosis, primary childhood Hodgkin’s disease or soft-tissue sarcoma, female gender, and increased exposure to anthracyclines and/or epipodophyllotoxins.18
HIV-ASSOCIATED MALIGNANCIES

Review Questions

1. Describe which malignancies occur most commonly in children with HIV?
2. What are some of the regional variations in the incidence of HIV-related malignancies?
3. Which viruses play a role in the pathogenesis of HIV-related malignancies?
4. Name the types of lymphoproliferative disorders associated with HIV infection.
5. What are some of the side effects of chemotherapy and radiation therapy?

Exam Questions

1. Kaposi's sarcoma affects which of the following organ systems?
   a. Skin
   b. Lymph nodes
   c. Lungs
   d. Intestines
   e. All of the above

2. The following statements are true regarding leiomyosarcomas EXCEPT:
   a. Leiomyosarcomas are very rare in non-HIV-infected children.
   b. Surgery is the treatment of choice for isolated tumors.
   c. EBV and HIV-related leiomyosarcoma appear to be linked.
   d. Leiomyosarcoma is classified as a CDC Category C symptom in children.

3. The pathogenesis of Kaposi's sarcoma is linked to which of the following viruses?
   a. HHV-5
   b. HHV-6
   c. HHV-7
   d. HHV-8

4. The following statements regarding cervical cancer are true EXCEPT:
   a. The CDC classifies invasive cervical cancer as an AIDS-defining illness in adolescents with HIV infection.
   b. HPV types 16 and 18 are associated with an increased risk of cervical cancer.
   c. Pap smear is the initial screening test of choice for cervical cancer.
   d. Recommendations for cervical-cancer screening are the same for HIV-positive and HIV-negative adolescents.

5. Which of the following groups is at highest risk of developing Kaposi's sarcoma?
   a. HIV-infected children
   b. HIV-infected hemophiliacs
   c. HIV-infected IV drug users
   d. HIV-infected homosexual men

6. The following modalities would be acceptable for the treatment of isolated Kaposi's sarcoma lesions EXCEPT:
   a. Radiation therapy
   b. Intralesional chemotherapy
   c. Surgical excision
   d. Systemic chemotherapy

7. Which of the following would be considered in the differential diagnosis of Kaposi's sarcoma?
   a. Bacillary angiomatosis
   b. Congenital hemangiomas
   c. Pyogenic granuloma
   d. Nevi
   e. All of the above

Answers: 1e, 2d, 3d, 4d, 5d, 6d, 7e

Objectives

The purposes of this module are to:
1. Review central and peripheral nervous-system abnormalities associated with HIV infection.
2. Evaluate the pathogenesis of neurologic manifestations of HIV.
3. Identify clinical, pathologic, and radiologic determinations of nervous-system abnormalities in children with HIV infection.
4. Review guidelines for the care of children with neurologic and psychiatric manifestations of HIV.

Key Points

1. Central-nervous-system (CNS) abnormalities may result from direct invasion of the CNS by HIV or by indirect effects of the virus on the CNS.
2. Patients with HIV who are severely immunosuppressed may develop opportunistic CNS infections.
3. Children with HIV are at increased risk of developing focal CNS neoplasms such as lymphoma.
4. Psychiatric manifestations of HIV infection may occur in children.

Introduction and Pathophysiology

The nervous system is a frequent target of HIV infection, and the consequences of nervous-system involvement in HIV infection are serious. Nervous-system involvement typically occurs in conjunction with profound immunosuppression and in the presence of other AIDS-defining illnesses. HIV-associated neurologic disorders can, however, be the first problems with which children and adults with AIDS appear for treatment. Various abnormalities of the central nervous system (CNS) and peripheral nervous system (PNS) are associated with HIV and AIDS. These abnormalities may be attributable to the following causes: HIV infection, complications related to immunosuppression, neurotoxic effects of antiretroviral treatments, and other systemic complications of HIV that affect brain function.

Neurologic disorders in people with HIV infection include peripheral neuropathies (nerve disorders that affect the limbs or feet and hands), myelopathy (disorders of the spinal cord), focal cerebral mass lesions (brain tumors such as CNS lymphoma), CNS complications of opportunistic infections, vascular (blood vessel) abnormalities, seizures, and
encephalopathies. Developmental delays and regressions are also important CNS-related problems in HIV-infected children. These are discussed in detail in the growth and development chapter. In some cases, children and adults with HIV suffer similar neurologic and psychiatric manifestations. The ongoing growth and development of children, however, sometimes leads to unique nervous-system presentations of HIV disease in these patients. In this chapter, we focus on neurologic and psychiatric manifestations of HIV as they relate to pediatric patients.

HIV has been found in the brain and spinal fluid of children infected by HIV. Microglia, astrocytes, oligodendroglia, and cells of the monocyte-macrophage lineage are known to have CD4+ receptors, allowing for direct infection by the virus.

A selective barrier (the blood-brain barrier, or BBB) between circulating blood and brain tissues prevents many damaging substances from reaching the brain. Certain compounds readily cross the BBB; others are completely blocked. HIV has the ability to cause changes in the BBB and to enter the CNS. The neurons themselves are not infected by HIV, but neuronal function is indirectly impaired via complex mechanisms. Monocytes and microglial cells serve as the main CNS reservoirs for HIV. Once infected, these cells secrete a number of substances (such as TNF-alpha and nitric oxide) that are toxic to the brain. HIV infected microglial cells secrete chemokines (mainly MCP-1) that amplify recruitment of HIV infected monocytes, leading to a self-perpetuating feedback loop.

Some of HIV’s effects on the brain occur without the virus itself having to cross the BBB. The viral coat protein gp120 can enter the CNS independent of the rest of the virus and is directly neurotoxic. Brain endothelial cells react to substances associated with HIV infection, such as Tat and cytokines, by releasing neurotoxic substances at the surface abutting the brain.

Since HIV does not directly infect neurons, its effects on the peripheral nervous system (PNS) are also related to indirect effects of infection. Neurotoxic side effects of antiretroviral medications also have a major effect on the PNS.

Central and Peripheral Nervous System Abnormalities

Progressive Encephalopathy (PE)

PE in HIV-infected children is represented by a well-defined triad: 1) impaired brain growth, 2) progressive motor dysfunction, and 3) loss or arrest of age-appropriate neurodevelopmental milestones. HIV-related encephalopathy can occur in the absence of other signs and symptoms. Periodic neurologic and cognitive assessment can help with the recognition and monitoring of PE. HIV-infected children with PE can proceed along a variable neuro-developmental course, with periods of spontaneous improvement and stabilization. Treatment with antiretroviral medications and early intervention programs for children with neurologic impairments and developmental delays can help mitigate the symptoms and improve the course of PE.

Impaired brain growth in children with PE can be observed both clinically and radiographically. In children under the age of 2 years, a plateau in serial measurements of head circumference is an indicator of impaired brain growth. In older children whose cranial sutures are closed, measurements of head circumference are not as useful. If available, computed tomography (CT) imaging may be used to detect loss of brain tissue. Radiological findings may demonstrate signs of cerebral atrophy: enlargement of the sulci, the subarachnoid space, and the ventricles. Brain atrophy has been shown to be a significant predictor of HIV-related disease progression.

Progressive motor dysfunction typically begins with the inability to perform fine movements with the hands and fingers, such as handwriting or sewing. As the condition worsens, bigger muscle groups become involved, and the person may lose the ability to walk...
or sit. The muscles may become either rigid or flaccid. Involuntary movements and spasms often occur. Children with PE do not achieve significant motor milestones, such as walking or feeding themselves, at appropriate ages. In severe cases, previously ambulatory and functional children become spastic, are unable to walk, and require assistance with activities of daily living. Motor deficits in children with PE usually involve both sides of the body equally. This is in contrast to the motor deficits observed in patients with inter-cranial neoplasms, which tend to have asymmetric effects.

Neurodevelopmental decline manifests itself in young children as the loss or arrest of age-appropriate neurodevelopmental milestones. School-aged children are at risk of cognitive impairments that lead to the loss of the ability to learn and understand and resultant academic failure. Developmental delay may also be related to environmental, psychosocial, and nutritional factors. Whenever possible, neurodevelopmental testing should be coordinated with clinical examination, laboratory data, and radiographic information to confirm the appropriate diagnosis.

**Static Encephalopathy (SE)**

Fixed, non-progressive neurologic or neurodevelopmental deficits can also occur in children with or without HIV infection. These are termed static encephalopathies. SE is often related to identifiable historical CNS

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**Figure 1: Progressive HIV Encephalopathy**

*This is a 5-year-old girl with HIV infection and severe, progressive HIV encephalopathy. The girl is non-communicative and spastic. This condition may progress rapidly for a period of time and then stabilize or improve spontaneously. However, eventually neurologic deterioration will occur.*

**Figure 2: Generalized Brain Atrophy**

*This is a computerized tomographic (CT) scan of the brain of an 8-year-old boy with HIV infection and generalized brain atrophy. Cerebral atrophy is observed commonly among children with HIV-associated encephalopathy, but it also may be observed among children who are normal neurologically and Developmentally.
insults, such as premature birth, intrauterine exposure
to infections or toxins, genetic factors, or head trauma. Children with SE may manifest developmental delay but not regression; static motor deficits but not progressive motor dysfunction; and microcephaly (abnormally small head size). Children with HIV infection and SE may spontaneously improve over time, may remain stable, or may experience neurologic deterioration. This makes it difficult to tell the difference between an HIV-infected child with SE and one with slowly progressive PE.

**Seizures**
Seizures in children with HIV infection can have a variety of causes. Seizures in the context of HIV should raise suspicion of intracranial opportunistic infections, mass lesions, and vasculopathies. Metabolic imbalances, drug side effects or interactions, and cortical structural changes can also trigger seizures. Suspicion of a focal CNS lesion should be heightened whenever a focal neurologic deficit is discovered on history, physical exam, or electroencephalogram (EEG).

Unless neuroimaging (CT, MRI) is available, it may be difficult to determine the etiology of seizures. Laboratory studies may detect electrolyte or metabolic imbalances, and lumbar puncture may help to confirm suspected infection.

Anticonvulsant medications are available to help control seizures. Their use in HIV-positive patients should be coordinated by providers knowledgeable about possible interactions between anticonvulsants and antiretroviral medicines.

**Strokes**
Strokes are more commonly seen in children with advanced HIV disease or HIV encephalopathy. HIV produces inflammation of blood vessels, including those in the brain. Children with HIV are at an increased risk of suffering strokes and seizures due to the effects of the HIV virus on the vessels of the brain. Many cases of stroke are hemorrhagic, due to HIV-associated thrombocytopenia and idiopathic thrombocytopenic purpura or CNS neoplasia. Arteriovenous malformations (AVMs) are known to increase the risk of stroke in the context of HIV infection. When AVMs occur in immuno-suppressed, HIV-positive patients, highly active antiretroviral therapy (HAART) may help lead to their resolution.

**Opportunistic Infections (OIs)**
Adults with HIV infection are more likely than children to develop an OI in the CNS. However, these infections can also occur in pediatric patients. OIs that involve the CNS are often not readily apparent and should be considered in cases of acute or chronic behavioral or mental status changes, as well as in children with persistent headaches, malaise, or fever. The most common pathogens that cause CNS

<table>
<thead>
<tr>
<th>Disease</th>
<th>Clinical</th>
<th>Neuroimaging</th>
<th>Location of Lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral toxoplasmosis</td>
<td>Acute onset of symptoms</td>
<td>Common</td>
<td>Multiple</td>
</tr>
<tr>
<td>Primary CNS lymphoma</td>
<td>Insidious onset of symptoms</td>
<td>Usually Absent</td>
<td>One or few</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>Insidious onset of symptoms</td>
<td>Common</td>
<td>One or few</td>
</tr>
<tr>
<td>Cryptococcosis, cryptococcal meningitis</td>
<td>Acute onset of symptoms</td>
<td>Common</td>
<td>Variable</td>
</tr>
</tbody>
</table>
Infections in immunocompromised patients include toxoplasmosis, cryptococcus, herpes simplex, and cytomegalovirus. JC virus, which leads to progressive multifocal demyelinating leukoencephalopathy (PML) in about 5 percent of adults with AIDS, is extremely rare in children.

HIV-infected children who develop OIs in the CNS may develop significant symptoms, including signs of increased intracranial pressure (severe headache, nausea, vomiting, confusion, coma), focal neurologic signs (hemiparesis, visual changes, gait instability, fine or gross motor abnormalities), malaise, fever, behavioral or personality changes, seizures, and meningitic signs (headache, neck pain and nuchal rigidity). The neurologic impairment most frequently observed in children with HIV is due to the HIV infection itself, rather than to opportunistic infections or CNS tumors. CNS OIs must always be considered in HIV-infected children with CNS manifestations, because if these infections go untreated, death may occur.

**CNS Neoplasms**
Non-Hodgkin's lymphoma is the most common CNS neoplasm in children with AIDS. CNS lymphomas may be confused with other CNS conditions, such as toxoplasmosis or cryptococcosis. They tend to grow rapidly and to lead to headaches, nausea/vomiting (primarily upon arising in the morning), altered mental status, focal neurologic signs, and increased intracranial pressure. Epstein-Barr virus (EBV) infection is involved with the pathogenesis of non-Hodgkin's lymphoma in HIV-infected children. HAART and anti-cancer chemotherapies, especially corticosteroids, can improve prognosis.

Leiomyosarcomas have been reported with increased frequency in children with HIV infection. The most common sites of the lesion are the lungs, spleen, and gastrointestinal tract. Leiomyosarcomas can be found in the brain as well. Symptoms of intracranial leiomyosarcoma are the same as those seen with other CNS mass lesions.

**HIV Myopathy and Myelopathy**
Myopathy is characterized by muscular pain and proximal muscle weakness. HIV-associated myopathy is more common in adults than in children. With the increased use of antiretroviral nucleoside analogues (e.g. zidovudine) in children, however, myopathies are occurring more frequently as a side effect of these medications. Myopathy can also be caused by direct effects of the HIV virus or by secondary infections (e.g. CMV). Diagnosis of myopathy may be made based on clinical observations and evidence of myopathic changes on electromyogram (EMG). Elevated serum creatine kinase (CK) levels are also associated with myopathies. Myopathies in HIV-infected patients may also be related to the use of corticosteroids or statin drugs (used to treat lipid disorders) or to hypothyroidism. Treatment involves addressing the causative agent.

Myelopathy is characterized by functional disturbance or pathologic changes in the spinal cord. Demyelinating changes of the corticospinal tracts and vacuolar changes may be seen. Progressive difficulty walking and weakness in the lower extremities may be observed. The child may develop sensory disturbances and urinary incontinence. As with myopathy, myelopathy is more commonly seen in HIV-infected adults than in children. Myelopathy often results from a reactivated infection with measles or CMV. The treatment for HIV-related myelopathy is antiretroviral therapy. Myelopathies may also be related to spinal-cord tumors and epidural abscesses. These etiologies should be ruled out as part of the diagnosis and management of HIV-infected children with myelopathy.

**Peripheral Neuropathy**
There are many causes of peripheral neuropathies in children with HIV infection. Common etiologies include viral pathogens, autoimmune effects, vitamin and mineral deficiencies, and side effects of antiretroviral agents. The symptoms of peripheral neuropathy range from mild numbness or tingling to debilitating pain. HIV sometimes causes peripheral
neuropathy by generating a tissue-specific autoimmune attack on the peripheral nerves. Varicella zoster virus causes symptoms along a sensory dermatome (shingles) more commonly in immunosuppressed patients. Cytomegalovirus-related polyradiculoneuropathy (inflammation of the nerve roots) also leads to peripheral neuropathy. HIV-infected children sometimes develop peripheral neuropathies related to vitamin B-12 or pyridoxine deficiency. Certain antiretroviral nucleoside analogues (ddC, ddI, d4T, 3TC) are neurotoxic and may exacerbate or trigger peripheral neuropathy.

### Sleep Problems
Both quality and quantity of sleep are important to normal growth, development, and health of children. Sleep disturbances occur more commonly among HIV-infected children and adults than among non-infected individuals. Fatigue during regular daily activities is also more commonly reported among people living with HIV. Sleep disturbances have been found to occur early in the course of HIV infection. Medications and diet may also have effects on sleep quality, but HIV itself is thought to affect sleep via several mechanisms. Animal studies have suggested that HIV gp120 protein directly alters sleep architecture.

#### Table 2: Neurologic Manifestations of Pediatric HIV Infection

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>Clinical Findings</th>
<th>Diagnostic Studies</th>
</tr>
</thead>
</table>
| **Focal Cerebral Mass Lesions**    | Headache, nausea/vomiting, motor deficits (usually asymmetric), discoordination, visual changes, altered mental status | • CT/MRI: enhancing lesions  
• Lumbar puncture: Cerebrospinal fluid (CSF) may reveal abnormal cytology or Epstein-Barr virus (EBV) via PCR  
• Brain biopsy: sometimes needed to confirm diagnosis |
| **Myelopathy**                     | Gait disturbances, lower-extremity weakness/spasticity, incontinence, sensory abnormalities, abnormal lower-extremity reflexes | • CT/MRI: no mass lesions seen; nerve-root thickening may be present  
• CSF: polymorphonuclear pleocytosis |
| **Myopathy**                       | Muscle weakness, muscle soreness, weight loss          | • EMG: irritative myopathy  
• Muscle biopsy: inflammation, degeneration |
| **Opportunistic Infections**       | Headache, nausea/vomiting, fever, seizures, altered mental status, malaise | • CT/MRI: multiple enhancing lesions (toxoplasmosis), periventricular and meningeal abnormalities (CMV)  
• Lumbar puncture: CSF may be positive for pathogens and abnormal cells  
• Serologies for specific pathogens |
| **Peripheral Neuropathy**          | Distal symmetric neuropathy:  
• Distal numbness/pain  
• Stocking/glove sensory loss  
Inflammatory demyelinating polyneuropathy:  
• Progressive weakness  
• Areflexia  
Progressive polyradiculopathy:  
• Lower-extremity weakness  
• Urinary incontinence and retention  
• Paresthesias  
• Decreased ankle reflexes | Distal symmetric neuropathy:  
• EMG: distal axonopathy  
Inflammatory demyelinating polyneuropathy:  
• EMG: demyelination  
Progressive polyradiculopathy:  
• EMG: polyradiculopathy  
• Serum: increased creatine kinase |
| **Progressive Encephalopathy**     | Fine and gross motor deficits (usually symmetric), abnormal tone, neurodevelopmental delay, microcephaly, altered mental status | • CT/MRI: brain atrophy, white-matter abnormalities |
| **Seizures**                       | Focal or generalized seizures, post-ictal state (fatigue and confusion following seizure) | • EEG: abnormal patterns  
• CT/MRI and CSF studies: mass lesions may be seen via imaging, and CSF may be positive for pathogens and abnormal cells if etiology is infectious or neoplastic  
• Lumbar puncture: may reveal infection |
| **Strokes (Cerebral Vascular Accidents)** | Rapid onset of focal neurological signs, seizures, altered mental status | • CT/MRI: extent of bleeding seen (in ischemic strokes, CT may not show changes during the first 24 hours); contributing factors such as CNS neoplasms may be identified  
• Lumbar puncture: with subarachnoid hemorrhages, blood will be present in the CSF |
IL-1, which is considered a somnogenic lymphokine, is also produced in higher levels in the presence of HIV infection.

**Psychiatric Manifestations of HIV in Children**

CNS manifestations related to HIV infection commonly include some of a psychiatric nature. Children and adolescents with HIV infection are at increased risk of developing psychiatric problems. It is important to note that among horizontally infected patients, the incidence of primary psychiatric disorders is also higher. Primary psychiatric disorders may precede the HIV infection and may actually lead to behaviors that put the person at risk of acquiring HIV. The rate of horizontal acquisition of HIV infection is higher among people who engage in risky behaviors such as unsafe sexual practices and needle-sharing. Since some psychiatric conditions (mood disorders, anxiety disorders, psychotic disorders, and substance-abuse problems) are associated with a higher rate of these risk-taking behaviors, these psychiatric illnesses

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>Care Guidelines</th>
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<tbody>
<tr>
<td><strong>Focal Cerebral</strong>&lt;br&gt;Mass Lesions</td>
<td>- Assess for signs of increased intercranial pressure, fever, focal neurological signs, behavioral changes.  &lt;br&gt;- Administer chemotherapy or antibiotics as needed.  &lt;br&gt;- Provide support to family and education regarding specific medications needed by patient.</td>
</tr>
<tr>
<td><strong>Myelopathy</strong></td>
<td>- Assess for pain, muscle weakness, lower-extremity weakness, incontinence, and spasticity.  &lt;br&gt;- Administer muscle relaxants as needed.  &lt;br&gt;- Provide physical therapy for weakened muscles and to maintain range of motion.  &lt;br&gt;- Teach exercises to family to help patient at home.</td>
</tr>
<tr>
<td><strong>Myopathy</strong></td>
<td>- Assess for pain, muscle weakness, and range of motion.  &lt;br&gt;- Consider discontinuing medications that may be contributing to condition.  &lt;br&gt;- Administer corticosteroids and pain medications as needed.  &lt;br&gt;- Provide physical therapy for weakened muscles and to maintain range of motion.  &lt;br&gt;- Teach exercises to family to help patient at home.</td>
</tr>
<tr>
<td><strong>Opportunistic</strong>&lt;br&gt;Infections</td>
<td>- Assess for signs of increased intercranial pressure, fever, focal neurological signs, behavioral changes.  &lt;br&gt;- Administer appropriate medication based on suspected or confirmed pathogen:  &lt;br&gt;- Toxoplasmosis: pyrimethamine, sulfadiazine, clindamycin  &lt;br&gt;- Cryptococcosis: fluconazole, flucytosine, amphotericin B  &lt;br&gt;- Herpes simplex: acyclovir  &lt;br&gt;- Cytomegalovirus: ganciclovir, foscarnet</td>
</tr>
<tr>
<td><strong>Peripheral</strong>&lt;br&gt;Neuropathy</td>
<td>- Assess for numbness, paresthesias, pain, weakness.  &lt;br&gt;- Administer analgesics, tricyclic antidepressants, anticonvulsants, steroids as needed.  &lt;br&gt;- Provide support to family and education regarding progression of symptoms.</td>
</tr>
<tr>
<td><strong>Progressive</strong>&lt;br&gt;Encephalopathy</td>
<td>- Assess for progressive motor dysfunction, failure to reach or loss of age-appropriate milestones.  &lt;br&gt;- Administer antiretroviral medications and muscle relaxants as needed.  &lt;br&gt;- Assist with ambulation and activities of daily living.  &lt;br&gt;- Provide information to family regarding progression of symptoms.</td>
</tr>
<tr>
<td><strong>Seizures</strong></td>
<td>- Assess for seizure activity.  &lt;br&gt;- Protect patient from injury during seizure activity.  &lt;br&gt;- Monitor respiratory status; suction airway and administer oxygen as needed.  &lt;br&gt;- Administer anticonvulsant medications as needed.  &lt;br&gt;- Provide support to family during seizures.  &lt;br&gt;- Educate patient and family regarding long-term use of anticonvulsant medications and seizure precautions (i.e. patients with seizures should never swim alone or climb to high places from which they could fall during a seizure).</td>
</tr>
<tr>
<td><strong>Strokes</strong></td>
<td>- Intensive care, including neurosurgical intervention, is often needed immediately after a stroke occurs.  &lt;br&gt;- Look for contributing factors, such as low platelet levels, which may be correctable.  &lt;br&gt;- Assess for seizures.  &lt;br&gt;- Assist with ambulation and activities of daily living.  &lt;br&gt;- Provide physical therapy as needed.  &lt;br&gt;- Provide support and education to the family regarding long-term prognosis.</td>
</tr>
</tbody>
</table>
tend to be disproportionately represented among adolescents with horizontally acquired HIV infection.

Secondary psychiatric conditions among patients with HIV result from the effects of HIV on the brain, the effects of secondary infections on the CNS, metabolic abnormalities, vitamin deficiencies, and side effects of medications used to treat HIV. Numerous case studies involving patients with late-stage HIV infection have documented psychotic and mood symptoms. In most of these cases, the cause of the psychiatric symptoms is not clearly defined. In some patients, however, symptoms have improved when antiretroviral therapy was initiated.

While antiretroviral medications often have a beneficial effect on psychiatric symptoms in late-stage HIV patients, the antiretroviral medicines themselves can also cause psychiatric symptoms. Efavirenz, in particular, has been associated with a number of adverse psychiatric side effects. Studies of the neuropsychiatric effects of efavirenz treatment have shown that nearly 50 percent of patients developed neuropsychiatric side effects. These include depressed mood, sleep disturbances, anxiety, psychosis, impaired concentration, vivid dreams, and nightmares.

Depressed mood is rarely, if ever, due to direct effects of HIV on the brain. Therefore, the etiology of the mood symptoms should be intensively sought in patients with HIV and depression. Vitamin B12 and folate deficiencies have been associated with depression. Patients with HIV infection have an increased risk of vitamin B12 deficiency due to malabsorption and altered metabolism. Hypothyroidism, likewise, can cause depression. Thyroid dysfunction has been seen at an increased rate among HIV-infected children. These conditions should be ruled out before the diagnosis of a primary mood disorder is made.

The evaluation of patients with HIV infection and psychiatric disorders should always include a full medical evaluation. The diagnosis of a primary psychiatric disorder should be one of exclusion: Medical conditions that may lead to secondary psychiatric manifestations should be ruled out.

Primary psychiatric disorders in patients with HIV may be treated with the same psychotropic medications that have proven to be effective in non-infected patients. Dosing may have to be altered, however, due to the presence of interactions between certain psychotropic and antiretroviral medications. When a secondary psychiatric disorder is determined to be present, the primary cause of the problem should be addressed. Psychotropic medications may also be used in these cases, however, to aid in the control of symptoms.
1. List neurological disorders that are seen in children with HIV.

2. Describe how HIV directly and indirectly affects the nervous system.

3. List infections and tumors that are more common among HIV-infected children.

4. Describe care guidelines for children with neurologic and psychiatric abnormalities related to HIV infection.

1. Common opportunistic CNS infections that may cause neurologic complications include all of the following EXCEPT:
   a. Toxoplasmosis
   b. Cytomegalovirus
   c. Candida albicans
   d. Herpes simplex

2. Which of the following cancers is most likely to cause focal cerebral mass lesions in children with HIV?
   a. Kaposi’s sarcoma
   b. Non-Hodgkin’s lymphoma
   c. Leiomyosarcoma
   d. Optic glioma

3. The following statements are true regarding the influence of antiretroviral drugs on HIV-infected patients with psychiatric illnesses EXCEPT:
   a. Certain antiretroviral drugs may be the cause of the psychiatric symptoms.
   b. Antiretroviral drugs may lead to the resolution of the psychiatric symptoms in patients whose psychiatric condition is due to the direct effects of HIV on the brain.
   c. Antiretroviral drugs can cure primary psychiatric illnesses.
   d. Medications used to treat primary psychiatric diseases can be used along with antiretroviral drugs.

Answers: 1c, 2b, 3c
A 2-year-old HIV-infected girl has been coming to your clinic for health care since birth. Several months ago, her mother noticed that she began to lose the ability to speak, and her motor function became impaired. During the clinic visit today, the mother tells you that these symptoms have progressively worsened, and now she is no longer able to walk or crawl. She can still say a few words, but her ability to speak continues to decline. Her head circumference is less than the 5th percentile for her age, but her height and weight are at the 50th percentile.

**Question:** This young child most likely has which of the following neurologic manifestations of HIV infection?

- a. Myopathy
- b. Seizures
- c. Progressive encephalopathy (PE)
- d. Intracranial lymphoma

**Answer:** c. PE in HIV-infected children is represented by impaired brain growth, progressive motor dysfunction, and the failure to reach or loss of neurodevelopmental milestones. PE can proceed along a variable course with periods of spontaneous improvement, although eventually neurologic deterioration will occur.

**Question:** Which of the following is an indicator of impaired brain growth in children whose cranial sutures have NOT closed?

- a. A plateau in serial measurements of head circumference
- b. Muscular pain and proximal muscle weakness
- c. Unilateral motor deficits
- d. Numbness and tingling in the hands and feet

**Answer:** a. Impaired brain growth in children with PE can be observed both clinically and radiographically. In children less than 2 years of age, a plateau in serial measurements of head circumference is an indicator of impaired brain growth. In older children whose cranial sutures are closed, measurement of head circumference is not as useful. If available, CT imaging can be used to detect loss of brain parenchymal volume.

**Question:** All of the following are care guidelines for children with PE, EXCEPT:

- a. Assist with ambulation and activities of daily living.
- b. Provide passive range of motion exercises and teach these to the mother.
- c. Assess for progressive motor dysfunction and failure to reach or loss of developmental milestones.
- d. Do not discuss the child’s deteriorating neurologic condition with the mother.

**Answer:** d. A complete developmental and neurologic assessment of a child with PE is essential in planning care. The mother needs to be aware of the status of the child’s neurologic condition in order to be able to plan for daily activities and the care regimen (including any medications required and daily exercises).

**Question:** Which of the following medications can slow or arrest the progression of PE?

- a. Antiretroviral agents
- b. Antibiotics
- c. Muscle relaxants
- d. Pain medications

**Answer:** a. When given in appropriate combinations and doses, antiretroviral medications can slow or stop PE. Muscle relaxants and pain medications are useful in treating the associated symptoms, but they do not slow or arrest progression. Antibiotic therapy is not useful in treating PE.
Case Study #2

A 22-year-old HIV-infected woman comes to your clinic complaining of difficulty walking, leg weakness, and sensory disturbances ( inability to distinguish hot from cold) in the lower extremities. She is diagnosed as having myelopathy and is started on a muscle relaxant. The doctor tells her that her symptoms may worsen.

Question: What other symptoms might she experience that are related to the myelopathy?
   a. Headache
   b. Incontinence
   c. Seizures
   d. Fever

Answer: b. Myelopathy is characterized by functional disturbances, or pathologic changes in the spinal cord. Different symptoms will occur depending on which level of the spinal cord is involved. This condition may be associated with progressive difficulty in walking, lower-extremity weakness and loss of sensation, and incontinence.

Question: In addition to muscle relaxants, which of the following may provide relief from the symptoms of myelopathy for this young-adult woman?
   a. Physical-therapy exercises
   b. Trimethoprim-sulfamethoxazole
   c. Chemotherapy
   d. Anticonvulsants

Answer: a. Physical-therapy exercises can strengthen weakened muscles and may help to prevent spasticity. These exercises can be taught to the patient and family members and be done daily at home.

Case Study #3

A 16-year-old girl presents to your clinic for evaluation and treatment after receiving positive results on a screening test for HIV. She ran away from home approximately one month ago and has been living on the street. Prior to running away from home, she began to have auditory hallucinations and was diagnosed with a psychotic disorder.

Question: Which of the following is true regarding her psychiatric symptoms and HIV diagnosis?
   a. Her psychiatric symptoms may be secondary to the effects of HIV on her brain.
   b. Her psychotic symptoms may have led her to take part in high-risk activities that resulted in her infection with HIV.
   c. If her psychiatric condition is secondary to the effects of HIV on the brain, antiretroviral medications are likely to help improve her symptoms.
   d. All of the above

Answer: d. Psychotic problems are among those that lead patients to engage in behaviors that put them at high risk of HIV infection. In this patient, since the timing and staging of her HIV infection are unknown, we cannot yet rule out the possibility that her psychotic symptoms are secondary to effects of HIV on the brain.

References


2. Banks WA. Protector, prey, or perpetrator: the pathophysiology of the blood-brain barrier in NeuroAIDS. NeuroAIDS. 2000;3(3).
The purposes of this module are to:
1. Discuss the metabolic changes associated with HIV infection and antiretroviral therapy, specifically dyslipidemia, lipodystrophy, insulin resistance, lactic academia, and decreased bone density.
2. Discuss the etiology and mechanisms of these changes.
3. Discuss treatment strategies.

Key Points
1. HIV infection and its treatment are associated with a variety of endocrine and metabolic abnormalities.
2. The etiologies of these abnormalities are multifactorial.
3. These abnormalities may result in life-threatening complications.
4. These abnormalities may be responsible for non-adherence to antiretroviral therapy.

Overview
HIV infection is associated with a wide array of endocrine and metabolic abnormalities, including adrenal insufficiency, hypoaldosteronism, thyroiditis, insulin resistance, diabetes mellitus, osteopenia, osteoporosis, hypercholesterolemia, hypertriglyceridemia, hypogonadism and hypopituitarism (see Figure 1).

The pathophysiology of these changes is equally varied: direct damage by HIV, opportunistic infection, malnutrition, systemic inflammatory responses, neoplasms, and the complications of HIV therapy. These abnormalities may also increase the possibility of more long-term, secondary diseases, such as cardiovascular disease. Furthermore, adherence to potent anti-retroviral therapy may be compromised. An understanding of the adverse events and their management will help to maximize the effectiveness of available treatment.

Dyslipidemia
Dyslipidemia involves changes in lipid metabolism. Total cholesterol levels in the blood are increased. Other signs of dyslipidemia include increases in low-density lipids (LDL cholesterol), increases in very low-density lipids (VLDL cholesterol), increases in triglycerides, and occasional decreases in high-density lipids (HDL cholesterol).

It is important to note that these changes can be caused by HIV disease independent of antiretroviral therapy. Studies have shown that early during the course of HIV infection, HDL levels decrease. As immune function declines, a decrease in LDL level occurs, which is followed by an increase in very low-density lipoprotein particles at the time of transition.
to AIDS. The increase in VLDL leads to hypertriglyceridemia. The increase in triglycerides is mediated by interferon-α, which also participates in host response to HIV infection. These changes in lipid metabolism have also been found to be typical of the acute phase of response to infection and inflammation. Therefore, restoration of immune health should lead to a reversal of these changes, e.g., an increase in LDL cholesterol. With the advent of antiretroviral therapy, several changes in lipid metabolism were noted. Protease inhibitor (PI) therapy is known to cause increased VLDL, LDL, and triglyceride levels. Nucleoside reverse transcriptase inhibitors (NRTIs) have also been implicated in increasing cholesterol and triglycerides. Non-nucleoside reverse transcriptase inhibitors (NNRTI) are least likely to increase cholesterol levels. Thus it is clear that dyslipidemia is a result of a combination of HIV disease, HIV treatment, and restoration of immune-system health.

Dyslipidemia can increase the risk of coronary heart disease. An increase in coronary heart disease has been noted in HIV-infected patients. The assessment of dyslipidemia must include information about other risk factors for coronary heart disease (CHD). Such risk factors include a family history of hypercholesterolemia (elevated total cholesterol levels above 240 mg/dL or 6.3 mmol/L), hypertension (blood pressure greater than the 95th percentile for height or history of anti-hypertensive medications), low HDL cholesterol levels (less than 40 mg/dL or 1.1 mmol/L), a family history of premature CHD (in males under 55 years of age or females under 65 years of age), age (above 45 years for males, above 55 years for females), and cigarette smoking. The National Institutes of Health have developed a calculation that can assist in determining a patient’s 10-year risk of CHD. When available, this risk assessment can be combined with the aforementioned risk factors. Once the assessment is made and risk factors are determined, a goal LDL-cholesterol level should be determined based on Table 1. In general, a triglyceride level greater than 500 mg/dL (5.6 mmol/L) is abnormal.

The treatment of dyslipidemia begins with lifestyle changes. These include smoking cessation, decreased alcohol consumption, increased exercise, decreased fat

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Table 1: Assessment of Goal LDL and Management of Elevated LDL

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Goal LDL Mg/dL (mmol/L)</th>
<th>Lifestyle Change Indicated Mg/dL (mmol/L)</th>
<th>Drug Therapy Indicated Mg/dL (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary heart disease or equivalent</td>
<td>&lt;100 (2.5)</td>
<td>100-130 (2.5-3.3)</td>
<td>&gt;130 (3.3)</td>
</tr>
<tr>
<td>≥2 risk factors, 10-year 10-20%</td>
<td>&lt;130 (3.3)</td>
<td>≥130 (3.3)</td>
<td>≥130 (3.3)</td>
</tr>
<tr>
<td>≥2 risk factors, 10-year &lt;10%</td>
<td>&lt;130 (3.3)</td>
<td>≥130 (3.3)</td>
<td>≥130 (3.3)</td>
</tr>
<tr>
<td>0-1 risk factors</td>
<td>&lt;160 (4.1)</td>
<td>160-190 (4.1-4.9)</td>
<td>≥190 (4.9)</td>
</tr>
</tbody>
</table>
intake, and weight loss if appropriate. Diet modification in children must be closely monitored, because children require a certain caloric intake for proper growth. Increased dietary fiber, especially soluble fiber, has a modest cholesterol-lowering effect. Monounsaturated fats lower LDL cholesterol levels while maintaining or increasing HDL cholesterol levels. Foods that contain monounsaturated fats include olive oil, avocados, and many kinds of nuts (such as cashews) and seeds (such as sesame). Patients with HIV/AIDS who have elevated LDL and whose triglyceride levels are above normal (200-500 mg/dL or 2.2-5.6 mmol/L) may use pravastatin 10-40 mg per day or atorvastatin 10 mg per day, as these drugs are least likely to interact with antiretroviral medications. Patients with triglyceride levels above 500 mg/dL (5.6 mmol/L) regardless of LDL-cholesterol levels may be treated with gemfibrozil 600 mg twice daily or fenofibrate 54-160 mg per day. There are no established pediatric doses for these medications.

**Lipodystrophy**

Lipodystrophy is defective metabolism or distribution of fat. Features of lipodystrophy may include increased fat stores, or lipohypertrophy, in the abdomen for men, breast enlargement for women, and buffalo hump for both (Figure 2). Other features include lipoatrophy, which involves loss of subcutaneous fat, particularly in the extremities, the neck, and the face.

Lipodystrophy is not clearly associated with organ dysfunction. Many studies suggest that lipodystrophy is more highly associated with highly active antiretroviral therapy (HAART) than with the pathogenesis of HIV disease. Drugs implicated in the etiology include PIs and NRTIs, especially stavudine. One of the suggested etiologies for such dysfunction is that the antiretroviral medicines, particularly NRTIs, cause mitochondrial toxicity leading to a change in fat metabolism or even fat-cell apoptosis or cell death. Patient awareness of the disfiguring side effects of antiretroviral therapy can be a significant hindrance to adherence. In addition, the fact that lipodystrophy can be readily recognized worldwide causes some patients to be fearful of the effects of stigmatization.

Clinical manifestations of lipodystrophy include lipoatrophy or fat accumulation in certain regions of the body. The severity of lipodystrophy can be graded on a scale developed as part of the HIV Outpatient Study (HOPS). The scale is as follows:

- **Grade 0**: Absence of any lipodystrophy
- **Grade 1**: Mild signs that are only noticeable on close inspection
- **Grade 2**: Moderate lipodystrophy that is readily noticeable by a patient or a health professional
- **Grade 3**: Severe lipodystrophy that is readily noticeable by a casual observer

The HOPS scale is quite subjective and difficult to validate but is still useful in trying to characterize lipodystrophy.

Other diagnostic methods include the use of Dual-Energy X-ray Absorptiometry (DXA) to determine the trunk-to-limb fat ratio. A single-slice abdominal CT can be used to determine the ratio of visceral adipose tissue to subcutaneous adipose tissue (VAT:SAT).

Treatment of lipodystrophy includes decreasing the amount of fat in the diet and exercise to increase the
muscle-to-fat ratio. Hormone therapy has been attempted in some studies, particularly the use of testosterone, growth hormone, or steroids. Cosmetic surgery has also been employed. If therapy permits, changing from a PI-containing regimen or from a stavudine-containing regimen might have some benefit. Any change in antiretroviral therapy must be balanced against the risk of decreasing the effectiveness of the regimen and subsequent resurgence of HIV-associated illnesses.

Many studies have examined the impact of lipodystrophy on HIV-infected adults. Although not as abundant, some research has looked at lipodystrophy in HIV-infected children. The results have varied, but much of the literature suggests that children, especially pre-pubertal, are less susceptible to lipodystrophy syndrome than post-pubertal adolescents and adults. Subjects receiving pediatric dosing regimens were less likely to develop lipodystrophy than those receiving adult dosing regimens.

**Insulin Resistance**

HIV disease and HIV treatment can alter glucose homeostasis. A number of studies have demonstrated hyperinsulinemia in HIV-infected patients. However, it is difficult to distinguish the contributions of HIV disease itself from those of HIV antiretroviral regimens.

Insulin resistance occurs when there are higher circulating levels of insulin than are needed for maintaining normal glucose homeostasis. This occurs at the level of skeletal muscle, liver, and adipose tissues, which develop decreased sensitivity to the effects of insulin. The etiology for this insulin resistance has often been attributed to protease inhibitors. Studies done on HIV-negative patients treated with PIs demonstrated definite signs of insulin resistance. However, it seems possible that a number of factors contribute to insulin resistance. These factors include changes in fat distribution (VAT:SAT ratio), age, and body mass index (BMI). Patients who acquire insulin resistance may have a higher risk of Type 2 diabetes mellitus. There may also be an increased risk of atherosclerotic disease.

A diagnosis of insulin resistance can be made through a combination of physical and laboratory findings, such as polydipsia, polyphagia, polyuria, and increased fasting blood glucose or a suspicious glucose-tolerance test. If insulin resistance is suspected, an intravenous insulin-tolerance test can be conducted to verify the diagnosis. Treatment of insulin resistance includes dietary changes, sensible weight reduction, and exercise. Medical management includes metformin at 500 mg twice daily and cessation of PI use in antiretroviral therapy.

**Lactic Acidemia**

Lactic acidemia is defined as a serum lactic acid level of more than 2.1 mmol/L. Patients with lactic acidosis may be asymptomatic or may present with nausea, vomiting, fatigue, diminished exercise tolerance, shortness of breath, tachypnea, and abdominal pain. Serious manifestations include lethargy, liver failure, increased risk of cardiac arrhythmias, hypotension, shock, and even death. Lactic acidemia is usually associated with NRTI therapy, including ddI, d4T, and AZT, because of its inhibition of mitochondrial replication by disrupting mitochondrial DNA and oxidative phosphorylation. However, it is important to assess other causes of lactic acidosis, including hypoperfusion, severe anemia, and hypoxemia. These can be indications of other co-morbid and potentially fatal illnesses.

Laboratory studies will show signs of anion gap acidosis, including a low bicarbonate. Serum lactic acid will be elevated. Studies have been unable to determine clear risks associated with asymptomatic lactic acid elevation, and routine testing of lactic acid is controversial. Treatment includes supportive care and correction of acid-base imbalance or other possible underlying causes. If lactic acidemia is severe, one should discontinue the offending antiretrovirals. Investigational therapy includes riboflavin (vitamin B2) and thiamine.
Bone-Density Disorders in HIV Infection

Osteopenia, osteoporosis, and osteonecrosis are the most significant bone disorders affecting patients with HIV and AIDS. They represent decrease in bone mineral density, or BMD. Such abnormalities have been observed in both adults and children. Bone loss in children can be particularly serious, as most bone creation takes place prior to the age of 30. The etiologies of bone loss are unclear. Some evidence points to HIV infection itself, while some evidence suggests that treatment regimens are the cause. Still other evidence suggests that antiretroviral therapy might be protective. The pathogenesis seems to be multifactorial. Figure 3 shows some factors that may contribute to decreased BMD in HIV-infected patients.

A DXA scan is used to assess BMD. Individual results are often summarized as a t score, which refers to the number of standard deviations above or below the mean BMD of a young adult (usually about age 30) at peak bone density. The World Health Organization (WHO) criteria for osteoporosis are based on t scores from DXA scans:

- >-1: normal
- -1 to -2.5: indicative of osteopenia
- <-2.5: indicative of osteoporosis

As the t score declines below 0, the risk of fracture increases continuously. The BMD data may also be summarized as Z scores, which are similar to t scores but are normalized to patients the same age as the subject. Several recent studies have shown significant...
decreases in BMD in HIV-infected children, both on and off antiretroviral therapy.\textsuperscript{13,14} Up to 66 percent of children in one study were found to have bone loss on DXA scan.\textsuperscript{15}

When osteopenia is evaluated, vitamin D deficiency and hormonal imbalance must be ruled out, along with renal pathology. Management may include weight-bearing exercise, decreased alcohol consumption, smoking cessation, and vitamin D and calcium supplementation. Some suggest the use of alendronate 5-10 mg per day. Alendronate acts by inhibiting osteoclast bone resorption.

\section*{Adherence}

The impact of these adverse effects on adherence cannot be understated. For some, the task of having to take medicines every day for the rest of their lives without missing a dose is daunting. The difficulty is compounded by the idea that these medicines can cause such adverse physical reactions, especially the cosmetic changes. There is still stigma attached to HIV, and the fear that members of the community can identify someone’s serostatus simply by noticing lipoatrophy can be socially debilitating. Patient and health care workers must understand the adverse effects of antiretroviral therapy as well as their management. This understanding is paramount in maximizing the effectiveness of adherence counseling as well as maximizing the benefits of available treatment regimens.

\section*{Conclusion}

Many endocrine and metabolic changes have been noted in HIV-infected patients. Often these are associated with long-term use of antiretroviral therapy. The morbidity and rare mortality associated with these disorders must be balanced against the often severe morbidity and mortality in HIV-infected patients who are not treated with antiretrovirals. Antiretroviral medications prolong life and improve the quality of life for most patients. Patients should be screened for metabolic abnormalities regularly. Screening can often be accomplished through history taking and physical examination. Many of the first-line treatments for metabolic abnormalities include diet and lifestyle changes. Such changes should be encouraged for all HIV-infected patients on antiretroviral treatment.
MANAGEMENT OF METABOLIC CHANGES RELATED TO ANTIRETROVIRAL TREATMENT

Review Questions

1. Why are elevations in cholesterol and triglycerides considered a health risk for HIV-infected patients?

2. Define lipodystrophy and explain how it might affect patient adherence to medications.

3. What are some cost-effective interventions health professionals can recommend to patients experiencing metabolic changes?

4. Why is bone-density loss particularly dangerous for children?

Exam Questions

1. A 45-year-old man who is HIV-infected comes for a regular screening visit. He is currently on antiretroviral therapy containing a protease inhibitor. As you assess his risk of coronary heart disease, which of the following factors is NOT relevant?
   a. Family history of high cholesterol
   b. History of cigarette smoking
   c. Number of sexual partners
   d. Presence of hypertension

2. A 35-year-old woman has been on antiretroviral therapy, including a protease inhibitor, for five years. On this visit, she says that for the past several months she has noted an increasing thirst and has been urinating more frequently. Which test would you consider ordering?
   a. Fasting blood glucose
   b. Full blood count
   c. Blood culture
   d. Liver-function tests

3. An 8-year-old boy comes to your office. His mother states that in the past several months he has broken his arm twice, both times in seemingly minor falls. He was horizontally infected with HIV and has been in highly active antiretroviral therapy for three years. What might you suggest to the caregiver?
   a. Keep the child inside at all times.
   b. If feasible, obtain a DXA scan.
   c. Supplement his diet with additional vitamin D and calcium.
   d. None of the above
   e. b and c

Answers: 1c, 2a, 3e
Case Study

Jackson is a 17-year-old male with HIV who has been on antiretroviral therapy for about seven months. His regimen includes d4T, ddI, and efavirenz. His viral load has been undetectable, and he has gained 2 kg since starting his therapy. He presents to your clinic complaining of having two weeks of malaise, fatigue resulting in decreased exercise tolerance, nausea, and shortness of breath. He says he has been very compliant with his medicines, missing only one dose in the past month. On physical exam, he is tachypneic with some abdominal tenderness to palpation.

**Question:** Which of the following is the most appropriate diagnostic test to order at this time?

- a. Blood culture
- b. Antistreptolysin titers
- c. Serum cryptococcal antigen
- d. Serum lactate
- e. Serum triglyceride level

**Answer:** d. These vague complaints of fatigue, diminished exercise tolerance, nausea, and shortness of breath, together with the physical findings and his antiretroviral regimen including d4T and ddI, are all very suspicious for lactic acidemia. An elevated anion gap and a low serum bicarbonate are suggestive of metabolic acidosis. A serum lactate level greater than 2.1 mmol/L gives the diagnosis.

**Question:** The lactate level was found to be 6 mmol/L. Of the following, which is the most important course of action?

- a. Trial of L-carnitine
- b. Reassurance
- c. Discontinue the current antiretroviral regimen
- d. Give vitamin B complex orally
- e. None of the above

**Answer:** c. The treatment of severe lactic acidosis secondary to NRTI therapy is supportive. Although there have been studies suggesting a role for administration of co-factor supplementation such as vitamin B complex, L-carnitine, and others, the most important thing to do at this time is to remove the offending cause, i.e. the antiretroviral drugs d4T and ddI.

References


12. Glesby, M. Bone disorders in human immunodeficiency virus infection. 


**GASTROINTESTINAL MANIFESTATIONS OF HIV INFECTION**

Nancy R. Calles, B.S.N., R.N., A.C.R.N.

Jeannie Y. Chang Pitter, M.D.

**Objectives**

The purposes of this module are to:

1. Review specific subjective and objective information important in the assessment of nausea, vomiting, and diarrhea in patients with HIV/AIDS.
2. Analyze the possible causes of diarrhea in patients with HIV/AIDS.
3. Classify the signs of dehydration in relation to their level of severity.
4. Identify the appropriate rehydration plan for use with patients experiencing dehydration.
5. Describe the specific symptoms associated with wasting syndrome in patients with HIV/AIDS.

**Key Points**

1. Patients with HIV/AIDS are at risk of gastrointestinal complications.
2. Careful assessment using subjective and objective information is important when evaluating patients with HIV/AIDS who are experiencing nausea, vomiting, or diarrhea.
3. Patients with diarrhea and/or vomiting should be monitored carefully for signs and symptoms of dehydration.
4. Oral-rehydration fluids should be used when possible for patients with dehydration.
5. Wasting syndrome is a severe form of weight loss associated with HIV/AIDS.
6. Hepatitis is a common co-infection in HIV-infected patients.

**Overview**

People infected with HIV have a higher likelihood of developing complications from gastrointestinal infections than people with normal immune systems. Diarrhea is the most common gastrointestinal manifestation in HIV-infected patients. Others include vomiting, weight loss, esophagitis, malabsorption, jaundice, and failure-to-thrive. Worldwide, many patients with HIV experience diarrhea; in Africa, it is estimated that 60 percent to 97 percent of children with AIDS suffer diarrhea. Gastrointestinal manifestations may be caused by HIV; by other viruses such as cytomegalovirus (CMV), *Mycobacterium avium* complex (MAC), and hepatitis; by bacteria such as salmonella and shigella; by parasites such as cryptosporidia and giardia; and by fungi such as candidiasis. This module will discuss the treatment and management of gastrointestinal manifestations in HIV-infected patients.

**Nausea and Vomiting**

Nausea and vomiting are common physical complaints with many causes. Causes include infection and/or inflammation of the gastrointestinal (GI) tract, an overfilled stomach, gastroesophageal reflux (GER),
protein intolerance, urinary-tract infection (UTI), pregnancy, increased intracranial pressure, meningitis, hepatitis, pancreatitis, malignancies, mechanical obstruction, sepsis, food poisoning/toxins, and altered metabolism. Nausea and vomiting can also be caused by medications, such as antiretroviral agents, drugs used to treat or prevent opportunistic infections (OIs), and antineoplastic (anti-cancer) drugs. (Please refer to the chapter on antiretroviral treatment for a list of specific medications that may cause nausea and vomiting, hepatitis, or pancreatitis as side effects.)

Assessment
Assessment of a patient with nausea and vomiting should include both subjective and objective data.

Subjective Data:
1. Onset of the vomiting, quantity of emesis, presence of blood or bile
2. Relationship of the vomiting to meals, time of day, activities, or medications
3. History of trauma or ill contacts
4. Presence of associated signs and symptoms, such as diarrhea, fever, pain, dysuria, flank or abdominal pain, vision changes, headache, seizures, high-pitched cry (especially in an infant), jaundice, irritability, behavior changes, polydipsia, polyuria, polyphagia, or anorexia
5. Changes in patterns or quantity of urination and amount of oral intake

Objective Data:
1. Patient’s current weight and last known weight
2. Volume of intake and output, and vital signs (temperature, heart rate, blood pressure, respiration rate)
3. Assessment of skin turgor, mucous membranes, and the presence or absence of tears
4. Nuchal rigidity, level of consciousness, and any behavioral changes, such as irritability or lethargy
5. When laboratory studies can be obtained, a complete blood count, serum pH, electrolytes, BUN, creatinine, AST, ALT, bilirubin, amylase, lipase, urine analysis, and urine culture may be helpful in determining the cause of nausea/vomiting and degree of dehydration.

Clinical Considerations
Considerations for patients with nausea and vomiting include identifying the cause of the nausea and vomiting and restoring or maintaining adequate hydration. The patient and family should be educated about the signs of dehydration and the importance of maintaining adequate fluid intake.

The patient’s weight, intake, and output should be assessed daily. Intake should include all oral and intravenous fluids; output should include urine, stool, and emesis. Antiemetic medications may be harmful in the pediatric setting and are not recommended.† Hydration fluids should be administered as available. The types of fluids are discussed in the next section. Patients should be instructed to drink fluids frequently, small volumes at a time; to eat five to six small meals a day; to avoid greasy, high-fat foods; and to eat food at room temperature.

Diarrhea
Diarrhea is defined as an excessive loss of fluid and electrolytes in the stool resulting in three or more loose stools in a 24-hour period.† Acute diarrhea persists for up to 14 days, while chronic diarrhea continues for two weeks or longer.

Diarrhea can be caused by infections, toxins, medications, anatomic abnormalities such as tumors, and dietary intolerance. Infectious causes of diarrhea are the most common. These may be of bacterial, viral, fungal, or parasitic origin. Infections can be classified as causing predominantly watery, large-volume diarrhea due to a predominant small-bowel infection or bloody, small-volume dysentery due to a predominant colonic infection. Pathogens that infect the GI tract are similar worldwide, but the likelihood of infection depends on the patient’s age, immune status, geographic location, and exposure history. Watery diarrhea is commonly caused by agents such as rotavirus, Norwalk virus,
adenoviruses, enteroviruses, Vibrio cholerae, enterotoxigenic E. coli, giardia, and cryptosporidium. Dysentery, characterized by bloody, mucousy stool that may contain white blood cells, may be caused most commonly by shigella and can also be caused by typhoid and non-typhoid salmonella, yersinia, campylobacter, Clostridium difficile, enterohemorrhagic and enteroinvasive E. coli, and the parasite Entamoeba histolytica. Dysentery may be accompanied by systemic symptoms such as fever and an elevated white-blood-cell count. Campylobacter species, salmonella, shigella, and MAC are particularly common bacterial causes of diarrhea in the setting of AIDS. Diarrhea caused by enteric viruses is no more common among children with AIDS than in the general population, although CMV and herpes simplex virus (HSV) may cause opportunistic infection. Candida albicans can infect the gastrointestinal tract of people with AIDS, and parasites such as cryptosporidium and isospora are more likely to cause chronic diarrhea in an immunosuppressed host.

Food- or water-borne pathogens may cause diarrheal infections in immunocompromised hosts at a smaller inoculum than needed to infect healthy hosts, and they may also cause opportunistic infections. Opportunistic AIDS-defining diarrheal illnesses include chronic cryptosporidium (lasting more than one month), CMV disease, histoplasmosis, isosporiasis, MAC, and septicemia from salmonella. (More details regarding these infections and their treatment can be found in the chapter on opportunistic infections.)

Diagnosis of the cause of diarrhea is often difficult because of the many pathogens that produce infection. Whenever possible, appropriate enzyme immunoassays (EIAs) and bacterial, parasite, and special stool cultures should be sent for definitive diagnosis. Bacterial, mycobacterial, and CMV blood cultures may facilitate diagnosis in febrile patients with HIV/AIDS and diarrhea.

Bacterial toxins present in food may also cause acute diarrhea, usually in the setting of vomiting. S. aureus, B. cereus, and C. perfringens can cause food poisoning. Management of toxin ingestion is supportive care. Other causes of diarrhea include medications, such as antiretrovirals, which may cause diarrhea as a side effect. (Please refer to the chapter on antiretroviral treatment for a listing of specific medications that are associated with diarrhea.) Many antibiotics also cause loose stools due to their effect on normal flora, and C. difficile infection may occur in the setting of recent broad-spectrum antibiotic therapy. Inflammatory processes such as celiac sprue (malabsorption syndrome characterized by marked atrophy and loss of function of the small intestinal lining), surgical procedures, and tumors can change the anatomy and function of the intestines and result in diarrhea. (Please refer to the chapter on HIV-associated malignancies for more information about Kaposi's sarcoma and smooth-muscle tumors such as leiomyosarcomas and leiomyomas, which may present with diarrheal symptoms in patients with HIV/AIDS.) Osmotic diarrhea can occur with lactose deficiency and overfeeding, whereas bloody stools may occur with allergy to cow's milk or soy protein.

Many of the above causes of diarrhea may cause chronic diarrhea in children and adults with AIDS. Other causes of chronic diarrhea include HIV enteropathy (“villous atrophy and malabsorption in the absence of identifiable pathogens”), postinfectious enteritis, chronic intestinal infections, inflammatory bowel disease, thyrotoxicosis, encopresis, and pancreatic or liver disease causing fat malabsorption.

Assessment

Assessment of a patient with diarrhea should include both subjective and objective information.

Subjective Data:
1. Onset, duration, amount, frequency, odor, and appearance of stool
2. Presence of any associated symptoms, such as fever, pain, vomiting, cramping, flatus, abdominal distention, tenesmus, and mucus or blood in the stool
3. Dietary changes that might correlate with the increase in the amount of stool

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Assessment of a patient with diarrhea should include both subjective and objective information.

Subjective Data:
1. Onset, duration, amount, frequency, odor, and appearance of stool
2. Presence of any associated symptoms, such as fever, pain, vomiting, cramping, flatus, abdominal distention, tenesmus, and mucus or blood in the stool
3. Dietary changes that might correlate with the increase in the amount of stool
4. Family members with similar illness or other GI diseases and any unusual exposure history (travel, animals, antibiotics)

**Objective Data:**
1. Assess for signs of dehydration, such as sunken fontanel in the infant, poor skin turgor, dry mucous membranes, lack of tears, decreased urine output, and changes in level of consciousness.
2. Compare patient’s current weight with the patient’s previous weight
3. Assess for alterations in tissue perfusion (e.g. tachycardia, delayed capillary refill, hypotension)
4. Examine stool for color, consistency, blood, mucus, pus, odor, and volume
5. If possible, evaluate stool for ova and parasites, bacterial culture, and white blood cells

**Clinical Considerations**
Fluid and electrolyte replacement and maintenance are the mainstays of diarrhea management. Educate the patient and family about the signs of dehydration and the importance of maintaining adequate fluid intake. Administer hydration fluids as available. The management of dehydration is discussed in the next section. Dietary changes may alleviate diarrhea; high-protein, high-calorie foods that are low in fat and free of lactose and caffeine may be helpful. Patients should increase soluble fiber and avoid hot, spicy foods.

Antimicrobial agents may be indicated for the treatment of diarrhea in some situations. Table 1 shows common antimicrobial treatment regimens. Patients should be instructed on the importance of finishing all antimicrobial medications prescribed.

Good perineal hygiene to prevent skin breakdown and frequent handwashing to prevent transmission of infection should be emphasized. Antidiarrheal medications such as loperamide are useful for the management of diarrheal side effects of medications, but they may prolong infections. Bismuth

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**Table 1: Antimicrobial Therapy for Infectious Diarrhea**

<table>
<thead>
<tr>
<th>Organism</th>
<th>Indication for Therapy</th>
<th>Antimicrobial Choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Campylobacter</td>
<td>Early in illness</td>
<td>Macrolide or fluoroquinolone</td>
</tr>
<tr>
<td>Clostridium difficile</td>
<td>Moderate to severe symptoms</td>
<td>Metronidazole or vancomycin</td>
</tr>
<tr>
<td>Entamoeba histolytica</td>
<td>Treat all symptomatic cases.</td>
<td>Metronidazole followed by iodoquino or paromomicin</td>
</tr>
<tr>
<td>Enteroinvasive E. coli</td>
<td>Treat all cases.</td>
<td>Trimethoprim-sulfamethoxazole (TMP-SMX) or fluoroquinolone</td>
</tr>
<tr>
<td>Enterohemorrhagic E. coli</td>
<td>E. coli 0157:H7 should not be treated due to the risk of hemolytic-uremic syndrome.</td>
<td>None</td>
</tr>
<tr>
<td>Enteropathogenic E. coli</td>
<td>Nursery epidemics or severe symptoms</td>
<td>TMP/SMX or fluoroquinolone</td>
</tr>
<tr>
<td>Enterotoxigenic E. coli</td>
<td>Severe or prolonged course</td>
<td>TMP/SMX, fluoroquinolone, or azithromycin</td>
</tr>
<tr>
<td>Giardia</td>
<td>Treat all symptomatic cases.</td>
<td>Metronidazole or Alinia</td>
</tr>
<tr>
<td>Salmonella</td>
<td>Intestinal infections in the immunocompromised and infants under 3 months of age should be treated, as well as typhoid fever and invasive disease.</td>
<td>Ampicillin, TMP/SMX, cefotaxime, ceftriaxone, or fluoroquinolone</td>
</tr>
<tr>
<td>Shigella</td>
<td>Treat all cases. Resistance testing should be performed.</td>
<td>TMP/SMX, Azithromycin, Ampicillin, fluoroquinolone, ceftriaxone, or cefixime</td>
</tr>
<tr>
<td>Vibrio cholerae</td>
<td>Treat all symptomatic cases.</td>
<td>Tetracycline, doxycycline, TMP/SMX, or fluoroquinolone</td>
</tr>
<tr>
<td>Yersinia enterocolitica</td>
<td>Treat all symptomatic cases.</td>
<td>TMP/SMX, aminoglycoside, fluoroquinolone, cefotaxime, chloramphenicol, doxycycline, or tetracycline</td>
</tr>
</tbody>
</table>

Adapted from Table 17.4, Antimicrobial Therapy for Children with Bacterial Enteropathogens.
subsalicylate compounds should be avoided in the setting of vomiting or flu due to their possible association with Reye’s syndrome.

**Dehydration**

Dehydration occurs when water output exceeds water intake. Patients with vomiting and diarrhea are at high risk of dehydration. The patient’s weight and intake and output should be assessed daily. Intake should include all oral and intravenous fluids; output should include urine, stool, and emesis. Dehydration can be classified as mild, moderate, or severe (see Table 2). As dehydration develops, signs and symptoms include a sunken fontanel in infants, poor skin turgor, dry mucous membranes, lack of tears, decreased urine output, changes in the level of consciousness, increased heart rate, and decreased weight.

**World Health Organization Treatment Plan A**

The World Health Organization (WHO) has outlined the treatment of diarrhea at home as Treatment Plan A. Early intervention at home may prevent dehydration and nutritional deficits.

Plan A should be used to treat patients who have:
1. Been seen at a health facility and found to have no signs of dehydration.
2. Been treated at a health facility with Treatment Plans B or C until dehydration was corrected.
3. Recently developed diarrhea but have not visited a health facility.

The three basic rules of home therapy using Plan A are to:
1. Give the patient more fluids than usual to prevent dehydration.
2. Give the patient plenty of food to prevent undernutrition.
3. Take the patient to a health facility if the diarrhea does not get better or if signs of dehydration or another serious illness develop.

**Administration Guidelines: Plan A**

**Which fluids to give:** Fluids that should be used at home to prevent dehydration include “recommended home fluids,” other drinks usually available in the home, and in some instances oral-rehydration salts (ORS) solution. Many countries have recommended specific home fluids for use in oral-replacement treatment. These include food-based drinks, such as undiluted cereal gruel, and sugar-salt solution (SSS). These fluids are suitable for home treatment of most children with diarrhea.

For patients who have been treated for dehydration at a health facility using Treatment Plans B or C (described later), ORS solution should also be used.

Two recipes for oral-rehydration solutions are

<table>
<thead>
<tr>
<th>Table 2: Degrees of Dehydration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Older child</td>
</tr>
<tr>
<td>Infant</td>
</tr>
<tr>
<td>Skin Turgor</td>
</tr>
<tr>
<td>Skin (Touch)</td>
</tr>
<tr>
<td>Buccal Mucosa/Lips</td>
</tr>
<tr>
<td>Eyes</td>
</tr>
<tr>
<td>Tears</td>
</tr>
<tr>
<td>Fontanelle</td>
</tr>
<tr>
<td>CNS</td>
</tr>
<tr>
<td>Pulse Rate</td>
</tr>
<tr>
<td>Pulse Quality</td>
</tr>
<tr>
<td>Blood Pressure</td>
</tr>
<tr>
<td>Capillary Refill</td>
</tr>
<tr>
<td>Urine Output</td>
</tr>
</tbody>
</table>

included below. Please remember to measure all quantities precisely; even minor deviations from these recipes could be dangerous.

### ORS Solutions

<table>
<thead>
<tr>
<th>Starch-Based Solution</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 quart clean water</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1/2 teaspoon table salt</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 ounces (about 1 cup) baby rice cereal</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sugar-Based Solution</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 quart clean water</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1/2 teaspoon table salt</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 teaspoons sugar</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**How much fluid and how often:** The following is a general guide for the amount of fluid to be given at home after each loose stool; continue using until diarrhea resolves.

1. Children ages 2 years or younger: 50-100 ml
2. Children ages 2-10 years: 100-200 ml
3. Children ages 10 years or older and adults: as much as they want

**Which foods to give:** Breastfeeding should be continued without interruption. For infants under 6 months of age who normally take formula or cow’s milk and are not yet taking soft foods, milk should be given at half strength (by diluting it with an equal amount of clean water) for two days. After two days, the usual formula or milk should be given. For other infants and children, the usual cow’s milk should be given throughout the illness.

Children who are 6 months of age or older, younger infants who have already begun to take soft foods, and adults should also be given soft or semi-solid weaning foods. During diarrhea, give the patient as much food as he or she wants. Offer food every three to four hours (six times a day). Small, frequent feedings are tolerated better than large feedings given less frequently.

**WHO Treatment Plan B, for Mild to Moderate Dehydration**

Treatment Plan B is often initiated in the clinic or outpatient setting.

1. Breastfeeding should continue.
2. Estimate the amount of ORS solution to be given during the first four hours with the formula
   \[ 75 \text{ ml} \times \text{weight (kg)} = \text{amount (ml)} \text{ ORS solution} \]
3. Show family members how to give the solution.
4. Monitor treatment and reassess the patient periodically until rehydration is completed.
5. Resume giving foods other than breast milk after four hours.
6. Identify patients who cannot be treated satisfactorily with ORS solution by mouth and adopt a more appropriate method of treatment.
7. Give instructions for continuing treatment at home after rehydration is completed, following Treatment Plan A.
8. If the patient wants more ORS than shown, give more.
9. For infants under 6 months who are not breastfed, also give 100-200 mL clean water during this period.
10. Reclassify patient to Plan A, B, or C after four hours.

**Administration Guidelines: Plan B**

1. Give one teaspoonful (5 mL) of fluid every one to two minutes to children under 2 years of age; offer frequent sips from a cup to older children and adults. Give the determined amount of fluid in a period of four hours.
2. If the patient vomits, wait 10 minutes, then continue giving ORS solution, but more slowly: a spoonful (5 mL) every two to three minutes.

**Monitoring Treatment**

1. Check to be certain that the mother or family member is giving ORS solution correctly and the patient is taking it satisfactorily.
2. Record the amount of solution taken and the number of diarrhea stools.
3. Observe for signs of worsening dehydration (e.g. further loss of skin elasticity, increasing lethargy) or increasing stools, and move to Plan C accordingly.
4. Observe for puffy eyelids, swollen digits, or wet, coarse breath sounds, which can indicate over-
hydration; if these are seen, ORS solution should be stopped, although breastfeeding and the provision of plain water should continue. When the puffiness disappears, return to Treatment Plan A guidelines if stable.

WHO Treatment Plan C, for Severe Dehydration

Patients with signs of severe dehydration can die quickly from hypovolemic shock. They should be treated immediately, following Treatment Plan C:

1. Decide how the fluid will be given: (a) by IV drip, (b) by nasogastric (NG) infusion, or (c) orally.
2. Decide how much IV fluid to give, then give the fluid and reassess the patient frequently.
3. Shift to Treatment Plan B or A when the patient is no longer severely dehydrated.
4. Treat suspected or confirmed cases of bacterial or parasitic infection with the appropriate medication.

Administration Guidelines: Plan C Intravenous Replacement

The treatment of choice for severe dehydration is IV rehydration, because it is the most rapid way to restore the depleted blood volume. Ringer’s Lactate Solution (also called Hartmann’s Solution for Injection) and normal saline (0.9 percent NaCl) are the preferred commercially available solutions (Table 3). If these are not available, half-strength Darrow’s solution with 2.5 percent or 5 percent dextrose or half-normal saline in 5 percent dextrose may be used. IV solutions containing only dextrose (glucose) should not be used.

Infants should be given IV fluid at a rate of 30 ml/kg in the first hour, followed by 70 ml/kg over the next five hours, providing a total of 100 ml/kg in six hours.

Older children and adults should be given IV fluid at a rate of 30 ml/kg within 30 minutes, followed by 70 ml/kg in the next 2.5 hours, providing a total of 100 ml/kg in three hours. After the first 30 ml/kg have been given, a strong radial pulse should be easily felt. If it is still very weak and rapid, a second infusion of 30 mL/kg should be given at the same rate; however, this is rarely necessary. Small amounts of ORS solution should also be given by mouth (about 5 ml/kg/hour) as soon as the patient is able to drink, in order to provide additional potassium and base. This is usually possible after three to four hours in infants and after one to two hours in older children and adults.

Nasogastric (NG) Replacement

If IV therapy is not possible, an NG tube can be used to give ORS solution, provided there is a person trained in the tube’s placement and maintenance. This approach is not as satisfactory as IV infusion, because the fluid cannot be given as rapidly, and additional time is required for it to be absorbed from the intestine. The maximum rate of fluid infusion is about 20 ml/kg/hour. When higher volumes are administered, abdominal distension and repeated vomiting are frequent problems.

Oral Replacement

If IV and NG therapy are not possible or will be delayed, and if the patient is able to drink, ORS solution should be given by mouth at a rate of 20 ml/kg/hour. This approach has the same disadvantages as NG therapy, and it cannot be used for patients who are very lethargic or unconscious. Children under 2 years should be given ORS solution by spoon, about one teaspoonful (5 ml) per minute. Older children and adults may drink the solution from a cup. Patients with abdominal distension caused by paralytic ileus should not be given ORS solution either orally or by NG tube.

Reassessing the Patient

Signs of a satisfactory response to rehydration are return of a strong radial pulse, improved level of consciousness, ability to retain oral fluids, improved skin turgor, and urinary output nearly equal to intake. When these signs are observed, the interval between assessments can be lengthened. If the signs of dehydration remain unchanged or worsen, and especially if the patient continues to pass watery stools, the rate of fluid administration and the total amount of fluid given for rehydration should be increased.
In addition to rehydration therapy, the patient’s normal need for water must be met. Breastfeeding should be resumed as soon as an infant can suck. Infants less than 6 months of age who are not breastfed should be given 100–200 mL of plain water during the first six hours if they are able to drink. Older children and adults should be given water to drink as soon as they desire it, provided that vomiting has subsided. This water is in addition to any ORS solution being given.

**Transition to Treatment Plans B and A**

At the end of the planned rehydration period outlined in Treatment Plan C (usually three to six hours), the patient’s hydration status should be carefully reassessed. If signs of severe dehydration are still present, rehydration therapy must be continued following Treatment Plan C. Otherwise, further treatment should follow Plan B if some signs of dehydration remain or Plan A if there are no signs of dehydration. In either case, ORS solution should be used. Before removing the IV line, however, it is wise to give ORS solution for at least one hour to be certain oral-replacement therapy is feasible. If possible, patients presenting with severe dehydration should be hospitalized until the diarrhea subsides. Otherwise, they should be observed for at least six hours after rehydration before returning home, to make sure that the mother or family member can maintain their hydration using the ORS solution.

**Wasting Syndrome**

Wasting syndrome is an AIDS-defining condition in both adults and children. Wasting is defined by a weight less than 80 percent of expected weight for height. Wasting causes loss of lean body mass. In developing countries in Africa, failure to gain weight and weight loss are the most common presenting signs of HIV disease. Wasting syndrome can be attributed to inadequate caloric intake, malabsorption of

### Table 3: Rehydration Plans and Fluids

<table>
<thead>
<tr>
<th>Indication</th>
<th>Route</th>
<th>Fluid Choice</th>
<th>Dose**</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Plan A:</strong> Prevention of Dehydration in the Setting of Diarrhea *</td>
<td>Oral</td>
<td>ORS solution, undiluted cereal gruel, sugar-salt solution (SSS)</td>
<td>Children &lt;2 years: 50–100 mL after each loose stool</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Children 2-10 years: 100–200 mL after each loose stool</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Children &gt;10 years and adults: as much fluid as desired after each loose stool</td>
</tr>
<tr>
<td><strong>Plan B:</strong> Mild to Moderate Dehydration</td>
<td>Oral</td>
<td>ORS solution, undiluted cereal gruel, SSS</td>
<td>Children &lt;2 years: 5 mL every 1-2 minutes by spoon. Total volume (mL) over 4 hours should equal about 75 mL x weight (kg).</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Children &gt;2 years and adults: 5-10 mL every 5-10 minutes; increase amount as tolerated. Total volume (mL) over 4 hours should equal about 75 mL x weight (kg).</td>
</tr>
<tr>
<td><strong>Plan C:</strong> Severe Dehydration</td>
<td>Intravenous</td>
<td>Ringer’s Lactate Solution (Hartman’s Solution for Injection)/ or normal saline (0.9% NaCl)</td>
<td>Infants: 30 mL/kg for 1 hour, then 70 mL/kg over 5 hours (total of 100 mL/kg over 6 hours)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Older children and adults: 30 mL/kg over 30 minutes, then 70 mL/kg over 2.5 hours (total of 100 mL/kg over 3 hours)</td>
</tr>
<tr>
<td><strong>Plan C:</strong> Severe Dehydration</td>
<td>Nasogastric (only if IV therapy is not available)</td>
<td>ORS solution, undiluted cereal gruel, SSS</td>
<td>20 mL/kg/hour for 6 hours (total of 120 mL/kg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Children &lt;2 years: 5 mL/minute by spoon</td>
</tr>
<tr>
<td><strong>Plan C:</strong> Severe Dehydration</td>
<td>Oral (only if alert and when IV/NG are not possible)</td>
<td>ORS solution, undiluted cereal gruel, SSS</td>
<td>Children &gt;2 years and adults: 20 mL/kg/hour for 6 hours (total of 120 mL/kg)</td>
</tr>
</tbody>
</table>

* See text for modifications in the setting of vomiting.
+ ORS solution: WHO solution, Pedialyte, Rehydralyte
† If not available, use half-strength Darrow’s solution with 2.5% or 5% dextrose or normal saline with 5% dextrose.
‡ “Repeat once if the radial pulse is still very weak or not detectable.”
** Decrease the rate if there is vomiting or abdominal distension.
nutrients from the GI tract, and/or increased metabolic rates.

Considerations for a patient with wasting syndrome include performing a nutritional assessment. The nutritional assessment should include growth measurements and dietary history (see chapter on nutrition). The patient should be assessed for any clinical signs or symptoms that suggest malabsorption, such as chronic diarrhea. Wasting can sometimes be alleviated with the use of antiretroviral agents and/or nutritional supplements. Oral supplementation should be offered to increase caloric intake. If oral supplementation fails, enteral supplementation should be used.

**Hepatitis**

Infection with two or more organisms is known as co-infection. A common co-infection is HIV and hepatitis. Many different viruses cause hepatitis, ranging from hepatitis A to E and G. Symptoms are similar regardless of which virus causes the disease. Patients may present with nausea, loss of appetite, vomiting, abdominal pain, and jaundice. If patients become jaundiced, they may develop pruritis (itching). Hepatitis A is a virus spread by oral-fecal route, often through contaminated food. Immunization to prevent Hepatitis A is recommended in HIV-infected patients with chronic hepatitis C infection. Hepatitis A infection is treated symptomatically and rarely progresses to liver failure. The easiest way to prevent transmission is to practice frequent handwashing and good hygiene.

Hepatitis B and C are transmitted by contact with blood or through sexual contact. Condoms can reduce the risk of transmission. Vaccination against hepatitis B is recommended for HIV-infected patients. Traditional treatment of hepatitis B with interferon is not as effective in HIV-infected people as in the non-infected. New treatments for hepatitis B are being utilized, including the antiretroviral medications lamivudine and Tenofovir disoproxil fumarate (TDF). TDF is recommended for the treatment of lamivudine-resistant hepatitis B. Studies are examining whether the combination of Tenofovir and lamivudine can decrease hepatitis B virus levels further in HIV-infected patients.

Hepatitis C co-infection with HIV is becoming more common worldwide. This is particularly true among intravenous drug users in the United States. In addition, perinatal transmission of hepatitis C has increased among women who are co-infected with HIV and hepatitis C. All infants born to women co-infected with HIV and hepatitis C should be screened for hepatitis C. Treatment for hepatitis C is available and does not appear to interfere with HIV treatment. It is recommended that treatment be started in patients with chronic hepatitis C progressing to cirrhosis. The two treatment regimens that are currently used are interferon alone and interferon in combination with ribavirin. A recent study of peginterferon alfa-2a plus ribavirin found that this combination was more effective in treating HIV/hepatitis C co-infected patients than the combination of interferon and ribavirin or peginterferon alpha-2a alone.
Review Questions

1. Name five important subjective or objective criteria to assess when a patient with HIV/AIDS is experiencing nausea and vomiting.

2. Name five important subjective or objective criteria to assess when a patient with HIV/AIDS is experiencing diarrhea.

3. Define the three classifications of dehydration severity and discuss which symptoms you would see for each class.

4. Identify the treatment for dehydration using the WHO Plan A. What is different in Plan B and in Plan C?

5. How is wasting syndrome defined in a patient with HIV/AIDS?

6. Name four important subjective or objective criteria to assess when a patient with HIV/AIDS is experiencing hepatitis.

Exam Questions

1. Which of the following fluids are acceptable for oral-rehydration therapy at home?
   a. Cow’s milk or formula/breast milk
   b. Rice water
   c. Commercial fruit drink
   d. Water only

2. Harish, aged 9 months, has had watery diarrhea for two days. He drinks cow’s milk and eats regular food. For the past two days, his mother has given him only boiled rice and tea. On physical examination, he shows no signs of dehydration. Which of the following recommendations are appropriate?
   a. Dilute the cow’s milk with an equal volume of water for the next two days.
   b. Encourage extra fluids after each watery stool.
   c. Begin giving an undiluted cereal gruel every four hours.
   d. Stop all solid foods until the diarrhea has resolved.

3. Juma, a 14-month-old boy, has had watery diarrhea for three days and has been assessed as having some dehydration. He has been treated with ORS solution at the clinic and is now ready to go home. Which of the following steps are appropriate?
   a. Give an antibiotic to stop his diarrhea.
   b. Stop all solid foods for two days.
   c. Encourage the mother to give him plenty of food.
   d. Begin giving commercial fruit juice every four hours.

4. Antimicrobial agents are never indicated for the treatment of diarrhea.
   a. True
   b. False

5. Treatment for hepatitis A includes:
   a. Supportive/symptomatic care
   b. Antimicrobials
   c. Interferon
   d. All of the above

Answers: 1a, 2b, 3c, 4b, 5d
Case Study

A 2-year-old toddler presents to clinic with a three-day history of diarrhea and decreased oral intake. On physical assessment, the nurse notes mottled skin color, very poor skin elasticity, parched mucous membranes, thready pulse, and delayed capillary refill.

**Question:** What should be the nurse’s assessment of the child’s level of dehydration?

- a. Mild
- b. Moderate
- c. Severe

**Answer:** c. The child has severe dehydration, as evidenced by the following signs and symptoms: mottled skin color, very poor skin elasticity, parched mucous membranes, thready pulse, and delayed capillary refill.

**Question:** According to WHO guidelines, what would be the most appropriate treatment plan?

- a. Treatment Plan A
- b. Treatment Plan B
- c. Treatment Plan C

**Answer:** c. Children with signs of severe dehydration can die quickly from hypovolemic shock. They should be treated immediately, following Treatment Plan C.

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References

HEMATOLOGIC MANIFESTATIONS OF HIV/AIDS

Nancy E. Kline, Ph.D., R.N., C.P.N.P., F.A.A.N.

Objectives

The purposes of this module are to:
1. Review the physiology of normal hematopoesis.
2. Evaluate the pathogenesis of hematologic manifestations of HIV.
3. Analyze specific laboratory determinations of anemia, neutropenia, and thrombocytopenia.
4. Identify the clinical manifestations of altered hematopoesis related to HIV.
5. Establish care guidelines for children with altered hematopoesis.
6. Formulate specific nursing-care guidelines for children with anemia, neutropenia, or thrombocytopenia.

Key Points

1. Altered hematopoesis in patients with HIV can affect all three cell lines (white blood cells, red blood cells, and platelets).
2. Anemia in children with HIV/AIDS can be caused by opportunistic infection, myelosuppressive drugs, or unknown factors.
3. Children with anemia demonstrate signs and symptoms of decreased oxygen-carrying capacity.
5. Children with neutropenia may develop signs and symptoms of infection.
6. The primary cause of thrombocytopenia in children with HIV/AIDS is idiopathic thrombocytopenic purpura (ITP).
7. Children with thrombocytopenia are at risk for bleeding.

Overview

Altered hematopoesis (blood-cell production) occurs in patients with HIV infection. This affects all three cell lines (red blood cells, white blood cells, and platelets) that come from stem cells in the marrow. Consequently, HIV-infected children may suffer from anemia (lowered levels of red cells), thrombocytopenia (lowered levels of platelets), neutropenia (lowered levels of white blood cells called neutrophils), or any combination of these three. The causes of these conditions are varied, and some are unknown. It has been suggested that HIV actually infects the progenitor cell or causes it to function abnormally. When progenitor cells cannot produce adequate hematopoetic growth factors (the substances that stimulate the production of blood cells in the bone marrow), decreased production of blood cells occurs. In addition, antiretroviral treatment for HIV infection and chemotherapy for treatment of HIV-associated malignancies also cause altered hematopoesis, which can contribute to the problem.

Normal Hematopoesis

To understand abnormal blood-cell production, it is important to know how normal hematopoesis (production of blood cells) occurs. To have normal hematopoesis, a progenitor cell (also called a stem cell)
must be present. The hematopoetic stem cell is the cell from which all blood cells will be derived during a person’s lifetime.

Stem cells are situated in the bone marrow, spleen, liver, and peripheral blood. Stem cells in the bone marrow produce the vast majority of blood cells, while the other sites only assist in times of undue stress. Only about 5 percent of the stem cells in the bone marrow are functioning at any one time, yet they are able to maintain the hematopoetic system for the lifetime of the person.

In addition to the stem cell, other stromal cells must be present for normal hematopoesis to occur. T-lymphocytes, macrophages, endothelial cells, and fibroblasts help to produce the hematopoetic growth factors that are needed for production and differentiation of normal white blood cells in the bone marrow. Erythropoietin, produced in the kidney, and thrombopoietin, produced in the liver, are necessary for proliferation and production of red blood cells and platelets, respectively.

Pathogenesis of Hematologic Manifestations of HIV Infection

Anemia
Anemia can be defined as a reduction below normal of the hemoglobin concentration and red blood cell mass. The etiology of anemia in children with HIV infection is not entirely clear and may be multifactorial in origin (Table 1). Anemia may be caused by opportunistic infection or myelosuppressive drugs. Either of these factors can suppress the bone marrow, which then fails to produce an adequate number of red blood cells (RBCs). The virus that causes HIV may in some way affect the physiologic cue that helps the bone marrow start making new RBCs (known as the erythropoietin feedback mechanism). If this mechanism is blunted, inadequate RBC production occurs. Patients with HIV infection often have lower-than-normal levels of vitamin B-12, folate, and iron. These substances are necessary for normal RBC production. If they are not available in adequate amounts, the child will become anemic.

Neutropenia
Neutropenia occurs when there is a decreased number of neutrophils in the peripheral circulation. It is defined as an absolute neutrophil count (ANC) of less than 1000/mm³ in infants 2 weeks to 1 year of age and of less than 1500/mm³ in children older than 1 year. The
risk of serious bacterial infection increases when the ANC falls below 500/mm$^3$. The ANC is calculated by multiplying the total white blood cell count by the sum of the percentages of segmented neutrophils and bands (two types of granulocytes).

Example:

\[
\text{WBC} = 3000/\text{mm}^3 \quad \text{Segs} = 24\% \quad \text{Bands} = 4\%
\]

\[
\text{ANC} = 3000 \times 0.28 = 840/\text{mm}^3
\]

Children with HIV or AIDS may develop neutropenia. Like anemia, neutropenia in children with HIV is caused by various factors. In some people with HIV infection, decreased levels of the factor that stimulates production of white blood cells (WBCs) in the bone marrow (granulocyte colony stimulating factor, or GCSF) are present. A deficiency of GCSF can cause chronic neutropenia. Many antiretroviral drugs that are given to treat HIV can cause neutropenia, as can antibiotics and antiviral drugs used to treat infection.

### Table 3: Care Guidelines for Children With Altered Hematopoiesis

<table>
<thead>
<tr>
<th>Anemia</th>
<th>Hemoglobin &lt;10 gm/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Monitor CBC for decreased hemoglobin</td>
<td></td>
</tr>
<tr>
<td>• Assess for tachycardia, heart murmur, pallor, tachypnea, dyspnea, level of consciousness</td>
<td></td>
</tr>
<tr>
<td>• Monitor for associated symptoms: irritability, fatigue, shortness of breath, chest pain with exertion, headaches</td>
<td></td>
</tr>
<tr>
<td>• Provide medical interventions as ordered</td>
<td></td>
</tr>
<tr>
<td>- Transfuse with PRBCs 10 ml/kg prn when symptomatic</td>
<td></td>
</tr>
<tr>
<td>- Provide oxygen during periods of respiratory distress</td>
<td></td>
</tr>
<tr>
<td>• Patient and family education</td>
<td></td>
</tr>
<tr>
<td>- Quiet activities are tolerated better during periods of anemia</td>
<td></td>
</tr>
<tr>
<td>- Signs and symptoms that signal anemia: irritability, change in skin color, increased heart rate and respiration, shortness of breath</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Neutropenia</th>
<th>ANC &lt;1000/mm$^3$ for age 2 weeks to 1 year or &lt;1500/mm$^3$ for children &gt;1 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Monitor CBC for decreased hemoglobin</td>
<td></td>
</tr>
<tr>
<td>• Assess for fever, skin ulcerations, pain, cough, tachypnea, rales, wheezing, stomatitis, perirectal fissures</td>
<td></td>
</tr>
<tr>
<td>• Provide antibiotic therapy as ordered for fever</td>
<td></td>
</tr>
<tr>
<td>• Monitor temperature</td>
<td></td>
</tr>
<tr>
<td>• NO rectal temperatures or exams</td>
<td></td>
</tr>
<tr>
<td>• Avoid intramuscular injections</td>
<td></td>
</tr>
<tr>
<td>• Avoid urinary catheterization</td>
<td></td>
</tr>
<tr>
<td>• Prep skin with povidone-iodine or alcohol prior to phlebotomy</td>
<td></td>
</tr>
<tr>
<td>• Patient and family education</td>
<td></td>
</tr>
<tr>
<td>- Avoid ill contacts</td>
<td></td>
</tr>
<tr>
<td>- Wash hands frequently</td>
<td></td>
</tr>
<tr>
<td>- Notify health care provider when fever is &gt;38.4°C</td>
<td></td>
</tr>
<tr>
<td>- Practice meticulous oral hygiene</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Thrombocytopenia</th>
<th>Platelet count &lt;100 000/mm$^3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Monitor CBC for decreased hemoglobin</td>
<td></td>
</tr>
<tr>
<td>• Assess for bleeding, bruising, petechiae, purpura</td>
<td></td>
</tr>
<tr>
<td>• Provide medical interventions as ordered</td>
<td></td>
</tr>
<tr>
<td>- Transfuse with platelets 6 units/m² prn for active bleeding that is not controlled</td>
<td></td>
</tr>
<tr>
<td>• Avoid intramuscular injections or lumbar puncture if possible</td>
<td></td>
</tr>
<tr>
<td>• Use pressure dressings if bone-marrow aspiration is necessary</td>
<td></td>
</tr>
<tr>
<td>• NO rectal temperatures or exams</td>
<td></td>
</tr>
<tr>
<td>• Patient and family education</td>
<td></td>
</tr>
<tr>
<td>- Quiet activities help to prevent bleeding associated with injury</td>
<td></td>
</tr>
<tr>
<td>- Encourage fluids to prevent constipation</td>
<td></td>
</tr>
<tr>
<td>- Notify health care provider if bleeding occurs and cannot be controlled</td>
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</tr>
</tbody>
</table>
and chemotherapeutic agents used to treat HIV-associated malignancies (Table 2).

**Thrombocytopenia**

Thrombocytopenia, or a low platelet count, means a decrease in the number of platelets in the peripheral blood to less than 100,000/mm³, regardless of age. Thrombocytopenia occurs in patients with HIV infection. The primary cause of thrombocytopenia in children with HIV is idiopathic thrombocytopenic purpura (ITP). ITP is caused by an abnormal process in which circulating platelets are coated with an antibody and ultimately removed from the peripheral circulation as they travel through the spleen. In addition, patients with HIV may not produce the same number of platelets as uninfected people.

**Clinical Manifestations of Altered Hematopoiesis**

All children with alterations in hematopoiesis should have a comprehensive patient history, physical examination, and complete blood count (CBC). Bone-marrow aspiration and biopsy may be necessary to determine the cause, because some children with HIV infection develop a malignancy that causes the altered hematopoiesis. The signs and symptoms of anemia, neutropenia, and thrombocytopenia are reviewed below, and care guidelines to manage these children are outlined in Table 3.

**Clinical Presentation of a Child With Anemia**

- Pale conjunctivae or palmar creases, jaundice
- Fatigue or irritability
- Decreased ability to concentrate
- Headaches, dizziness
- Tachycardia, heart murmur
- Cold or discolored extremities
- Glossitis
- Nailbed deformities

**Clinical Presentation of a Child With Neutropenia**

- May be asymptomatic
- Fever
- Skin ulcerations or lesions
- Tachypnea, cough, wheezing, rales
- Stomatitis, dysphagia
- Abdominal pain, diarrhea
- Perirectal pain or fissure

**Clinical Presentation of a Child With Thrombocytopenia**

- Bruising, petechiae, purpura
- Epistaxis
- Gingival bleeding
- Hematuria
- Hematochezia

**Nursing Care of a Child With Altered Hematopoiesis**

Nurses caring for children with HIV or AIDS need to understand normal hematopoiesis and to know that alterations in this process may occur in these patients. Altered hematopoiesis leads to significant morbidity in HIV-infected children and may even cause death. By monitoring laboratory values and identifying signs and symptoms of anemia, neutropenia, or thrombocytopenia, the nurse may be the first health care provider to initiate intervention. Care guidelines for these children are contained in Table 3.
HEMATOLOGIC MANIFESTATIONS OF HIV/AIDS

Review Questions

1. Review the physiology of normal hematopoiesis beginning with the stem cell.

2. Name the causes of anemia in a child with HIV/AIDS and the etiologies associated with them.

3. Identify the causes of neutropenia in a child with HIV/AIDS and the etiologies associated with them.

4. What are common signs and symptoms associated with anemia, neutropenia, and thrombocytopenia?

5. What are specific nursing interventions for the care of a child with anemia, neutropenia, and thrombocytopenia?

Exam Questions

1. Which of the following is a possible cause of anemia in a person with HIV/AIDS?
   a. Increased levels of iron
   b. CMV viral infection
   c. Antibody production
   d. Increased B-12 absorption

2. Children with HIV/AIDS who develop neutropenia are at risk for:
   a. Bleeding
   b. Shortness of breath
   c. Infection
   d. Malnutrition

3. Clinical manifestations of a child with thrombocytopenia include:
   a. Fever
   b. Pale conjunctivae
   c. Petechiae
   d. Stomatitis

Answers: 1b, 2c, 3c
**Case Study #1**

A mother brings her 4-year-old daughter to the clinic because she has noticed blood oozing from the child’s gingival tissue. The day before she came to the clinic, the daughter had a nosebleed that lasted 45 minutes. When you examine her, you notice she has a deep purple bruise on her right flank and other bruises scattered over her body. There are generalized petechiae on her trunk, extremities, face, and neck.

**Question:** A complete blood count reveals that her platelet count is 39,000/mm³. Which of the following terms characterizes a low platelet count?

a. Anemia  
b. Thrombocytopenia  
c. Neutropenia

**Answer:** b. Thrombocytopenia occurs when the platelet count in the peripheral blood is less than 100,000/mm³, regardless of age. Patients with HIV infection may not produce the same numbers of platelets as uninfected people. In addition, they may develop idiopathic thrombocytopenic purpura (ITP) that causes the platelet count to fall because the platelets are coated with an antibody and removed from circulation as they pass through the spleen.

**Question:** What are some of the signs and symptoms of thrombocytopenia?

a. Fever, malaise, cough  
b. Fatigue, tachycardia, pallor  
c. Bruising, hematochezia, hematuria, purpura

**Answer:** c. Thrombocytopenia causes spontaneous bleeding in the soft tissue, mucosa, and gingivae, and in some cases can lead to severe bleeding in vital organs, such as the brain. Bruises may appear on odd parts of the body, such as the flanks and buttocks.

**Question:** The mother is concerned that her daughter may have another nosebleed. What information can you provide her on how to treat a nosebleed at home?

a. Have the child lie flat. Apply a cool cloth to the forehead.  
b. Have the child bend forward and rest her head between her knees until the bleeding stops.  
c. Have the child remain upright. Wearing gloves or using a soft cloth, tightly pinch her nostrils against her nasal septum for at least 10 minutes.

**Answer:** c. Constant pressure that compresses the nares to the nasal septum helps slow the flow of blood and may cause it to cease. The child should not lie down while her nose is bleeding, because excess blood can drip into the nasopharynx, be swallowed, and cause nausea and vomiting. Resting the head between the knees will promote blood flow to the area and increase bleeding.

**Case Study #2**

You are examining a 16-year-old girl with HIV infection who is in the clinic because she has been feeling very tired. She tells you that she goes to school during the day and then works at the market until it closes. She has to help her mother by working so that they can afford to stay in their small house and feed her six brothers and sisters. She often does not eat, because she worries that her younger brothers and sisters will not have enough food. Lately she has had shortness of breath and headaches nearly every day. She has not had any recent infections, fevers, or other illnesses.
Question: A complete blood count shows that her hemoglobin is 9.6 g/dL, well below the lower limit of normal for her age, but her platelet count and white blood cell count are normal. The anemia in this young lady may be due in part to which of the following?

a. Drug-associated hemolytic anemia
b. Malignancy
c. Dietary deficiency

Answer: c. The etiology of anemia in individuals with HIV infection is not entirely clear and may be multifactorial. The virus that causes HIV may affect the way the body manufactures red blood cells. Although certain medications and malignancies can cause anemia, these two etiologies are not as likely based on her history and physical assessment data. However, persons who have HIV may also have lower levels of vitamin B-12, folate, and iron than uninfected individuals. If dietary intake of these substances is inadequate, then ineffective production of red blood cells is likely, causing anemia.

Question: Which of the following is NOT a clinical manifestation of anemia?

a. Nosebleeds
b. Tachycardia, heart murmur
c. Headaches, dizziness
d. Cold or pale skin

Answer: a. Although nosebleeds may ultimately cause anemia due to blood loss, a nosebleed is not a clinical sign of anemia. Patients who are anemic exhibit pallor, fatigue, irritability, decreased ability to concentrate, headaches, dizziness, tachycardia, heart murmur or gallop, and cold extremities. Patients who have chronic anemia exhibit all of the above manifestations as well as glossitis, nailbed deformities, and poor wound healing.

Question: The doctor at the clinic looks at the peripheral smear and tells you that the red blood cells are very small and pale, which may indicate she has iron-deficiency anemia. Which of the following would be the most important educational information to offer this young woman during this visit?

a. Measures to prevent bleeding
b. Nutritional counseling
c. Information on growth and development

Answer: b. The platelet count is normal, so there is no need at this time to review thrombocytopenic precautions. Information on growth and development is important to provide to all children and adolescents, but it is not the most important educational information that she needs at this time. Based on the presumed diagnosis of iron-deficiency anemia, nutritional counseling is the most important patient education that you can provide to help her try to select foods that are rich in iron.

Case Study #3

You are taking care of an 18-month-old girl with HIV infection whose mother says the child has had a persistent cough and now has sores in her mouth. She was seen by the doctor three weeks earlier and was given oral antibiotics for pneumonia. On physical examination, she has ulcers in her oropharynx, and her lung sounds are clear. Her temperature is normal. A complete blood count reveals a white blood cell count of 2400/mm³, a platelet count of 160 000/mm³, and hemoglobin of 12.6 gm/dL. The percentages of segmented neutrophils and bands equal 26 percent and 6 percent, respectively.
Question: **What is her absolute neutrophil count (ANC)?**

- a. 76.8  
- b. 0.768  
- c. 768  
- d. 76 800

**Answer:** c. The ANC is calculated by multiplying the total white blood cell count by the percentage of segmented neutrophils and bands. ANC = 2400 x 0.32 = 768/mm³. Neutropenia is defined as an ANC of less than 1500 in children older than 1 year.

Question: **Which of the following does NOT cause neutropenia?**

- a. HIV  
- b. Trimethoprim-sulfamethoxazole  
- c. ZDV  
- d. Ferrous sulfate

**Answer:** a. Like anemia, neutropenia in persons with HIV is caused by various factors. Decreased levels of granulocyte colony stimulating factor is present in some people with HIV, predisposing them to have fewer neutrophils in the peripheral circulation. Certain medications (e.g. antiretroviral agents, antibiotics, antiviral drugs, chemotherapy) may also cause neutropenia.

Question: **Which of the following educational points do you want to make to the mother to help decrease the likelihood that she will transmit an infection to her neutropenic child?**

- a. Avoid ill contacts  
- b. Wash hands frequently and always before touching or feeding the child  
- c. Practice meticulous oral hygiene  
- d. All of the above

**Answer:** d. People who are neutropenic often develop repeated infections. Avoiding contact with others who are obviously ill (e.g. have fever, upper respiratory infections, or gastrointestinal infections), practicing good handwashing before touching or feeding the child, and maintaining meticulous oral hygiene are all methods of preventing the transmission of illness.

### References


Objectives

The purposes of this module are to:
1. Describe the physiology of pain.
2. Review the causes of pain in people with HIV.
3. Identify key components of pain assessment.
4. Describe the WHO analgesic (pain-relief) ladder for pain management.
5. Understand the classifications of pain medications used for people with HIV.
6. Identify side effects related to pharmacologic pain management.
7. Describe pain from a psychological perspective.
8. Describe symptom management at end-of-life in people with HIV/AIDS, including management of nausea and vomiting, diarrhea, constipation, hiccups, pruritis, and dyspnea.

Key Points

1. Pain is both a sensory and an emotional experience associated with tissue damage.
2. Pain is defined as nociceptive when it results from ongoing activation of primary afferent neurons by noxious stimuli.
3. Pain in people with HIV is a serious problem and is often undertreated.
4. Pain management for people with HIV should follow the WHO analgesic ladder when possible and should also include behavioral interventions.
5. Symptom management at end-of-life is complex and requires ongoing assessment and intervention.

Physiology of Pain

Nociceptive Pain

The sensation of nociceptive pain occurs when the nerve endings in the periphery are activated by a noxious stimulus. Nociceptive pain generally is a response to direct tissue damage. The initial trauma causes the release of several chemicals, including bradykinin, serotonin, substance P, histamine, and prostaglandin. These chemicals facilitate the transmission of the pain impulse from the periphery to the spinal cord.

Small C fibers and large A delta fibers pick up messages at the site of injury and transmit signals to the dorsal horn of the spinal cord. Neurotransmitters (including glutamate, substance P, and adenosine triphosphate) allow the pain signals to ascend to the brainstem by the spinothalamic tract and enter the higher centers of the brain. The cerebrum and thalamus are known as the control centers that process and register the experience of pain. Once an impulse enters the higher centers of the brain, they process information about the pain, such as location and intensity, along with factors such as fear, past and present experiences, and the person's current emotional status. All these factors
are considered before a response attempts to stop the pain. The brain may respond by blocking further pain impulses from reaching the higher centers or by producing endogenous opioids (endorphins), which saturate pain-receptor sites along the spinal cord and in the brain, providing an analgesic effect.

**Neuropathic Pain**

Neuropathic pain is caused by altered excitability of the peripheral or central nervous system, usually caused by dysfunction or injury. Neuropathic pain is distinguished from nociceptive pain by its persistence over a longer period of time. Neuropathic pain is frequently described as a burning, stabbing, or shooting sensation. A complete neurologic exam is essential to evaluate sensory, motor, cranial nerve, reflex, cerebellar, cognitive, and emotional function. Sensory evaluation may reveal the presence of hyperalgesia (increased sensitivity to pain) or allodynia (pain caused by benign stimuli, such as touch). These findings are significant symptoms associated with neuropathic pain, especially when no apparent skin pathology is present.

**HIV-Related Pain**

Pain experienced by people with HIV is caused by the disease and by infections and cancers that occur because the disease has disabled the immune system. Lesions, such as those of Kaposi’s sarcoma or infections of the oral cavity, can cause nociceptive pain. So can visceral inflammation (e.g., gastritis, pancreatitis, and biliary tract disorders); deep somatic causes such as myopathies (muscle pains), arthralgias (joint pains), and back pain; and headaches (related to HIV-related meningitis or encephalitis). Drugs that are used to fight the virus, such as AZT, can also cause neuropathic pain. Neuropathic pain in people with HIV is most commonly associated with nerve pain after a herpes virus infection, with drugs used to fight HIV, and with associated diabetic neuropathy (see Figure 1).

---

**Figure 1: Sources and Locations of Pain in Persons With HIV**

Pain Assessment

Pain is both a sensory and an emotional experience. The patient’s emotional state can affect his or her perception of pain. For this reason, several assessment strategies are needed to provide qualitative and quantitative information about pain. Qualitative assessment is a description of the location, duration, and characteristics of the pain, as well as of factors affecting the pain (see Table 1). Quantitative assessment evaluates the intensity of the pain using a pain scale.

Special Considerations:
Assessment of Pain in Children
It can often be difficult to assess pain caused by HIV in children, particularly if the children are very young. Parents can provide important information to assist with the assessment of pain (see Table 2).

Pain Rating Scales
Pain rating scales are important assessment tools that can help determine the level of pain as well as whether pain-management strategies are working. A simple linear scale can be used in any setting to determine the perception of pain experienced by the person with HIV (Figure 2).

Table 1: Qualitative Pain Assessment

<table>
<thead>
<tr>
<th>Child Form</th>
<th>Parent Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tell me what pain is.</td>
<td>What word(s) does your child use in regard to pain?</td>
</tr>
<tr>
<td>Tell me about the hurt you have had before.</td>
<td>Describe the pain experiences your child has had before.</td>
</tr>
<tr>
<td>Do you tell others when you hurt? If yes, whom?</td>
<td>Does your child tell you or others when he/she is hurting?</td>
</tr>
<tr>
<td>What do you do for yourself when you are hurting?</td>
<td>How do you know when your child is in pain?</td>
</tr>
<tr>
<td>What do you want others to do for you when you hurt?</td>
<td>How does your child usually react to pain?</td>
</tr>
<tr>
<td>What don’t you want others to do for you when you hurt?</td>
<td>What do you do for your child when he/she is hurting?</td>
</tr>
<tr>
<td>What helps the most to take your hurt away?</td>
<td>What does your child do for him/herself when he/she is hurting?</td>
</tr>
<tr>
<td>Is there anything special that you want me to know about you when you hurt? (If yes, have child describe.)</td>
<td>What works best to decrease or take away your child’s pain?</td>
</tr>
</tbody>
</table>

Table 2: Children’s Pain Experience History

<table>
<thead>
<tr>
<th>Child Form</th>
<th>Parent Form</th>
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</thead>
<tbody>
<tr>
<td>Tell me what pain is.</td>
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<td>What helps the most to take your hurt away?</td>
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</tr>
<tr>
<td>Is there anything special that you want me to know about you when you hurt? (If yes, have child describe.)</td>
<td>What works best to decrease or take away your child’s pain?</td>
</tr>
</tbody>
</table>


Figure 2: Numeric Pain Scale

Scale uses a straight line with end points identified as “no pain” and “worst pain”; divisions along the line are marked in units from 0 to 5 (high number may vary). Scale may be used horizontally or vertically.

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Worst Pain</td>
</tr>
</tbody>
</table>
Assessment of pain in children can include a pain rating scale. The FACES pain scale has been used in many countries to assess children’s perceptions of pain. It can be used with children as young as 3 years of age (Figure 3).

**Physical Examination**
Performing a complete physical examination is vital to a thorough assessment of a patient’s pain. The physical examination should attempt to establish the relationship of the pain complaint to the disease. Special attention should be given to the abdomen and gastrointestinal system prior to initiation of narcotic therapy, because those drugs can cause constipation.

**Physiologic Measures and Diagnostic Studies**
Physiologic measures should be used only as adjuncts to self-reports of pain and behavioral observation. As with behavioral measures of pain, physiologic or biologic measures cannot discriminate well between physical responses of pain and other forms of stress on the body.

Physiologic responses include skin flushing, diaphoresis, elevated blood pressure, tachycardia (fast heart rate), tachypnea (quick breathing), restlessness, and dilation of the pupils. The occurrence and severity of these symptoms vary among patients.

Behavioral observation can be used with preverbal and non-verbal patients, and in addition to self-reports in all other cases. Observation includes vocalizations, verbalizations, facial expressions, motor responses, body posture, activity, and appearance. Pain is expressed differently depending on the age and developmental level of the patient.

Interpret behaviors cautiously. Behaviors such as watching television, playing, and sleeping can be distraction strategies used for coping with pain. In addition, patients with chronic pain may not show symptoms of the pain because they have adapted to it.

**Key Points to Remember for Pain Assessment**
Failure to assess pain is a critical factor leading to undertreatment. Assessment should occur:
- At regular intervals after initiation of treatment.
- At each new report of pain.
- After pharmacologic or non-pharmacologic intervention, at an appropriate interval (e.g. 15-30 minutes after parenteral therapy, one hour after oral administration); follow-up assessment is crucial.

It is essential to document the pain assessment on the patient’s medical record.

When there is uncertainty about the presence or amount of pain even after using assessment strategies (a common occurrence with infants and young children), a diagnostic trial of analgesics is appropriate.

**Pharmacologic Pain Management**
The current standard for the management of pain

---

**Figure 3: FACES Pain Scale**

```
0      1     2      3      4      5
No Hurt Hurts Little Bit Hurts Little More Hurts Even More Hurts Whole Lot Hurts Worst
```

Numbers for coding may vary. Recommended age: children from 3 years.

*FACES Pain Rating Scale (Whaley and Wong, 1987. Used with permission.*)
consists of four concepts: “by the ladder,” “by the clock,” “by the mouth,” and “by the person.” This means that pain management should follow the World Health Organization (WHO) analgesic ladder, be administered on a scheduled basis, be given by the least invasive route, and be tailored to the individual’s circumstances and needs.

By the Ladder
The WHO analgesic ladder is a multi-step approach to treating pain and a guide for initiating analgesic drugs and dosages that correspond to the patient’s reported level of pain (Figure 4). The ladder starts with non-opioid oral drugs for mild pain and progresses to strong opioids, adjuvants (e.g. antidepressants, anticonvulsants, anxiolytics, corticosteroids), and invasive therapies for severe or intractable pain. It is important to keep in mind that the potency of pain relief should be matched to the patient’s reported level of pain (Table 3). For example, patients who report severe pain should be started on a potent opioid such as morphine. It would be inappropriate to start a patient with severe pain on ibuprofen or a weak opioid and progress up the ladder from that point.

Overview of the Mechanism of Action of Analgesic Drugs

NSAIDs/Acetaminophen
Non-steroidal anti-inflammatory drugs (NSAIDs) have analgesic, anti-pyretic (fever-lowering), and anti-inflammatory effects. NSAIDs act peripherally to provide their analgesic effect by interfering with

Figure 4: WHO Therapeutic Ladder for Pain Management

the synthesis of prostaglandin through the inhibition of cyclooxygenase (COX).

There are two isoenzymes of COX, COX-1 and COX-2. The COX-1 isoform is expressed primarily in the kidney and gastro-intestinal tract and on platelets. In contrast, the COX-2 isoform is found in low levels in tissues and is induced during inflammation. By selectively inhibiting the COX-2 isoform, some NSAIDs influence the prostaglandin pathways, decreasing pain and inflammation and avoiding the toxicities of the inhibition of COX-1. Most NSAIDs are non-selective inhibitors of COX.

The side effects of nonselective NSAIDs include decreased platelet aggregation, which can cause bleeding problems, gastric irritation, and, with long-term use, a potential for toxicity affecting the kidneys. Patients who have low platelet counts or who are neutropenic (have low counts of white blood cells called neutrophils) should be monitored carefully when taking nonselective NSAIDs for pain relief.

Acetaminophen (paracetamol) has similar pain-relieving and fever-lowering effects as the NSAIDs, but it does not provide an anti-inflammatory effect. Acetaminophen does not affect platelet function or irritate the stomach but can, in high doses (>75 mg/kg/day or 4 g/day), damage the liver.

**Opioids**

The most commonly used class of opioids includes morphine, fentanyl, and codeine. These drugs provide high levels of pain relief, probably because they have an effect on the central nervous system (CNS). The more of such a drug one gives, the greater the pain relief. However, because these drugs can slow or even stop a patient from breathing and are physically addictive, the amount that can be prescribed to a patient is limited. Meperidine is also in this class of opioids, but its action is brief, and it can cause toxicity resulting seizures, even at low doses. Because of these factors, **meperidine should not be used for chronic pain control**. These opioids can be given in pill form, rectally, as subcutaneous or intravenous infusions, intramuscularly, transdermally, and directly into the CNS via epidural/caudal/intrathecal injection.

The most common side effects of opioid pain relief are constipation, sedation, itching, and nausea/vomiting. Respiratory depression and slowed breathing, although the most frequently cited concern of health care providers, are rare occurrences. The risk of respiratory depression decreases significantly when patients are on opioid pain relievers for prolonged periods of time. In the event that mild respiratory suppression occurs, it is easily managed by awakening the patient, giving oxygen, and decreasing further opioid doses by 25 percent.

Common negative effects of all opioids are tolerance, physical dependence, and addiction. Tolerance occurs when the opioid over time becomes less effective in relieving pain. Over time, opioids are also less likely to sedate the patient or to cause breathing to slow or stop. This is a beneficial form of tolerance, because it means the dose of the drug can be increased without endangering the patient.

Concerns about the development of tolerance should not lead health care providers to “save” opioid drugs for later use. Tolerance is easily managed by increasing...
the dose of the opioid, adding appropriate adjuvants, or switching to another opioid drug. In some cases, a person who has become tolerant to one opioid will be somewhat tolerant to another. When a patient is switched to the new opioid, the dose should be reduced to as little as 50 percent of the pain-relieving dose of the previous drug. From there, the health care provider can increase dosage until pain relief is adequate.

Adjuvants
Adjuvant drugs are used in combination with non-opioid and opioid drugs to enhance pain management, most frequently in complicated neuropathic pain syndromes. Adjuvant drugs can be divided into two categories: co-analgesic drugs and drugs that treat side effects. Co-analgesics include drugs from a variety of classes, such as antidepressants and sedatives/hypnotics. Drugs used to treat side effects include antihistamines, psychostimulants, laxatives, neuroleptics, and antiemetics.

Some medications are very useful in combinations with analgesics or pain relievers:

- **Steroids**
  Steroids can help reduce edema (swelling) and inflammatory responses and thereby ease pressure on surrounding structures. In the head, such pressure can cause headache, nausea, and vomiting. In other areas, it can cause bone pain, pain involving the covering of the lungs, and nerve and spinal-cord compression.

- **Muscle relaxants**
  Muscle spasms caused by nerve involvement can make pain worse. They may be relieved with local heat or massage. Diazepam (Valium) is a useful muscle relaxant, especially when given at night.

- **Drugs that act on the CNS**
  Anxiety often complicates the feeling of pain. Medications to relieve anxiety, such as diazepam, are therefore often useful. Phenothiazines may be combined with an opioid analgesic. Antidepressants (e.g. amitriptyline) can also help relieve pain associated with nerve destruction, as in herpes zoster or shingles.

**By the Clock**
One of the most common causes of undermedication of patients in pain is the use of PRN (pro re nata or “as needed”) dosing schedules. The goal of pain management is to optimize pain relief while minimizing undesirable side effects. When analgesics are administered on a scheduled basis, a steady therapeutic state is achieved, providing consistent pain relief and allowing tolerance to side effects to develop. When a PRN schedule is used, analgesia is frequently administered in a random pattern. This results in brief periods of pain relief followed by potentially long periods of pain with increasing undesirable side effects. While PRN dosing is ineffective as the only method of pain management, it can be appropriate when used to provide extra doses of a regularly scheduled analgesia to treat episodes of intense or severe “breakthrough” pain.

**Dosing**
The appropriate initial dose of opioid analgesic depends on the patient's prior exposure to opioids, the severity of the pain, and the route of administration. For patients with severe pain, it is necessary to titrate or change the opioid dose frequently to achieve pain relief as quickly as possible. The route used to administer medication to patients with HIV must be considered carefully. Generally, the least invasive route should be used.

The needs of the individual patient must be taken into account when determining dosages of pain medications. There is no standard dose that will work for everyone. The goal is to provide each patient with the dose of analgesic or pain-relieving medication that prevents recurrence of pain prior to the next dose, keeping the patient pain-free.

**Oral/Sublingual**
Patients who are able to swallow tablets can achieve excellent pain control with oral medications, and this route should be the first choice for administration of analgesic medication.
Oral opioids undergo a “first-pass effect” in the liver, so oral doses must be higher than parenteral doses. Drugs that can be administered sublingually prevent the first-pass effect as the drug is absorbed directly into the bloodstream and provides a more rapid effect.

**Rectal**

Many drugs are available in rectal suppositories. However, absorption of drugs by the rectal route can be inconsistent. The rectal route is also contraindicated in patients with neutropenia (deficiency of white blood cells called neutrophils) or thrombocytopenia (deficiency of platelets, the blood cells responsible for clotting) because of the risk of infection or bleeding.

**Management of Side Effects**

Opioids have side effects that can create discomfort. The most common side effects are constipation, sedation (sleepiness), pruritis (itching), and nausea/vomiting.

To prevent constipation, patients on opioids should immediately be started on a stool softener combined with a mild peristaltic stimulant (a medication that helps initiate the movement of food through the intestines). Constipation can be treated with increased fiber, such as bran cereals, and fluids, such as prune juice. Severe constipation may require the use of a cathartic drug that can stimulate a bowel movement. Enemas and suppositories are administered when other measures have not relieved the problem. The following guidelines can be used to prevent and manage constipation caused by opioid use:

- **Routinely assess the patient’s usual bowel habits, use of laxatives, and date of last bowel movement.** Optimally, bowel movements should occur a minimum of every two days.
- **Encourage the intake of fluids and fiber products (water, stewed prunes, fruits, bran products, grated beet root), but do not force their use.** They can worsen symptoms in the presence of an impaction (an accumulation of feces in a bowel that has not moved).
- **Begin a stool softener or laxative at the initiation of opioid use; a combined laxative and stool softener should be started if bowel movements are less frequent than every two days.**
- **Determine which medications to use based on the patient’s bowel movements.** For children on long-term or high doses of opioids, constipation can become a chronic problem. If a child has not had a bowel movement in more than three days despite the use of oral laxatives and stool softeners, consider the use of a suppository. If constipation persists, a strong cathartic such as oral magnesium citrate or an enema may be indicated.

Uncommon side effects of opioids include respiratory depression (slowed or stop breathing), seizures, dry mouth, myoclonus (involuntary muscle twitching or spasm), and urinary retention. If a patient is receiving a dosage of an opioid analgesic that provides pain relief but is accompanied by an undesirable side effect, consider switching to another opioid in a dose that provides equal pain relief or add a drug to treat the side effect.

**Comfort Measures**

Comfort measures can be a useful treatment option for reducing pain (Table 4). Comfort measures can be used as distractions to help relieve anxiety and fear associated with painful procedures. They often allow patients to feel more relaxed and at ease.

**Factors That Affect Perceptions and Experience of Pain**

Pain is generally associated with something negative and threatening. In Greek and Latin, words for “pain” also mean “punishment,” and the person suffering pain may perceive it that way. However, there are many factors that influence a person’s perceptions of pain and responses to it (see Table 5).
**Psychological Factors**
In some patients, fear of pain, injury, or loss of physical capacity may be more disabling than the pain itself. An attentional bias toward pain stimuli may increase the patient’s focus on pain cues from the environment, which may lead to anxiety and fear that in turn exacerbate the pain. Long-term feelings of depression, hopelessness, and helplessness may develop, associated often with emotional and behavioral regression and sometimes with suicidal ideation. About 50 percent of depressed patients report pain as a symptom, an indication of increased pain sensitivity in this group. In this context, the control of pain and associated anxiety are important goals of treatment.

Cognitive factors can affect patients’ experience of pain. Thoughts and images that spring to mind may engage negative emotions and lead to unhelpful reactions, as in a patient who thinks, “This pain is unbearable. It will never end. I cannot resist it. I am not capable of getting through this situation.”

Cognitive factors are linked with self-esteem and self-efficacy and are predictors of how quickly and how well a patient resumes normal functioning. Patients may also construct a variety of meanings for their experiences, including their illnesses and pain. One might see illness as a challenge, another as an enemy or a sign of being “damaged.” The meanings people assign to pain and illness stand in direct relationship with their acceptance of their situation. Generally, people who accept their illness as a positive challenge have significantly better mental health than those who do not.

In working with children in pain, developmental issues should be considered. There is evidence that children’s concepts of pain and reactions to pain differ at different ages (see Table 6). However, there is no clear evidence that the pain they actually experience in similar procedures differs by age.

Because infants and children express pain differently at different ages, many misconceptions about children’s pain are perpetuated. Common fallacies include the beliefs that infants do not feel pain, that children tolerate pain better than adults, that children always tell the truth about pain, and that children become accustomed to pain.

<table>
<thead>
<tr>
<th>Table 4: Comfort Measures</th>
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<tbody>
<tr>
<td>Comfort Measure</td>
</tr>
<tr>
<td>Quiet presence</td>
</tr>
<tr>
<td>Massage</td>
</tr>
<tr>
<td>Music</td>
</tr>
<tr>
<td>Heat</td>
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<tr>
<td>Cold/Ice</td>
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</table>

<table>
<thead>
<tr>
<th>Table 5: Factors That Affect Perceptions and Experience of Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor</td>
</tr>
<tr>
<td>Psychological</td>
</tr>
<tr>
<td>Family and Social</td>
</tr>
<tr>
<td>Life Stress</td>
</tr>
<tr>
<td>Religious and Spiritual</td>
</tr>
<tr>
<td>Culture</td>
</tr>
</tbody>
</table>
Each patient copes with pain in a unique way. Coping strategies that patients exhibit are related to their:
- Perceptions of self
- Previous experience with pain
- Expectations of pain management

**Family and Social Factors**
There is consistent evidence that social support can alter the way in which pain is expressed, for better but also for worse. Both children and adults can learn (e.g. from observation) helpful ways to tolerate and to express pain. On the other hand, family members seeking to protect and care for a loved one may unwittingly reward behavior appropriate to a sick person. This may have the effect of encouraging the patient to keep the sick role, i.e. to continue to live within the constraints and dependencies imposed by illness, even if it is no longer necessary.

Learning processes are likely to play a central role in the developmental trajectory of recurrent pain. Just as adults can learn, by observing role models, how to better tolerate pain, so children can learn pain behaviors and coping styles, both adaptive and maladaptive. Parents may provide direct instruction on the meaning of pain and appropriate responses. Evidence shows that children are sensitive to positive and negative reinforcement of pain behavior. In families where mothers and children report more encouragement for illness behavior, somatic symptoms are more frequent. Finally, the social acceptability of the body part involved in pain can affect the patient’s verbalization of pain. Shame, fear of prejudice, and criticism are correlated with inadequate pain expression and ineffective pain management.

**Life Stress Factors**
Many life factors can affect responses to pain (see Table 7). Children who are suddenly hospitalized without a significant familiar person by their side may have very intense pain reactions. Separation from family members, deaths in the family, and loss of body functions are severe life stressors.

**Cultural Factors**
A disabling medical condition may be regarded with shame or treated with denial by those surrounding the patient. Each culture defines both the type of pain response considered appropriate and the necessity for pain relief. Sexual stereotypes also may determine or reinforce how pain is perceived and how patients respond to it. In many cultures, for example, men and boys are expected to suppress natural responses to pain.

**Assessment of Psychological Factors**
While acute pain is mostly physical in nature, chronic

**Table 7: Life Stress Factors**
- Problems with primary support group (e.g. death of a family member)
- Problems related to the social environment (e.g. loss of a friend, retirement)
- Educational problems (e.g. bad scores)
- Occupational problems (e.g. unemployment)
- Housing problems (e.g. homelessness)
- Economic problems (e.g. extreme poverty, inadequate finances)
- Problems with access to health care services
- Problems with the legal system (e.g. arrest, victim of crime)

**Table 6: Age and Concept of Pain**

<table>
<thead>
<tr>
<th>Age</th>
<th>Concept of Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-6 years</td>
<td>Young children relate to pain primarily as physical, concrete experience and think of pain as magical. They may view pain as a punishment for wrongdoing. They tend to hold someone accountable for their pain and may even strike out at that person.</td>
</tr>
<tr>
<td>7-12 years</td>
<td>Children relate to pain physically but are also able to perceive psychological pain (e.g. someone dying). They fear bodily harm and death and may view pain as punishment.</td>
</tr>
<tr>
<td>13 years and older</td>
<td>Adolescents are able to give reasons for pain and perceive several types of psychological pain. Despite their mature understanding of pain, they have limited abilities to cope with it. They fear losing control during painful experiences (shame).</td>
</tr>
</tbody>
</table>
pain has a significant psychological component. This means that the assessment and treatment of chronic pain should include both medical and psychological interventions. To assess the effects of chronic pain on a person's life, we have to take into account both the person and the family. As a general guideline, the assessment should seek to identify the effects of pain with regard to:

- Social interactions
- Finances
- Family dynamics
- Cognition and mood
- Activities of daily living
- Job and family-role performance

**Psychological Interventions for Acute and Chronic Pain**

Psychological interventions should be used in accordance with the patient's age and preferences (see Table 8). Pain management must be individualized, as no one treatment is right for every person. The health care professionals involved in the patient's care must evaluate available options and together determine what is best.

**Symptom Management at End-of-Life**

Attention to palliative and end-of-life issues for patients with HIV/AIDS is an essential aspect of clinical care. Symptom management at end-of-life must address the physical, psychological, and social issues of patients who are dying. This section will describe selected symptoms at end-of-life (nausea and vomiting, diarrhea, constipation, hiccups, pruritis, and dyspnea) and suggest interventions to alleviate or decrease their severity.

**Nausea and Vomiting**

Nausea and vomiting can be very distressing and can lead to medication non-adherence, dehydration, electrolyte imbalances, malnutrition, and wasting. Obstruction of the bowel caused by constipation, dysmotility, infection, inflammation, medications, and psychological factors can lead to nausea and vomiting.

A thorough history should be obtained, with particular attention to associated symptoms and factors that increase or decrease these symptoms.

**Interventions:** The underlying cause of nausea and vomiting should be treated, if possible. Otherwise a number of palliative interventions may be used to help decrease symptoms and promote optimal hydration and nutrition:

- Avoid favorite foods when nauseated to prevent aversion to that food in the future.
- Avoid reclining or lying supine after eating, as reflux and nausea may occur.
- Eat (or serve) small portions of food at mealtime.
- Foods and liquids at cool temperatures may be better tolerated by someone who is nauseated.
- Avoid odors as much as possible.

**Diarrhea**

Patients with uncontrolled diarrhea are at increased risk of dehydration, electrolyte imbalance, skin breakdown, and fatigue. At end-of-life, the overuse of medications or supplements to alleviate constipation is a common cause of diarrhea. Other causes include partial intestinal obstruction, fecal impaction, and pancreatic insufficiency. Infectious diarrhea is especially common in HIV infection and is caused by the following pathogens: cryptosporidia, giardia lambila, entamoeba histolytica, and cytomegalovirus. A review of diet, medications, timing of bowel movements in relation to ingestion of food or liquids, and

<table>
<thead>
<tr>
<th>Specific Strategies</th>
<th>Therapeutic Approaches</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distraction techniques</td>
<td>Cognitive approaches use thoughts, emotions, and actions to assist the patient in adapting to living with a condition that may cause pain.</td>
</tr>
<tr>
<td>Relaxation</td>
<td>Behavioral approaches help patients plan activities to give them control without increasing their pain.</td>
</tr>
<tr>
<td>Guided imagery</td>
<td>Supportive approaches assist patients in grieving their loss of bodily integrity and developing a social-support network to learn to deal with pain.</td>
</tr>
<tr>
<td></td>
<td>Group therapy is an excellent way of overcoming feelings of loneliness, negative emotions, and lacking skills.</td>
</tr>
</tbody>
</table>
description, quantity, and quality of stool are important to assess when taking a patient history. When performing a physical exam, make sure to palpate the abdomen and do a rectal exam. Note that patients at end-of-life are at risk of developing the same diarrheal illnesses that occur every day in the general population (e.g. viral or bacterial gastroenteritis and adverse effects of medications).

**Interventions:** Infectious diarrhea should be identified and treated with appropriate antibiotics, if available. Adsorbent and bulk-forming agents (e.g. kaolin and pectin) can provide modest relief from diarrhea but may take up to 48 hours to produce an effect and can interfere with the absorption of certain medications. In general, the patient should receive adequate hydration by taking sips of clear liquids. Intravenous hydration may be required to reverse the dehydration associated with severe diarrhea. Simple carbohydrates (e.g. toast or crackers) will add back small amounts of electrolytes and glucose. Milk and other lactose-containing products should be avoided.

**Constipation**

Constipation is multifactorial, occurring in the presence of one or more of the following: too much or too little solid waste, decreased water content in the stool, and poor motility. Constipation is difficult for the patient to endure and may be difficult to treat. If the patient has been anorexic, a decrease in solid waste or water content may cause constipation. Being bed-ridden can cause motility problems, as can the use of certain drugs (e.g. opioids). The cause of the constipation needs to be identified prior to initiating treatment. A thorough patient history must be obtained, including assessment of diet, fluid intake, level of activity, and medications. Physical examination should include palpation of the abdomen and a digital examination of the rectal vault to assess for stool.

**Interventions:** Constipated patients on diets low in fiber may improve if fiber (e.g. psyllium) is added to their diet. However, it is important to note that patients with minimal fluid intake or poor gut motility at end-of-life may develop a fecal impaction from eating additional fiber. Patients’ stool water content depends on how much water they drink, their general hydration status, how much water is absorbed from and secreted into the intestine, and how fast stool moves through the bowel. Stool water content can be increased by raising the amount of fluid intake or adding osmotically active particles that retain water (e.g. magnesium salts, sorbitol, and lactulose). It is important to restrict the intake of concentrated fruit juices, as these may draw water into the gut and cause dehydration. Lubrication of the gut minimizes pain that can interfere with excretion. Mineral oil taken orally and glycerin suppositories or soap-based enemas given rectally increase lubrication and ease passage of stool.

**Hiccups**

Hiccups are distressing and interfere with the quality of life. A hiccup is an involuntary reflex involving the respiratory muscles of the chest and diaphragm. A single episode of hiccups can last for a few minutes or for hours. Hiccups lasting longer than 48 hours are considered persistent. Some people suffer from intractible hiccups, which last longer than one month. Physiologic causes include irritation of the vagus nerve or diaphragm, but hiccups may also be idiopathic or associated with stress, gastric distention, liver disease, uremia, and CNS abnormalities.

A thorough history, review of medications, focused review of systems, and physical exam may help guide the initial choice of treatment. Many drug and non-drug treatments have been used, but there is little evidence of any single superior approach to management; virtually all current data is anecdotal. If possible, treatment should be directed at the underlying cause.

**Interventions:** Chlorpromazine and haloperidol (given orally) are effective in relieving hiccups. Phenytoin has been effective in relieving hiccups in persons with CNS disorders, and metoclopromide is useful if stomach distention is present. Other medications
have been tried with modest success (e.g. valproic acid, baclofen, and carbamazepine). Well-known non-pharmacologic remedies include drinking or gargling water, biting a lemon, swallowing sugar, being startled or frightened, coughing, holding your breath, hyperventilation, and breathing into a paper bag.

**Pruritis**

Pruritis (itching) is a common and often distressing symptom near end-of-life. The itch sensation may arise from stimulation of the skin itch receptor or may be due to other causes (e.g. opioid-induced pruritus). Many skin diseases may produce itching with a rash as a prominent symptom; examples are hives, chicken pox, herpes zoster, and eczema. Some parasitic infestations of the skin, such as scabies and lice, may be very itchy. Other skin conditions have symptoms of pruritus without having an apparent rash. Pruritus is usually secondary to subtle dry skin, but it may be a manifestation of an internal condition. Several internal diseases may cause itching. The most common is kidney failure. Other internal diseases that may cause pruritus include some types of liver disease, such as hepatitis C; thyroid disease, including increased thyroid hormone levels; and HIV. Occasionally, lymphomas may have pruritus as a component. Neurologic conditions such as pinched nerves and strokes also may cause itching. Although pruritus is often a disrupting and even disabling symptom, it generally responds well to treatment.

**Interventions:** Although there are many causes for pruritus, some basics apply to most treatments. First, hot bathing and showering should be avoided; patients should bathe only in tepid or lukewarm water. Wearing lightweight clothing and keeping cool help reduce the severity of itching. Since soaps often dry out the skin, only mild soaps, if necessary, should be used. After bathing, the patient should rinse off the soap film completely, pat the skin lightly, and immediately apply a moisturizing lotion or cream. For itchy conditions where blistering or weeping of the skin is present (e.g. chicken pox or poison ivy), taking a cool oatmeal bath or using topical drying agents such as calamine may be helpful.

**Dyspnea**

Dyspnea at end-of-life typically occurs when the patient is bed-ridden and oral secretions that are not cleared (due to loss of the swallowing reflex) accumulate. An altered respiratory pattern, either fast or slow, is present. This can be very distressing for the patient and family. Dyspnea may be caused by an acute anxiety episode, severe pain, constipation, urinary retention, pneumothorax, or worsening pleural effusion.

**Interventions:** Opioids are the medication of choice to treat dyspnea. Antitussives can help with cough; anticholinergics (e.g. scopolamine, visteral) will help reduce secretions; and anxiolytics (e.g. diazepam) can reduce anxiety. If oxygen is available, a nasal cannula is usually better tolerated than a mask, although oxygen is not always helpful. Non-pharmacologic measures to alleviate dyspnea include upright positioning (or at least elevation of the head of the bed), increasing air movement in the room with a fan or open window, and use of relaxation techniques (e.g. distraction, deep breathing, and guided imagery). Restriction of fluid intake is also beneficial in reducing secretions.
HIV CURRICULUM FOR THE HEALTH PROFESSIONAL

Review Questions

1. How do you define nociceptive and neuropathic pain?
2. What are three causes of pain in patients with HIV?
3. What steps are included in the WHO analgesic ladder?
4. How do family and social factors affect the perception and experience of pain?
5. What are three factors that can cause constipation?
6. What interventions can be used for a patient with pruritis?
7. What are the physiologic causes of dyspnea at end-of-life?

Exam Questions

1. Which of the following statements regarding pain is true in children ages 2-7 years?
   a. The child is able to give a reason for why he or she is having pain.
   b. The child may view pain as a punishment for wrongdoing.
   c. The child is able to perceive psychological pain.
   d. The child feels ashamed if he or she loses control during painful procedures.

2. Which of the following non-pharmacologic measures helps decrease dyspnea?
   a. Supine positioning with the head flat on the bed
   b. Forcing fluids
   c. Increasing air movement in the room
   d. Warm clothing

3. How long do persistent hiccups last?
   a. More than 48 hours
   b. More than 24 hours
   c. More than one month
   d. More than a few minutes

Answers: 1b, 2c, 3a
Case Study

Winnie is a 20-year-old female with HIV who has pain and itching from a herpes zoster infection involving her back and side. She describes the pain as a deep burning sensation that shoots up her lower back.

**Question:** What kind of pain is she experiencing?
- a. Neuropathic pain
- b. Nociceptive pain
- c. Bone pain
- d. Visceral pain

**Answer:** a. Post-herpetic pain is classified as neuropathic pain, caused by altered excitability of the peripheral or central nervous system. This is usually due to dysfunction or injury. It is distinguished from nociceptive pain because of its duration and the presence of a burning, stabbing, or shooting sensation. Bone pain is classified as nociceptive pain; visceral pain is a subtype of neuropathic pain.

**Question:** Which non-pharmacologic intervention may decrease the itching associated with this rash?
- a. Using a strong soap to cleanse the skin
- b. Bathing in tepid or lukewarm water
- c. Wearing heavy clothing
- d. Bathing in hot water

**Answer:** b. Hot-water bathing increases circulation and therefore increases itching. Heavy clothing causes sweating and increased itching. Strong soaps irritate the skin and cause increased pain and itching. Bathing in tepid or lukewarm water may help decrease the itching.
Objectives

The purposes of this module are to:
1. Describe the risk factors that contribute to malnutrition in HIV/AIDS.
2. Explain how to conduct a nutritional assessment of children and adults.
3. Explain how to determine nutrient needs of children and adults.
4. Describe nutrition intervention strategies for problems associated with HIV/AIDS.
5. Emphasize the importance of preventing foodborne illness.

Key Points

1. HIV infection can frequently result in nutritional deficiencies and growth failure.
2. Malnutrition associated with HIV/AIDS can severely affect an already compromised immune system, leading to increases in rates of opportunistic infections and a decreased survival rate.
3. It is important to monitor and maintain adequate nutritional status in HIV-infected children and adults.

Causes of Malnutrition

Factors that contribute to malnutrition in people with HIV or AIDS include infection, fever, gastrointestinal illnesses, developmental problems, and economic and psychosocial issues.

Infection alters the metabolism of energy, carbohydrates, fats, proteins, vitamins, and minerals, increasing the body's need for these nutrients.

Fever increases calorie needs by 12 percent for each degree Centigrade above normal and 7 percent for each degree Fahrenheit above normal. Fever may also increase protein utilization. Sepsis (a generalized infection) increases calorie needs by 60 percent.

Gastrointestinal (GI) manifestations of HIV/AIDS include diarrhea and malabsorption; oral, esophageal, and gastric illnesses; and nausea and vomiting. Diarrhea and malabsorption (not always found together) can lead to vitamin, mineral, protein, fat, and carbohydrate losses as well as a decrease in oral intake. Diarrhea increases calorie needs by 25 percent. Malabsorption may occur without diarrhea because of metabolic changes associated with the disease, which lead to loss of nutrients.

Severe oral candidiasis (yeast) and herpes gingivostomatitis, viral esophagitis, and gastritis can make eating difficult and painful, leading to decreased oral intake or feeding refusal. Nausea and vomiting caused by drugs, infection, and/or illness can lead to poor oral intake as well as loss of nutrients.

Feeding and eating problems can occur with HIV/AIDS. Infants with HIV can have a weak suck, leading to inadequate intake of breast milk or formula. Older children can have poor chewing and feeding...
skills. Difficulty swallowing can lead to poor oral intake or complete refusal to eat. There is a risk of aspiration and pneumonia with swallowing problems. Children or adults with HIV/AIDS can lose feeding skills due to neurological deterioration, leading to inadequate intake of nutrients.

Economic issues that can lead to inadequate nutrient intake include a limited food supply, loss of household income or livelihood (such as farming) due to illness, as well as limited cooking and storage facilities. Also, parents may be too ill or uninterested to care for themselves and their children. Depression in an adult or child can also lead to poor nutrient intake.

**Nutrition Assessment**

Once malnutrition risk factors are identified, a nutrition assessment can be done. An assessment includes examining weight gain and linear growth, growth failure, nutrition laboratory values if available, and diet and feeding history.

For children, weight gain and linear growth are important components of a nutrition assessment. The weight of the pediatric patient in kilograms (kg) and the length or height in centimeters (cm) are valuable assessment tools. For children up to age 3, measurement of the frontal occipital (head) circumference (FOC) in centimeters is also a valuable tool to assess growth. Weight alone is adequate to assess growth when no other measurements are available.

To assess growth, the health care provider should plot the patient’s weight and height/length on a growth chart. Any prior weights and lengths that are available, including birth weight, are helpful to plot trends in the patient’s growth. The World Health Organization (WHO) recommends using the U.S. National Center for Health Statistics (NCHS) growth charts. The most recently updated set of growth charts is available at the end of this chapter and at the U.S. Centers for Disease Control and Prevention Web site on the Internet: http://www.cdc.gov/growthcharts/. The growth charts include body mass index (BMI) charts for up to 20 years of age for males and females.

Growth failure is defined as:

1. Crossing two major percentile lines on the NCHS growth charts over time. The charts show the 97th, 95th, 75th, 50th, 25th, 10th, 5th, and 3rd percentile lines. If, for example, a patient’s weight or length falls from the 25th to below the 5th percentile, the patient has crossed two percentile lines on the growth chart.

2. For a child whose weight is below the 5th

---

*A Ugandan girl drinks formula by cup.*
percentile for age: failing to follow along a normal upward growth curve on the growth chart. If there is no weight gain or inadequate weight gain, there is no indication of growth along a normal curve – the line on the growth chart would be flat or drop.

3. Loss of 5 percent or more of body weight.

Acute and chronic degrees of malnutrition for children are assessed using the Waterlow Criteria, as follows:

**Acute malnutrition** = 
\[
\text{actual weight} \times \frac{100}{\text{50th percentile weight/length on NCHS chart}}
\]

Stage 0 (normal): >90 percent  
Stage I (mild): 81-90 percent  
Stage II (moderate): 70-80 percent  
Stage III (severe): <70 percent

**Chronic malnutrition** = 
\[
\text{actual length/height} \times \frac{100}{\text{50th percentile height/age on NCHS chart}}
\]

Stage 0 (normal): >95 percent  
Stage I (mild): 90-95 percent  
Stage II (moderate): 85-89 percent  
Stage III (severe): <85 percent

When length/height measurements are not available, the Gomez Criteria can be used to determine degree of malnutrition, but these fail to assess the proportion of weight to height. The Gomez Criteria are used as follows:

Determine the weight for age at the 50th percentile on the NCHS growth chart (ideal weight).

**Percent of ideal body weight** = 
\[
\frac{\text{actual weight}}{\text{ideal weight}} \times 100
\]

Determine the degree of malnutrition:

<table>
<thead>
<tr>
<th>Degree of Malnutrition</th>
<th>Percent of Ideal Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st</td>
<td>75-85</td>
</tr>
<tr>
<td>2nd</td>
<td>64-74</td>
</tr>
<tr>
<td>3rd</td>
<td>&lt;64</td>
</tr>
</tbody>
</table>

To assess the nutritional status of an adult, a formula for determining ideal body weight is:

**Male:** 48 kg + 1.07 kg/cm if height is over 152 cm  
**Female:** 45.5 kg + .9 kg/cm if height is over 152 cm

For an adult, malnutrition can be defined as involuntary weight loss greater than 10 percent or weight less than 90 percent of ideal weight.

Laboratory values that are helpful when doing a nutrition assessment, in both the pediatric and adult populations, are the complete blood count (CBC), total protein, albumin (dehydration can lead to falsely elevated serum levels), and prealbumin (which has a half life of several days, versus about two weeks for albumin). Albumin and prealbumin assess visceral protein status (muscle mass).

Dietary intake and feeding history are important aspects of a nutrition assessment. The adequacy of nutrient intake can be assessed based on a 24-hour patient diet recall (a list of what the patient normally eats and/or ate in the past 24 hours) or a three-day food intake record (kept in writing by the patient or a caretaker). It is important to interview the patient/caretaker to find out the types and estimated amounts of foods/formula/fluids/breast milk consumed. Other important information includes the length of time it takes the patient to eat; the patient’s appetite; any chewing, sucking, or swallowing problems; any nausea, vomiting, diarrhea, and abdominal pain; and any feeding refusal, food intolerance, allergies, and fatigue. If the patient is a child, who feeds the child and provides the food for the child should be known.

### Determining Nutrient Needs of Children and Adults

Reversing weight loss, malnutrition, and wasting can
help boost the immune system of a child or adult who is HIV-positive. An easy approach to determining increased calorie needs of an HIV-positive child or adult is to use the U.S. Recommended Dietary Allowance (RDA) general population energy guidelines (see tables 1, 2, and 3) and increase the number of calories (kcal/day) to at least 150 percent of recommended energy levels.

To determine more exact calorie needs of an HIV-positive child, a few things need to be considered. Is the child ill? Has she lost weight, and has her linear growth been affected? Does she exhibit malnutrition based on the Waterlow or Gomez criteria? Is she severely wasted? A method to determine calorie needs for a child who has not been gaining weight or growing is to assess the child’s energy needs for catch-up growth. Catch-up growth means weight gain and growth to catch up to within normal limits for the child’s age. The formula to determine energy needs for catch-up growth is:

\[
\text{ideal body weight (kg)} \times \text{RDA kcal/kg for age current weight (kg)}
\]

These are starting points and need to be adjusted if there is fever, sepsis, lack of weight gain/growth, or continued weight loss.

For HIV-positive adults, increased calorie needs can be determined more precisely using kcal/day in Table 3 or the basal energy expenditure (BEE), along with activity and injury factors. The BEE, a measure of energy expenditure in a body at rest after fasting for at least 12 hours, can be calculated using the Harris Benedict formula:

For women:
\[
655.1 + (9.6 \times \text{weight in kg}) + (1.7 \times \text{height in cm}) - (4.7 \times \text{age in years})
\]

For men:
\[
665.5 + (13.8 \times \text{weight in kg}) + (5 \times \text{height in cm}) - (6.8 \times \text{age in years})
\]

Once the BEE is calculated, activity factors and injury factors need to be determined. These are multiplied with the BEE to estimate calorie needs.

\[
\text{BEE} \times (\text{activity factor}) \times (\text{injury factor}) = \text{estimated calorie needs}
\]

<table>
<thead>
<tr>
<th>Activity Factors</th>
<th>Injury Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bed rest 1.2</td>
<td>Minor surgery 1.2</td>
</tr>
<tr>
<td>Ambulatory 1.3</td>
<td>Skeletal trauma 1.35</td>
</tr>
<tr>
<td></td>
<td>Major sepsis 1.6</td>
</tr>
<tr>
<td></td>
<td>Severe burns 2.1</td>
</tr>
</tbody>
</table>

If a child or adult is bed-ridden, the resting energy expenditure (REE) in tables 1, 2, and 3 can be used to determine calorie needs. The REE, based on a body at rest after a meal, will vary from patient to patient depending on factors such as fever and infections.

HIV/AIDS also increases losses of protein. To determine protein requirements of children, the same
formula as for catch-up growth can be used, substituting RDA protein for calories (see tables 1 and 2):

\[
\text{ideal body weight (kg) x RDA protein (g/kg) for age current weight (kg)}
\]

For children with HIV/AIDS, protein may need to be increased to twice the RDA for protein but should not exceed 4 grams/kg/day to prevent azotemia (too much urea in the blood).

For adults, protein requirements are:

<table>
<thead>
<tr>
<th>Status</th>
<th>Estimated Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>0.8 – 1 g/kg/day</td>
</tr>
<tr>
<td>Moderately stressed</td>
<td>1 – 2 g/kg/day</td>
</tr>
<tr>
<td>Severely stressed</td>
<td>2 – 2.5 g/kg/day</td>
</tr>
</tbody>
</table>

For adults with HIV, starting at 2-2.5 g/kg/day of protein is recommended.

**Dietary Intervention**

If an illness is causing increased energy and/or protein needs, it is important to treat the underlying illness. It is also important to provide a high-calorie, high-protein diet and to teach the family how to increase nutritious foods in the diet that are high in vitamins and minerals.

Foods high in calories help to maintain body weight and promote weight gain. Starchy foods make up a large part of the diet and are a good inexpensive source of calories. These foods include bread, pap, porridge, mealies, sorghum, rice, potatoes, sweet potatoes, samp, millet, and pasta.

**Table 2: Estimated Energy and Protein Requirements for Adolescents Based on Weight**

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age (years)</th>
<th>Reference Weight (kg)</th>
<th>REF (kcal/kg)</th>
<th>RDA Energy (kcal/kg)</th>
<th>Energy (kcal/day)</th>
<th>Protein (gram/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>11-14</td>
<td>45</td>
<td>30</td>
<td>55</td>
<td>2500</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>15-18</td>
<td>66</td>
<td>30</td>
<td>45</td>
<td>3000</td>
<td>0.9</td>
</tr>
<tr>
<td></td>
<td>19-24</td>
<td>72</td>
<td>25</td>
<td>40</td>
<td>2900</td>
<td>0.8</td>
</tr>
<tr>
<td>Females</td>
<td>11-14</td>
<td>46</td>
<td>30</td>
<td>47</td>
<td>2200</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>15-18</td>
<td>55</td>
<td>25</td>
<td>40</td>
<td>2200</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td>19-24</td>
<td>58</td>
<td>25</td>
<td>38</td>
<td>2200</td>
<td>0.8</td>
</tr>
</tbody>
</table>

**Table 3: Estimated Energy and Protein Requirements for Adults Based on Weight**

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age (years)</th>
<th>Reference Weight (kg)</th>
<th>REF (kcal/kg)</th>
<th>RDA Energy (kcal/kg)</th>
<th>Energy (kcal/day)</th>
<th>Protein (gram/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>25-50</td>
<td>79</td>
<td>23</td>
<td>37</td>
<td>2900</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>51+</td>
<td>77</td>
<td>20</td>
<td>30</td>
<td>2300</td>
<td>.9</td>
</tr>
<tr>
<td>Females</td>
<td>25-50</td>
<td>63</td>
<td>22</td>
<td>36</td>
<td>2200</td>
<td>.8</td>
</tr>
<tr>
<td></td>
<td>51+</td>
<td>65</td>
<td>20</td>
<td>30</td>
<td>1900</td>
<td>1.0</td>
</tr>
<tr>
<td>• Pregnant</td>
<td>1st trimester</td>
<td></td>
<td></td>
<td></td>
<td>+0</td>
<td>60 g/day</td>
</tr>
<tr>
<td></td>
<td>2nd trimester</td>
<td></td>
<td></td>
<td></td>
<td>+300</td>
<td>60 g/day</td>
</tr>
<tr>
<td></td>
<td>3rd trimester</td>
<td></td>
<td></td>
<td></td>
<td>+300</td>
<td>60 g/day</td>
</tr>
<tr>
<td>• Lactating</td>
<td>1st 6 months</td>
<td></td>
<td></td>
<td></td>
<td>+500</td>
<td>65 g/day</td>
</tr>
<tr>
<td></td>
<td>2nd 6 months</td>
<td></td>
<td></td>
<td></td>
<td>+500</td>
<td>62 g/day</td>
</tr>
</tbody>
</table>
Foods high in protein help maintain muscle mass. Sources of protein include meat (beef, mutton, pork), organ meats, fish, chicken, eggs, milk, dairy products such as yogurt and cheese, and mopari worms and other insects. Inexpensive sources of protein include legumes such as beans and peas, nuts, peanut butter, and seeds, as well as grains such as rice, maize, barley, oats, wheat, rye, sorghum, millet, and corn. Grains and legumes need to be combined with each other or eaten in the same day or eaten with another protein source such as meat. If these foods are not combined or eaten on the same day, the protein they provide is considered incomplete. Vegetables and fruits are important sources of essential vitamins and minerals, especially vitamins A and C, and need to be eaten daily. Table 4 provides a list of important vitamins and minerals and their sources.

Fats and oils are also an important part of the diet, providing calories and essential vitamins and fatty acids. Sources of fat include butter, margarine, cooking oils, cream, mayonnaise, and salad dressings. Sugar, sweets, and desserts are good sources of calories but should not be used in place of more nutritious foods. They can be used in addition to a healthy diet to provide extra calories.

Patients with HIV/AIDS often lack vitamins and minerals because of inadequate dietary intake, infection, and malabsorption. Vitamins A, C, E, and B are important for immune function. Vitamins A and C are important for wound healing, and vitamin A for vision. The B vitamins are also important for energy production, red blood cell production, and growth. Vitamin E is important in red blood cell production. Minerals such as zinc and selenium are important in immune function and, along with other minerals such as iron, magnesium, potassium, phosphorus, and copper, are often depleted in association with HIV infection. Because vitamins and minerals play such an important role in the body, a daily multiple vitamin/mineral supplement is of benefit to HIV-positive patients, whether they are symptomatic or asymptomatic. If a vitamin is not feasible, it is especially critical to promote a healthy diet with a variety of foods.

Table 5 shows a list of clinical signs of vitamin and mineral deficiencies.

<table>
<thead>
<tr>
<th>Vitamin/Mineral Deficiencies</th>
<th>A and C</th>
<th>B</th>
<th>E</th>
<th>Zinc</th>
<th>Selenium</th>
<th>Iron</th>
<th>Magnesium</th>
<th>Potassium</th>
<th>Phosphorus</th>
<th>Copper</th>
</tr>
</thead>
<tbody>
<tr>
<td>B-12</td>
<td>Macrocytic (larger-than-normal red blood cells) anemia, neurologic disturbances, altered mental status</td>
<td>Meats, whole grains, milk, eggs, and legumes</td>
<td>Vegetable oils, dark green leafy vegetables, legumes, and nuts</td>
<td>Meat, legumes, and whole-grain cereals</td>
<td>Meat, seafood, and cereals</td>
<td>Meat, fish and poultry, whole-grain cereals, dark green leafy vegetables, and legumes</td>
<td>Green leafy vegetables, legumes, and whole grains</td>
<td>Meats, poultry, fish, fruits and vegetables, including bananas, potatoes, carrots, tomatoes, and oranges</td>
<td>Meats, milk, and whole-grain cereals</td>
<td>Organ meats, shellfish, legumes, nuts, and whole-grain cereals</td>
</tr>
<tr>
<td>B-6, niacin, riboflavin</td>
<td>Cheilosis (fissures, redness, sores around lips)</td>
<td>Thin, brittle, concave fingernails</td>
<td>Night blindness, xerophthalmia (dryness of the eyes), loss of appetite</td>
<td>Cardiomyopathy (abnormalities of the heart muscle)</td>
<td></td>
<td></td>
<td></td>
<td>Growth retardation, dermatitis (inflammation of the skin evidenced by itching, redness, and lesions), diarrhea, hair loss</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Nutrition Interventions for Specific Issues

Breastfeeding
When a mother who is HIV-positive breastfeeds, she risks transmitting the virus to her child. About one in seven infants are at risk of having HIV transmitted during breastfeeding. If the mother must breastfeed, she needs to take certain precautions to reduce the risk of transmission. She should exclusively breastfeed, meaning that no water, juices, or foods should be given while the child is breastfed, as these may introduce bacteria that could lower immune response, thus increasing the risk of transmission of HIV. The child can be given medications. (Also see the chapter on mother-to-child transmission of HIV.)

The WHO suggests the following guidelines for breastfeeding:

• When replacement feeding is affordable, feasible, acceptable, sustainable, and safe, avoidance of all breastfeeding by HIV-infected mothers is recommended.
• When replacement feeding is not possible, then exclusive breastfeeding is recommended.
• To minimize HIV transmission risk, breastfeeding should be discontinued as soon as feasible, taking into account the local circumstances, the individual woman’s situation, and the risks of replacement feeding (including infections other than HIV and malnutrition).

The mother must protect herself from sexually transmitted diseases. It is also important that the mother eat well and stay healthy, as her milk production can be affected by her health. A breastfeeding mother needs at least 500 extra calories per day. If she doesn’t get enough calories, she can become malnourished and lose bone.

If a baby refuses to breastfeed or spits up a lot of milk, he or she may have esophageal reflux and need medications.

Other Issues
To treat acute diarrhea and malabsorption, give clear fluids for 12-24 hours, then soft solids. Encourage fluids to prevent dehydration, but avoid excessive juices, and consider there may be temporary or long-term lactose (milk sugar) intolerance. Avoid high-fat foods.

To treat nausea and vomiting, recommend small frequent meals, cold foods and beverages, low-fat foods, and bland, non-spicy foods.

For oral lesions and esophageal pain, recommend smooth-textured non-spicy foods, cold foods, drinking through a straw to bypass sores, and mild sauces and gravies on foods to make swallowing easier.

When a patient has developmental delay or neurological deterioration, a feeding and swallowing evaluation should be conducted. If the patient has problems chewing or swallowing, it may help to puree the food. A parent or caretaker may need to feed the patient. Enteral (tube) feedings are also helpful if a patient cannot eat.

Foodborne illness can cause serious problems for HIV-infected patients. For this reason, it is important to teach patients and caretakers to wash their hands before and during food preparation, especially if handling raw meat; to wash fresh produce with clean water; to cook foods thoroughly; to avoid raw meat, fish, and eggs; to try to avoid unpasteurized dairy products and soft cheeses; to boil bottles and nipples if used; and to store foods at proper temperatures.

Assessing and maintaining adequate nutritional status is an important component of care for patients with HIV/AIDS. For many patients, good nutrition can help fight infections and prolong life.
Body mass index-for-age percentiles:
Boys, 2 to 20 years

SOURCE: Developed by the National Center for Health Statistics in collaboration with
the National Center for Chronic Disease Prevention and Health Promotion (2000).
CDC Growth Charts: United States

Stature-for-age percentiles:
Boys, 2 to 20 years

SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000).
CDC Growth Charts: United States

Weight-for-age percentiles:
Boys, 2 to 20 years

SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000).
CDC Growth Charts: United States

Weight-for-length percentiles: Boys, birth to 36 months

Revised and corrected June 8, 2000.
SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000).
CDC Growth Charts: United States

Head circumference-for-age percentiles:
Boys, birth to 36 months

SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000).
CDC Growth Charts: United States

Weight-for-age percentiles: Boys, birth to 36 months

SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000).
CDC Growth Charts: United States

Length-for-age percentiles: Boys, birth to 36 months

SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000).
CDC Growth Charts: United States

Weight-for-stature percentiles: Girls

Revised and corrected November 21, 2000.
SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000).
Body mass index-for-age percentiles:
Girls, 2 to 20 years
CDC Growth Charts: United States

Stature-for-age percentiles: Girls, 2 to 20 years

SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000).
CDC Growth Charts: United States

Weight-for-age percentiles: Girls, 2 to 20 years

SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000).
CDC Growth Charts: United States

Length-for-age percentiles:
Girls, birth to 36 months

SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000).

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CDC Growth Charts: United States

Head circumference-for-age percentiles:
Girls, birth to 36 months

SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000).
Weight-for-age percentiles: Girls, birth to 36 months

SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2002).

CDC Growth Charts: United States
CDC Growth Charts: United States

Weight-for-length percentiles: Girls, birth to 36 months

Revised and corrected June 8, 2000.
SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000).
Review Questions

1. Review the specific factors that contribute to malnutrition in people with HIV/AIDS.

2. What are the increased energy requirements associated with illness in people with HIV/AIDS?

3. What are the essential components of a nutritional assessment for children and adults with HIV/AIDS?

4. How do you assess nutritional status based on a person’s weight and height?

5. How do you calculate the nutritional needs of child and adolescents with HIV/AIDS?

6. What are the appropriate nutritional interventions to support increased energy and/or protein needs for a person with HIV/AIDS?

Exam Questions

1. All of the following are factors contributing to malnutrition in HIV/AIDS except:
   a. Increased energy requirements
   b. Infection
   c. Developmental problems
   d. Exercise

2. Which measure of growth is essential for evaluation of children?
   a. Frontal occipital circumference for children older than 5 years
   b. Height plotted on a growth chart
   c. Frontal occipital circumference for children up to 3 years old
   d. Weight compared to ideal body weight

3. Effective methods to increase calories when illness is present include:
   a. 250 percent increase in recommended calories
   b. Increase fats and starches in the diet
   c. Increase intake of fruits and vegetables
   d. Increase intake of water

4. In order to meet protein needs for children with HIV/AIDS, how much can the daily protein intake be increased?
   a. Not to exceed 2 gm/kg/day
   b. Not to exceed 6 gm/kg/day
   c. Not to exceed 4 gm/kg/day
   d. Not to exceed 1 gm/kg/day

5. Growth failure in children is defined as:
   a. Crossing three major percentile lines of the NCHS growth charts over time
   b. Failure to follow growth curve on a growth chart
   c. Loss of 1 percent or more of body weight
   d. Chronic diarrhea and vomiting

Answers: 1d, 2d, 3b, 4c, 5b
Case Study #1

B.D., age 7, comes into the hospital with fever (38°C) and respiratory distress. His weight is 15 kg, and his length is 109 cm. B.D. has a good appetite and eats well but has been losing weight, according to his grandmother, who is his primary caretaker. BD’s mother is deceased and had AIDS. BD was recently diagnosed with HIV and started antiretroviral therapy.

Question: What is the first step in a nutrition assessment?

Answer: Plot anthropometrics on CDC growth charts and determine degree of malnutrition, if any.

- Wt: 15 kg (<3rd percentile)
- Ht: 109 cm (<3rd percentile)
- Wt/Ht: <3rd percentile
- IBW: 18.1 kg
- Current wt percent of IBW: 83 percent
- Current ht percent of ideal ht for age:
  - 109 cm/122 cm = 89 percent

Question: Does this patient exhibit any signs of malnutrition based on the Waterlow Criteria?

Answer: Yes, Stage I (mild) acute malnutrition (based on his weight) and Stage I (mild) chronic malnutrition (based on his height).

This indicates that the malnutrition is not severe, but the fact that his height has been affected indicates a need for prompt intervention.

Question: What are the next steps?

Answer:
1. Determine the patient’s calorie and protein needs.
   - For catch-up growth calories:
     - 18.1 kg (IBW) x 70 cal/kg (RDA for age) / 15 kg (current weight) = 84 kcal/kg
     - Fever 12 percent x 1 degree above normal
     = 12 percent x 84 kcal = 10 calories
     10 + 84 = 94 kcal/kg/day (minimum)
   - For catch-up growth protein:
     - 18.1 kg IBW x 1 g pro/kg (RDA for age) / 15 kg = 1.2 g protein/kg per day + fever
     = 1.4 g pro/kg/day

2. Do a diet recall, which is an interview with the parent, caretaker, or patient to determine what the patient normally eats in a day or what he ate in the past 24 hours. Also do a calorie and nutrient assessment while the patient is in the hospital to determine his actual food and nutrient intake. If necessary, adjust his diet to increase calories and protein.
3. Take daily weights while he is hospitalized.
4. At discharge, instruct the grandmother on ways to increase calories and protein in his diet at home.
5. After discharge, follow up weight checks at pediatrician office or clinic.
6. If the patient does not gain weight, he may need supplemental feedings by mouth or nasogastric tube.

Case Study #2

C.F., a 4-month-old girl, is admitted to the hospital with diarrhea and dehydration. C.F. has a history of failure to thrive and hospitalizations for various illnesses, including pneumonia. She tests positive for HIV while in the hospital. Her mother has not been tested for HIV and has been healthy. C.F.’s weight is 3.2 kg. Her birth weight was 2.8 kg. Her length is 52 cm; her birth length was 47 cm. Her head circumference (FOC) is 40 cm; it was 34.4 cm at birth.

Question: What would be the first step in a nutrition assessment?

Answer: Anthropometrics and Waterlow Criteria assessment:
Wt: 3.2 kg is <3rd percentile for age
Length: 52 cm is <3rd percentile for age
Wt/length is at the 3rd percentile
FOC: 25th percentile (was at the 50th percentile at birth)
IBW: 3.7 kg; actual wt is 86 percent of IBW
Ideal ht for age: 61 cm; actual ht is 85 percent of ideal ht

**Question:** Is there any evidence of malnutrition? 
(See the Waterlow Criteria.)

**Answer:** Yes, this infant has Stage I (mild) acute malnutrition and Stage II (moderate) chronic malnutrition.

**Next steps:**
- Find out what the baby is eating – breast milk or formula?
- If the baby is breastfeeding, find out how long she takes at a feeding, whether the mother is introducing other foods/fluids; and whether the mother is malnourished and not producing enough milk.
- If the baby is on formula, what type and how much does she drink at a feeding? How long does she take to drink a bottle?
- Does the baby get tired easily while feeding?
- Does the baby cry and arch her back with feedings? (Possible gastroesophageal reflux?)
- How long has the baby had diarrhea? Is the infant getting enough fluids?

The baby will need to be tested for pathogens in the stool. If pathogens are the cause of her diarrhea and she is treated, the infant can probably be kept on her current type of feeding, but volume and possibly calorie concentration will need to be increased. If pathogens are not present, the baby may need to be put on an elemental formula, if available, to aid absorption and decrease diarrhea. If the baby is unable to eat enough by mouth, a nasogastric tube may need to be placed to provide enough calories and fluids for the child. Formula can be concentrated and have additives to increase calories and protein.

**Question:** What are C.F.’s current calorie and protein needs?

**Answer:**

\[
\text{IBW: } 3.7 \text{ kg} \times 108 \text{ kcal/kg} / 3.2 \text{ kg} = 125 \text{ kcal/kg/day} \\
+ \text{calorie needs for diarrhea (25 percent, or 31.2 calories)} \\
= 156 \text{ kcal/kg/day} \\
3.7 \times 2.2 \text{ g pro/kg} / 3.2 = 2.5 \times 25 \text{ percent} \\
= 3.1 \text{ g pro/kg/day}
\]

Regular weight and length checks are important to determine whether the nutrition intervention is working. If nasogastric feeds are necessary for more than eight weeks, a gastrostomy may need to be considered.

**Case Study #3**

A 30-year-old man comes to the clinic complaining of a cough of three weeks’ duration with fatigue and weight loss. His partner was recently diagnosed as HIV-positive, and this patient does not know his HIV status. He has had little appetite and complains of pain when he swallows. His weight is 55 kg, and his height is 178 cm. He is found to have tuberculosis and candidiasis, and testing shows he is HIV-positive.

**Question:** What is an appropriate weight for this man?

**Answer:** Approximately 75 kg (see Page 259 for calculation)

**Question:** What are his current calorie needs?

**Answer:** His BEE is calculated to be 2283 calories, and his activity factor is ambulatory (1.3). His stress factor is equivalent to sepsis (1.6), considering his HIV status and tuberculosis. Based on this, the man would need 2283 x 1.3 x 1.6 = 4750 calories per day. This is only an estimate. It may be helpful to do a diet recall and assess his current food intake to determine what he needs to add to his diet.
to gain weight and to receive an adequate amount of both macro and micronutrients.

**Question:** Will the candidiasis affect his food intake?

**Answer:** Yes, this could be why he has pain with swallowing, as the candidiasis may be affecting his esophagus. Soft non-spicy, and cold foods may help reduce the pain. Also, cold liquids that are not acidic are recommended.

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**Bibliography**


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Objectives

The purposes of this module are to:
1. Define complementary and alternative medicine (CAM).
2. Review various types of CAM used in treating HIV-infected patients.
3. Discuss risks and benefits associated with the use of CAM by HIV-infected patients.
4. Explore prevalent patient attitudes regarding CAM.

Key Points

1. Health care professionals must be knowledgeable about CAM therapies to assist patients in making informed choices regarding their use.
2. CAM therapies are used in conjunction with conventional treatments for HIV/AIDS patients.
3. The risks and benefits of all therapies, including CAM options, should be considered by patients and health care providers prior to the start of treatment.
4. When treatment failures and adverse effects of therapy are seen, the possible influence of complementary therapies needs to be considered.

Overview

Complementary and alternative medicines (CAM) are used by a majority of HIV-infected patients worldwide. The World Health Organization (WHO) reports that in Africa, North America, and Europe, three out of four people living with HIV/AIDS use some form of CAM therapy. Among the general populations of most countries of the world, use of CAM is also common. In the United States alone, more than $27 billion per year were spent on CAM therapies in the late 1990s. For patients in many parts of the world, standard Western medical therapies are not easily accessible. In Western countries where conventional medicines are more readily available, the number of people using CAM therapies has nevertheless been increasing over the past few decades. The implications of the widespread use of CAM are great in terms of both potential benefits to patients and potential risks.

CAM includes a wide range of therapies not usually integrated into standard Western medical practice. Complementary methods are those used in conjunction with conventional medical practices. Those employed instead of conventional practices are considered alternative. A variety of approaches to diagnosis, treatment, and care that fall outside of conventional methods can be classified as CAM.

Defining CAM in a multicultural context presents certain difficulties. What is considered conventional in one setting may be out of the ordinary in another. The list of practices that are considered to be CAM changes as some CAM therapies that are proven safe and effective become a part of mainstream medicine.
It is important for health care providers to have an appreciation of CAM modalities commonly used by their patients. Some commonly used CAM modalities are listed and defined in Table 1. For some of these treatments, certain benefits and risks with regard to their use in HIV-infected adults and children have been identified through research studies. These studies and their potential implications for HIV-infected children are discussed in the table and later in this chapter.

**Traditional Healers**

In some countries, up to 90 percent of the population relies on traditional medicine for basic health care.2,5 Traditional healers are often the most accessible of all health care providers, especially for rural communities. In Ghana, for example, there is one traditional medicine practitioner for every 400 people, but only one conventional medical doctor for every 12,000 people.3

Surveys have shown that in Africa, about 70 percent of people see traditional providers first when confronted with health-related problems. A 2001 study of HIV-infected people in Cambodia revealed that a majority consulted a traditional healer for care.6 The role and influence of traditional healers have been acknowledged and studied by international bodies such as WHO and UNAIDS. Many international and

| Table 1: CAM Modalities Commonly Used in HIV/AIDS Patients – Definitions and Potential Benefits |
|------------------|-------------------------------------------|
| **Therapy**      | **Theory and Uses**                        |
| Acupuncture      | Acupuncture is a component of traditional Chinese medicine. It is based on the theory of vital energy that circulates through the body in channels called meridians. Disease occurs when the flow of vital energy is disrupted, and healing occurs when the flow is restored through stimulation of specific points along the energy meridians. Stimulation occurs through a variety of techniques, including needle insertion and cupping. Acupuncture is commonly used for the treatment of pain. Studies have shown acupuncture to be effective in relieving some HIV-related symptoms, including HIV-related peripheral neuropathy. |
| Bioenergetic Therapies | Reiki and other forms of therapeutic touch operate on the belief that an invisible energy can be transmitted from the healer to the patient. Practitioners of this form of therapy work either by direct physical contact or through visualization and energy transfer. Some HIV-infected patients report an increased sense of well-being following bioenergetic treatments. |
| Chiropractic     | Chiropractic is based on an association between the spine and the nervous system and on the self-healing properties of the human body. Chiropractors believe that misalignment of the joints, particularly the spine, is a major source of morbidity. Through manipulations of the spine and other joints, they seek to re-establish normal body functions. Chiropractic manipulations have been used in children to treat joint and gastrointestinal symptoms and to strengthen the immune system. |
| Faith Healing    | Faith healing is a component of many traditional healing modalities. Some Christian communities stress that faith in God allows miraculous healing to take place. Numerous studies have looked at the effects of faith and prayer on health outcomes. In some cases, clear benefits have been seen among patients using faith healing modalities. |
| Herbs and Supplements | A multitude of herbal remedies are used throughout the world for the maintenance of health and treatment of disease. Vitamins and mineral supplements are sometimes added to or used with herbal treatments. Many conventional medicines are derived from natural plant products. Numerous ongoing studies are evaluating the safety and efficacy of commonly used herbal treatments. |
| Homeopathy      | Homeopathy is a system of medical treatment that operates based on the Law of Similars and the Law of Dilutions. The Law of Similars is the belief that a substance that would cause a symptom in a healthy person can treat the same symptom in a sick person (“like cures like”). According to the Law of Dilutions, the more a substance is diluted, the more powerful it becomes as a therapy. Thus, a very dilute solution made with poison Ivy extracts would be a potential homeopathic remedy for an itchy rash. A few small-scale studies have suggested a trend toward the improvement of immune functions and quality of life among HIV/AIDS patients using certain homeopathic remedies. |
| Massage         | A number of different types of massage aim to improve circulation, alleviate pain, promote relaxation, and stimulate the immune system. In early 2005, HIV-infected children ages 3-7 were being enrolled in a study in the Dominican Republic to assess whether massage therapy can increase their well-being and immune function. |
| Mind-Body Exercise | Yoga, tai chi, and qi gong are among exercises that are recommended to reduce stress and improve psychosocial function. These techniques can improve fitness and overall sense of well-being. |
| Traditional Healers (Curanderos, Shamans, Witch Doctors, etc.) | In many societies, certain people are believed to be endowed with special healing powers. Traditional healers are widely used for spiritual support, problem-solving, and health care. Healing techniques are often passed from one healer to another through apprenticeships. Traditional healing may take place in the form of a community ceremony or as a private healing ritual or treatment for a sick person. |
regional groups are working to improve collaborations between traditional healers and government-sponsored health networks. In Uganda, a non-governmental organization called Traditional Healers and Modern Practitioners Together Against AIDS (THETA) has been a regional leader in building effective partnerships between traditional and modern practitioners for the care of patients with HIV infection. Their work has included training traditional healers in modern understanding of HIV pathogenesis and treatments as well as studies to document the efficacy of selected traditional herbal remedies. In Botswana, traditional healers are organized into the Dingaka (“doctors”) Association of Botswana. Efforts to train Dingaka Association members regarding the spread of HIV have resulted in increased STD prevention counseling in the communities they serve.\(^{14,15}\)

The education of traditional healers in conventional medical theories and treatments can play an important role in stemming the transmission of HIV. A three-year study of the practices of traditional healers in Nigeria revealed that 77 percent of their treatments involved incisions made with unsterilized blades. “Herbal preparations were then rubbed into these actively bleeding skin cuts, using unprotected fingers, which were in direct contact with the patient’s blood.”\(^{17}\) Both healers and their patients are at great risk for contracting HIV and other infections through such practices. As antiretroviral medications (ARVs) become more widely available in areas where traditional healers work, it will be important for the healers to be trained in basic principles of their use. The problem of antibiotic resistance has been exacerbated by the misuse of antibacterial drugs by untrained practitioners,\(^{18}\) such as the mixing of low doses of antibiotics into herbal remedies. Similar practices using antiretroviral drugs would harm patients by leading to the development of viral resistance to the ARVs.

Their holistic approach makes traditional healers especially well-suited to the management of symptoms and the maintenance of patients’ general well-being. By providing education and regarding traditional healers as partners in the care of HIV-infected individuals, benefits to the patient can be maximized, and potential harm can be minimized. Traditional healers should be sensitized to the potential risk of infection to themselves as a result of certain practices.

**Attitudes Regarding CAM**

The use of CAM modalities is widespread among HIV-infected people around the world.\(^{5,6,15,19-22}\) While no study has focused on the prevalence of CAM use for HIV-infected children, it is known that CAM is widely used to treat children with other chronic diseases.\(^{23}\) It is therefore likely that CAM use is prevalent among HIV-infected pediatric populations. Because of the likely high prevalence, the importance of CAM to families, and the potential for interactions between CAM and conventional medicines, asking about CAM use should be a part of medical history-taking for all pediatric HIV patients.

There are many reasons why people choose to use CAM.\(^{5,9,25-27}\) Commonly cited reasons for CAM use include:

- Ease of access
- CAM providers’ use of culturally familiar ways to explain the causes of ill health
- Perception of efficacy
- Perception of safety
- Lower cost
- Preference for natural over synthetic medicine
- Greater sense of patient autonomy
- Greater use of physical touch
- Belief that CAM providers can heal both the body and the spirit
- Pleasant therapeutic experiences
- Rejection of science and technology
- Failure of conventional therapy to provide a cure
- Dissatisfaction with practitioners of conventional medicine
- Frustration with side effects of conventional medicines
- Desperation
Most patients who use CAM do not discuss this use with their mainstream health care providers unless asked specifically in a non-threatening manner. Patients cite many reasons for not discussing their CAM use with nurses, physicians, and other mainstream providers, including:

- They are not asked specifically about the use of CAM therapies.
- They think of the CAM therapies as separate from mainstream therapies and do not recognize that one may change the efficacy of the other.
- They fear that mainstream providers will perceive their CAM use negatively.
- They fear that mainstream providers will provide lower quality of care if they know of their CAM use.
- The use of CAM modalities provides them with an increased sense of control over the illness that may be compromised by disclosure to a paternalistic medical provider.

Despite the widespread use of CAM therapies, many health care providers do not routinely discuss CAM use with their patients. To best serve the interests of their patients, health care providers should establish and maintain trusting relationships with patients and their families; guard against personal biases; and provide balanced, evidence-based advice about therapeutic options. When evidence regarding the safety and efficacy of a treatment choice is lacking, the uncertainty should be discussed openly, and likely risks and benefits should be considered.

**Evaluating CAM Therapies**

It is important for health care providers to inform patients about known treatment-related risks and to be aware that unknown toxicities or interactions may exist. Health care providers should seek information about CAM therapies their patients are using. When studies related to the therapies are available, their quality and results should be reviewed. The providers of CAM therapies can often be contacted to help clarify the merits and the risks of the treatment approaches they recommend.

Many herbs and supplements contain undeclared pharmaceutical drugs, heavy metals, and other contaminants. A study of 260 Asian patent medicines sold in the United States revealed that one-third contained undeclared pharmaceuticals and/or heavy metals. The origin, contents, and quality of all remedies ingested or applied to the body should be investigated. Care should be taken to ensure that patients are not unknowingly consuming products that are likely to be harmful to them.

The potential risks and benefits of all therapies should be considered by patients and health care providers. Part of this evaluation should include reflection regarding how different therapies may interact with each other. Just as certain prescription drugs should not be given together due to potential adverse effects, some CAM therapies should not be used in conjunction with prescription medications. In HIV-infected patients on ARVs, some herbs have been shown to hasten the progression of HIV infection due to their effects on ARV concentrations (see Table 2). This is most likely due to induction and inhibition of various cytochrome P450 (CYP) enzymes involved in ARV metabolism. When patients fail to respond to prescribed therapies, the possibility of such interactions should always be considered.

Patients stand to gain much by increased understanding of the benefits and risks associated with CAM use. In 1998, the National Institutes of Health (NIH) of the United States established the National Center for Complementary and Alternative Medicine (NCCAM) to help bridge some of the gaps between conventional and CAM providers. Through scientific studies, NCCAM investigates which CAM practices are effective and why. As of June 2004, 13 NCCAM trials were looking at the efficacy of CAM treatments in HIV-infected people. These included studies related to the use of acupuncture to treat chronic diarrhea in HIV patients, Reiki to improve quality of
life in patients with advanced AIDS, and massage to improve immune function and quality of life in HIV-infected children. Patients and health care providers can look for the results of these and similar studies to guide them in the rational evaluation of CAM therapies.

### Table 2: Selected Potential Side Effects of CAM in Children With HIV/AIDS

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Common Uses</th>
<th>Risks or Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acupuncture</td>
<td>See Table 1</td>
<td>Complications are rare, but infections and serious tissue trauma (heart rupture, liver injury) have occurred in children due to acupuncture treatments.²⁶</td>
</tr>
<tr>
<td>Chiropractic Manipulations</td>
<td>See Table 1</td>
<td>Upper spinal manipulations have been associated with serious adverse events in children, including paralysis, strokes, and vertebral artery dissection.²⁷</td>
</tr>
<tr>
<td>Cutting and Blood-letting</td>
<td>Purging the body of hazardous substances, creating a dermal opening for the application of herbal remedies</td>
<td>Unsterile conditions and re-use of cutting instruments and other tools may lead to the spread of infections, including HIV.</td>
</tr>
<tr>
<td>Herb: Chaparral (Larrea tridentate)</td>
<td>Antioxidant, antifungal, also used for arthralgias, neuralgias, respiratory infections, rashes</td>
<td>Multiple cases of liver damage, including cirrhosis and fulminant liver failure, have been reported.³⁷</td>
</tr>
<tr>
<td>Herb: Coneflower (Echinacea sp.)</td>
<td>Immune stimulant</td>
<td>Use in HIV-positive patients is controversial; some in vitro studies suggest that it might aid progression of HIV disease.</td>
</tr>
<tr>
<td>Herb: Ephedra/Ma Huang</td>
<td>Stimulant, increases energy level</td>
<td>Increases blood pressure, heart arrhythmias, has led to strokes and death</td>
</tr>
<tr>
<td>Herb: Garlic (Allium sativum)</td>
<td>Antibacterial and antiviral properties, inhibits platelet aggregation</td>
<td>Decreases plasma concentrations of protease inhibitors²²,³⁴, increases bleeding tendencies</td>
</tr>
<tr>
<td>Herb: St. John's Wort</td>
<td>Used for the treatment of mood disorders, particularly depression</td>
<td>Reduces the concentration of certain protease inhibitors and NNRTIs,²,²²,²⁶,²⁸,³² (St. John's Wort is a potent inducer of CYP3A4 and inhibits several other CYPs.)³⁰</td>
</tr>
<tr>
<td>Homeopathy</td>
<td>See Table 1</td>
<td>Most but not all homeopathic remedies are diluted beyond the threshold of toxicity. A case has been reported of an infant suffering from mercury poisoning after ingesting homeopathically diluted mercury.²⁷</td>
</tr>
</tbody>
</table>
HIV CURRICULUM FOR THE HEALTH PROFESSIONAL

**Review Questions**

1. List CAM modalities used by HIV-infected patients.

2. Discuss reasons why HIV-infected patients choose to use CAM.

3. Identify reasons why HIV-infected patients may not tell health care providers about their CAM use.

4. Review the risks associated with some commonly used CAM therapies.

**Exam Questions**

1. Which of the following is a reason why patients are often reluctant to tell their conventional health care providers that they are using or seeking CAM therapies?
   - a. The health care providers are required to report them to the health district.
   - b. CAM providers usually tell people not to share their secrets with other health care providers.
   - c. Patients worry that their health care providers will not approve of their choice to use CAM.

2. Herbal therapies have been used to treat common illnesses and chronic conditions for centuries. Which of the following statements about herbal therapies is true?
   - a. Herbal therapies are always as effective as conventional medications.
   - b. Herbal therapies should be used cautiously because they can cause adverse reactions and side effects.
   - c. Herbal therapies should never be used in conjunction with modern medical treatments.

3. Which of the following is a reason why people in some parts of Africa seek care from a traditional healer before seeing a conventional health care provider?
   - a. Studies show that traditional remedies are usually more effective than conventional medicines.
   - b. There are more traditional healers than conventional doctors.
   - c. Traditional healers are always regulated by the government to ensure that their treatments are safe.
Case Study #1

A 6-year-old HIV-infected girl and her mother visit you in your clinic. The little girl was very sick when she first started coming to the HIV clinic. Since starting antiretroviral medications (nelfinavir, zidovudine, and lamivudine) 2 years ago, the child has been doing very well. Her growth and development have been good, and she seems happy and healthy.

During this visit, you note that the mother seems to have lost weight and appears to be tired. She mentions that she has been to the traditional healer, who gave her a mixture of herbs to make into a tea to help increase her energy and appetite.

**Question:** The mother asks you if it is safe to give the herbal tea to her daughter. Which of the following would be appropriate to tell the mother regarding the use of herbal remedies in children with HIV infection?

- a. It is definitely safe for children because it is made from herbs, which are natural.
- b. You cannot tell her whether the herbal mixture is safe without knowing exactly which herbs are in it.
- c. All herbal remedies are dangerous, and she should never consider using them for herself or her child.

**Answer:** b. Many herbs are safe for use in both adults and children, but some can be dangerous. Health care providers should look for evidence regarding the safety of herbal remedies that their patients are using.

**Question:** The girl’s mother returns one week later with a list of the herbal contents of the tea mixture given to her by the traditional healer. The list includes the herbs Hypericum perforatum and Ephedra. What should you tell her about the safety of this herbal remedy for her daughter?

- a. The herbal remedy will help the child’s body fight the HIV infection.
- b. There are no known risks associated with the use of Ephedra.
- c. The herbal remedy may cause the child’s antiretroviral drugs to stop working effectively.

**Answer:** c. The herb Hypericum perforatum reduces levels of protease inhibitors and NNRTIs in the blood. This child would be at increased risk for developing resistance to her antiretroviral regimen if she were to take an herbal preparation that led to inadequate serum levels of one or more of her ARVs.

Case Study #2

A 7-year-old HIV-positive boy who previously was doing well on antiretroviral medicines was taken off of his medicines when he came to live with his aunt. His aunt is aware that he is HIV-positive, and she believes that by praying for him every day, she will be able to keep him healthy. She has been providing him with a healthy diet and is teaching him to perform mind-body exercises to help him relax and improve his overall health. Since he stopped taking his medicines, the boy’s viral load has risen dramatically, and his absolute CD4 count has fallen to 160 (<15 percent). He now has oral thrush and diarrhea.

**Question:** Which of the following statements is most likely to be helpful in communicating to the aunt the necessity for her nephew to be put back on antiretroviral medications?

- a. You need to stop the mind-body exercises because they obviously are not helping him.
- b. The techniques you are using to maintain his health are good ones, but his declining condition proves that he needs additional help.
- c. If you do not put him back on his antiretroviral medicines, the doctor will not see him anymore.
**Answer:** b. It is important to show respect to patients by communicating with them in a non-threatening manner. Certain complementary therapies may not be sufficient to maintain the long-term health of an HIV-positive patient. If families believe them to be helpful and they are clearly not harmful to the patient, the use of particular complementary therapies should not be discouraged.

**Case Study #3**

You are providing health care to an HIV-exposed child. Her HIV-infected mother was put on a short course of antiretroviral therapy prior to the birth of this child. She declined the option of substitute feeds for her child because of widespread stigma within her neighborhood. The exposed child has tested HIV-negative at the age of 18 months. The mother is pregnant with her second child. She has not disclosed her HIV status to her husband. Although she is receiving prenatal care, including another short course of antiretroviral therapy, she has decided to have her second delivery conducted by a traditional birth attendant (TBA) because TBAs are not as inquisitive about HIV as conventional health care providers.

**Question:** Which of the following approaches would be best to take to help the unborn infant benefit from the short course of antiretroviral therapy and to help protect the woman's husband and the TBA from exposure to HIV?

a. Impress upon the HIV-infected mother the importance of disclosing her HIV status to both her husband and the TBA.

b. Discuss with the mother the possibility of bringing her husband to the clinic for couples counseling, with a view to empowering them to decide whom else to inform.

c. Take the initiative and inform both the husband and the TBA.

d. All of the above

**Answer:** b. This is the best option because it provides the best opportunity for partner involvement and possible support for protective choices later, such as substitute feeds.

**Case Study #4** (adapted with permission from a KHANA case study)

Srey lives with her husband and children in a large city in Cambodia. Her parents live in a small village nearby. Srey is a client of a home-care team and is open about her HIV status when she is in the city. She visited a kru khmer (traditional healer) whom she knew in her village. She says that she drinks his medicine every day and that it makes her better. She explains: “I don’t tell people in the village that I have HIV because they hate people with ‘AIDS.’ The kru gave me traditional medicine. It made me cold (reduced fever) and able to eat. I didn’t tell him that I have HIV, and my parents do not know, either. My parents guess that I have syphilis. My parents forbid talk about AIDS; they are embarrassed.”

**Question:** As a health worker with the home-care team, what advice would you give this patient?

a. Tell your parents that you have HIV.

b. Stop going to the traditional healer.

c. Invite some home-care team members to the village to brief the community (including your family) about HIV/AIDS in order to address the issue of stigma.

**Answer:** c. To create an environment in which Srey can disclose her status and enlist the support of her family and her traditional healer, the issue of stigma in the village must be addressed.


Objectives

The purposes of this module are to:
1. Identify psychosocial factors that affect children and adolescents infected with HIV/AIDS and how these factors relate to general chronic illness.
2. Identify sources of stigma and discrimination against children and adolescents and explore how stigma affects disclosure.
3. Examine issues of death and dying and the grief/bereavement process that follows for survivors.
4. Identify particularly vulnerable pediatric and adolescent populations and explore reasons why they are at increased risk of HIV/AIDS infection and progression.
5. Discuss special issues encountered by adolescents.

Key Points

1. HIV/AIDS progresses through many of the stages and stresses of other pediatric chronic and terminal illnesses.
2. Stigma affects all aspects of caring for children and adolescents infected and affected by HIV/AIDS, especially as they face the issue of disclosure.
3. Death and bereavement are important topics to help children deal with, even at an early age.
4. Orphans and girls are at increased risk of contracting HIV/AIDS and of receiving less support during their illness.
5. Adolescents are a unique population with a pivotal role in the future of the pandemic. They need special care and attention, including support and education.

Overview

HIV/AIDS takes an enormous physical toll on those infected by the virus as well as those who care for them. However, the psychological toll of the epidemic is just as significant. The psychological and social effects of HIV/AIDS are magnified in young people. Children and adolescents are an ever-growing part of the HIV/AIDS epidemic. In 2004, an estimated 2.2 million children under the age of 15 were living with HIV.1

Children involved in the epidemic face a set of psychological and social issues that must be addressed, not overlooked. This chapter will discuss how children and adolescents are affected by some of the important aspects of the HIV/AIDS epidemic, including stigma, disclosure, and death, and how health care professionals can support them in dealing with these challenges.
HIV/AIDS as a Chronic Illness

In many parts of the world, HIV/AIDS is still seen as a death sentence, a disease from which there is no recovery. But with the ever-improving availability of antiretroviral therapy, HIV is increasingly recognized as a chronic rather than terminal illness. This transition requires psychological adjustments, especially in the pediatric and adolescent populations.

A chronic illness can be defined as “a disorder with a protracted course which can be progressive and fatal or associated with a relatively normal life span despite impaired mental and/or physical functioning.” This broad definition encompasses multiple types of conditions, ranging from fatal to lifelong. It includes HIV/AIDS, which can but need not be fatal. Unlike acute conditions, which normally develop and resolve themselves quickly, chronic conditions are lifelong and usually have no cure. Of the main characteristics experienced by children with chronic illnesses or conditions, children with HIV infection may experience:

• Limitation of developmentally appropriate functioning
• Dependency on medication
• Need for more medical care than is normal for their age
• Disfigurement resulting from certain opportunistic infections or severe wasting accompanying progressive disease.

Because chronic illness persists for an extended time, affected children and their caregivers go through several stages that can be sources of great stress. These stages include:

• Initial diagnosis
• Disclosure to the child
• Difficulties resulting from long-term care, including financial and emotional strain
• Preparation for and acceptance of the patient’s eventual death.

The stressors of a chronic illness are more challenging when the ill patient is a child. This increases the necessity for primary caregivers and other family members to assist with medical care and with activities of daily living. Chronic illness creates a series of challenges for those involved in the child’s care. These challenges fall into three general areas: emotional, cognitive, and behavioral. Emotionally, the family must come to terms with the child’s diagnosis. This includes grief over the loss of the “idea” of their once-healthy child, as well as guilt, sadness, and anger. If the child was infected with HIV through mother-to-child transmission, the mother may feel enormous guilt and may even be blamed within the family for the child’s diagnosis.

The cognitive challenge is to educate the child’s family about HIV/AIDS, including transmission, disease progression, and treatment. Family members must understand how the child’s life will be affected on a daily basis. They must also understand the importance of adherence to the prescribed medication regimen. If they understand how the medications work, family members can become an informed asset to the team providing the child’s medical care. The family should also be educated regarding the symptoms of disease progression and possible side effects of medications. This way the family will know what to look for if the child falls ill or develops new symptoms.

The behavioral challenge consists of incorporating the child’s chronic illness in the daily life of the child and the family. Amidst the required behavioral changes, the child’s caregivers must also try to maintain a sense of normalcy for the child. The child’s medications and clinic visits need to be a part of daily living, though they often require major adjustments and place a strain on family relationships and routines. To develop as fully as possible, the child still needs rules, discipline, and routines. Routines are especially important for children dealing with stressful or new situations, because they help provide a sense of security.

Children with a chronic illness such as HIV/AIDS face unique challenges that make their lives more difficult. It is important to understand the long-term
effects these challenges can have on the children and their caregivers, whether that’s their parents, extended family, or others in the community. With proper support from their health care providers and their community, the burden of childhood with HIV/AIDS will seem less great.

**HIV/AIDS and Stigma**

A major factor that distinguishes HIV/AIDS from other chronic or terminal illnesses is the stigma associated with the disease. This stigma comes from a lack of knowledge about HIV and how it is transmitted. Stigma can adversely affect children and their caregivers in ways that have long-term negative psychological and social effects.

Stigma can be defined as “a negative, moral, or judgmental definition of a person or social situation, often connected to discredit, disgrace, blame, and ascription of responsibility for the conditions.”

Stigma alters the way people perceive and interact with the world around them. Stigma can have such a profound effect that it changes the way people think and feel about themselves. Stigma surrounding HIV/AIDS is not particular to one generation or one part of the world; it has been an important aspect of the disease since the first cases emerged in the early 1980s, and it has taken hold in all areas, even those untouched by the mass media.

HIV/AIDS stigma originated in the association of the disease with homosexual men and intravenous drug users, two marginalized groups in which the disease first came to public attention. Though beliefs that transmission was limited to these groups were soon proven false, stigma persisted and was reinforced by moral judgments of sexual promiscuity as a cause of transmission. Among some people, these associations have resisted widespread HIV education. HIV/AIDS stigma may be facilitated by the fact that the disease can be fatal, has no cure, and has noticeable physical effects during its advanced stages.

The pediatric population was not a prominent part of the initial phase of the pandemic. In the beginning, few children were recognized as being infected. The first groups of HIV-positive children to be recognized were those who had received infected blood products, particularly young boys with hemophilia, and children born to HIV-positive mothers. Today, those infected through mother-to-child transmission make up the vast majority of HIV-positive patients under the age of 15. Infection among adolescents (ages 15-24) is growing at an astounding rate, mostly through sexual transmission.

Three concepts are helpful in understanding stigma as it relates to the pediatric population: associative stigma, internalized stigma, and stigma management. Stigma is associative when it affects people because of their association with a stigmatized person (in this case, a person with HIV or AIDS). Associative stigma may affect caregivers who step in and help care for infected or affected children whose parents have died. Children may be affected by associative stigma if their parents are publicly known to be infected with HIV.

Stigma takes a particularly damaging form when it becomes internalized, which occurs when a person is aware of a social stigma and accepts, or internalizes, society’s negative views. This damages the person’s self-esteem and gives him or her a negative sense of self-worth. Internalized stigma has a big impact on the pediatric population through its influence on parents’ decisions about disclosure. If parents or caregivers have internalized the stigma and negative views of HIV/AIDS, their likelihood of telling the child about his or her diagnosis decreases significantly. If adolescents internalize the stigma regarding their diagnosis, they are more likely to become depressed and engage in denial regarding their HIV status.

Stigma management is a way of coping with HIV/AIDS stigma by being aware of possible negative reactions and finding ways to minimize them. Children who know their diagnosis may practice stigma management by choosing and limiting whom...
they disclose to in order to minimize the chance of negative reactions or rejection.

Stigma surrounding HIV/AIDS can severely impact those infected or affected by the virus. Prone to both stigma internalization and stigma management, they are less likely to seek social support for fear of rejection and isolation. In some areas, stigma has been reduced through education and outreach. In many parts of the world, however, stigma is still a harsh reality, sometimes barring children from school and other community activities. To safeguard a child from experiencing stigma, caregivers may delay disclosing the child’s diagnosis to the child; if children are unaware of their diagnosis, they are less likely to tell the “wrong” people. Data show that between 25 percent and 90 percent of school-aged HIV-positive children are unaware of their own HIV status. Many caregivers feel that if children know their diagnosis, they will internalize the stigma and give up. In this way, stigma leads to an atmosphere of secrecy within the family that the child often senses. Labeling the diagnosis a secret that must not be discussed only serves to increase the stigma. Many parents also are afraid to disclose the child’s HIV-positive status because of deep feelings of guilt or shame, especially when the route of transmission was from mother to child. The parents may feel guilty about their role in infecting the child and fear that the child will become angry or blame them.

These families need to be supported and educated, along with their communities. Through basic education about the virus and how it is transmitted, much of the stigma can be dispelled. With knowledge, longstanding myths and rumors can be laid to rest and the truth regarding HIV can replace fear and ignorance. Through support, families and children infected and affected by the HIV/AIDS epidemic will no longer feel alone in their struggle.

**Death and Bereavement**

Despite the increased availability of highly active antiretroviral therapy (HAART), death is still a common outcome of HIV/AIDS. Each year, millions of children lose one or both parents to AIDS. While relatives go to heroic lengths to provide orphans with food, shelter, and housing, oftentimes the children’s psychosocial needs are overlooked, and the children are not given full recognition or support after their loss. This is usually due to the belief that children are too young to understand what is happening or are better off not dwelling on their loss. Consequently, children are not properly supported in their time of mourning.

When a parent or caregiver approaches the end stages of AIDS, it is extremely important that a plan of care be created for the children. This is referred to as permanency planning. When this step is not taken, children are left in a state of uncertainty about who will care for them. This can compound the loss felt by the child after a parent’s death. The child may be separated from siblings and may experience frequent shifts from place to place in search of a proper home. Children whose parents do not complete permanency planning are at increased risk of developing emotional and behavioral problems.

For children who have lost parents or family members, grief can be overwhelming and hard to understand. Grief and bereavement experiences are unique to each individual. Grief can cause a series of different types of responses, including physical, emotional, behavioral, cognitive, spiritual, and social. Social responses are particularly important because of the high rate of stigmatization associated with HIV/AIDS. It is also imperative that grieving children be able to acknowledge their loss and be provided with an opportunity to release their grief. Without such as opportunity, they may experience psychological ramifications well into adult and may indeed never recover from their loss.

It is common for children to experience a regression in their behavior during their period of mourning. They may begin to display behaviors they have not exhibited in a long time, such as sucking on their
thumbs or becoming increasingly clingy – both actions that help increase their sense of security in a time of confusion. Some children will also try to gain attention through acting-out behaviors. Attention helps children remember they have not been forgotten. So children will act out to get this attention, even if the attention is negative in nature.

It is important to understand how children's views of death are shaped by their developmental age. For children 0-2 years of age, comprehension of death is very limited. However, they realize that the deceased person is no longer in the environment. These children may be more irritable than usual and may exhibit clinging behaviors. From 3 to 5 years of age, orphans believe that the deceased parent is just away for the time being and will eventually return. They have no comprehension of the finality of death.

Children ages 6-8 are curious and wonder what happened to the person who died. They believe the person is still alive and functioning, wherever he or she is, and they may ask whether the person can return someday. Children of this age also begin to exhibit forms of “magical thinking,” in which they believe they have the power to affect things with their thoughts or actions that in reality are out of their control. For example, a child who made his mother angry shortly before her death may believe he caused the mother’s death.

At ages 9-12, children come to realize that death is final and irreversible. The loved one will not return. These children are concrete thinkers and have trouble comprehending anything beyond the physical death that has occurred. During this period, children may show aggressive tendencies, display risky behaviors, or become excessively impulsive. During adolescence, ages 13-18, youths understand the concrete nature of death and also begin to understand death in an abstract sense. They think of death in terms of an afterlife as well as a physical death. Adolescents have powerful emotions regarding death and may exhibit these emotions for extended periods of time at random intervals. It may take years for a child to come to terms with parent’s death. (For more information on developmental stages and how children experience grief, see Table 1.)

For children of all ages, support is a key factor in the grieving process. This support can come from their families, friends, and communities. Rituals are a central part of death and grieving for communities around the world. Rituals are a central part of death and grieving for communities around the world. Often children have assigned roles during such rituals. Sometimes participating in rituals

<table>
<thead>
<tr>
<th>Age</th>
<th>Thoughts</th>
<th>Feelings</th>
<th>Actions</th>
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<tbody>
<tr>
<td>3-5 years</td>
<td>• Loved one will return.</td>
<td>• Fearful of separation</td>
<td>• Cry</td>
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<tr>
<td></td>
<td>• Loved one is just away.</td>
<td>• Anxious</td>
<td>• Temper tantrums</td>
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<td></td>
<td></td>
<td>• Confused</td>
<td>• Nightmares</td>
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<td></td>
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<td></td>
<td>• Regressive/clingy behavior</td>
</tr>
<tr>
<td>6-8 years</td>
<td>• Wonder if loved one can return</td>
<td>• Confused or anxious</td>
<td>• Temper tantrums</td>
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<tr>
<td></td>
<td>• Deceased can still function</td>
<td>• Fearful of separation</td>
<td>• Nightmares</td>
</tr>
<tr>
<td></td>
<td>• Magical thinking</td>
<td>• Fearful they might die, too</td>
<td>• Regressive/clingy behavior</td>
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<td></td>
<td></td>
<td></td>
<td>• Difficulty concentrating</td>
</tr>
<tr>
<td>9-12 years</td>
<td>• Understand finality and irreversibility of death</td>
<td>• Sad</td>
<td>• Aggressive/impulsive behavior</td>
</tr>
<tr>
<td></td>
<td>• Magical thinking</td>
<td>• Anxious</td>
<td>• Engage in risky behavior</td>
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<td>• Lonely</td>
<td>• Decline in school performance</td>
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<td></td>
<td>• Difficulty concentrating</td>
</tr>
<tr>
<td>13-18 years</td>
<td>• Understand finality of death</td>
<td>• Confused</td>
<td>• Aggressive/impulsive behavior</td>
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<tr>
<td></td>
<td>• Begin to look beyond physical death</td>
<td>• Withdrawn</td>
<td>• Engage in risky behavior</td>
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<tr>
<td></td>
<td>• Magical thinking</td>
<td>• Guilty</td>
<td>• Decline in school performance</td>
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<td>• Difficulty concentrating</td>
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<td></td>
<td></td>
<td></td>
<td>• Exhibit powerful emotional bursts</td>
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can help children with the transition and acceptance of a loved one's death. On the other hand, sometimes these roles can increase the trauma experienced by the child. Children must be supported before and after the ritual to reduce the amount of stress they experience. If participation in the ritual is optional, children should be allowed to choose whether they would like to participate.

When children face their own death, many experience anticipatory grief, “the grief expressed when the loss is perceived as inevitable”. Children may exhibit signs of anticipatory grief when they feel their death approaching. Often they will project their feelings onto others. For example, they may express fear that their caregivers might die. They will panic at the thought of anything traumatic happening to those persons, when in fact they are afraid of their own death and what will happen to their loved ones when they are gone. They may also show signs of knowing about their fate through symbolic play or art, for example through pretending toys are dead or by drawing death in their artwork. Children may become withdrawn, quiet, and increasingly irritable. They will inevitably feel a loss of control in the world around them.

To help children face this oncoming event, support is essential. Children must be given the opportunity to express what they are feeling and to ask questions about what might happen. These talks must be at a developmentally appropriate level so the child will understand. Children should be allowed to participate in decisions affecting them. They are the best resource for determining what they want and how much they can tolerate in the end stages of life.
Unfortunately, death and grief are harsh realities in this pandemic. Children's experience of losing parents and loved ones is often compounded by their own illness and by other factors surrounding the loss, such as secrecy and stigma. These families need additional support and care from their health care providers during their time of mourning.

**Orphans and Vulnerable Children**

All children need food, clothing, safe shelter, health care, and education. Young children depend on parents and caregivers to provide them with these necessities. However, for millions of children whose parents have died of AIDS, survival and well-being are in jeopardy. About 15 million children under the age of 15 have lost one or both parents to AIDS, most of them living in sub-Saharan Africa. By 2010, it is estimated that more than 25 million children around the world will be orphaned by the AIDS pandemic. In addition, AIDS has caused children to experience the loss of their siblings, friends, relatives, teachers, doctors, and other significant people in their lives.

Besides experiencing multiple losses, children orphaned by AIDS are likely to suffer economic hardship, malnutrition, illness, and loss of property and inheritance. Older orphans may drop out of school to work or care for younger siblings. Feeling powerless and lost, some orphans end up living on the streets, trading sex for money or food. Others live in orphanages or institutions, which often fail to provide adequately for the physical and psychosocial needs of children. Institutions also cost more than direct monetary assistance to families that foster orphans. Recognizing the frequent poor outcomes and expense of long-term institutionalized care, several countries have chosen to support family-based care models rather than institutions.

**Gender Issues**

Worldwide, young women (ages 15-24) are 1.6 times as likely as young men to be HIV-positive, according to the UNAIDS 2004 Report on the Global AIDS Epidemic. Figure 1 shows the gender ratios by region. In sub-Saharan Africa, young women are three times as likely as men to be HIV-positive. In many cases, young women may lack access to education and prevention programs due to sociocultural factors. In a survey in sub-Saharan Africa, half of the young women did not know that a healthy-looking person can have HIV. In addition, UNICEF found that more than half of the adolescents surveyed in 17 countries could not name a single method of protecting themselves against HIV. Sadly, many young women are coerced or forced into unprotected sex. A girl's vaginal tissue tears easily, putting her at high risk of contracting HIV from unprotected sex. Violence, forced prostitution, incest, and rape, including marital rape, all put girls and women at risk.

The story of 17-year-old Nicole and her 14-year-old brother, John, illustrates the many social challenges that orphaned and vulnerable children (OVC) face. The two live in the small, bleak apartment they once shared with their parents. John, infected vertically with HIV, receives excellent medical care and treatment at a nearby clinic. Nicole attends school, helps her brother with homework, and does all the household cooking and cleaning. Nicole's biggest fear is that without her care, John will die. Their uncle is trying to take their property and the small inheritance they have. They need legal aid but cannot afford to hire a lawyer. Nicole wants to attend school next year, too, but cannot afford the fees. Imagine a charming older man who is sexually experienced, possibly infected, pursuing Nicole with expensive gifts and hints of marriage. Would she choose to abstain, ask whether he's been tested, discuss whether he is faithful, or insist on condoms every time? In such situations, young women like Nicole may lack the confidence, power, knowledge, and skills to keep themselves safe.

In regions where the HIV epidemic is at an early stage, more young men than young women are infected. In Latin America, the epidemic is centered among men.
who have sex with men.\textsuperscript{14} In Central and Eastern Europe, injection drug use is driving the spread of HIV.\textsuperscript{14} However, trends indicate that as the epidemics in these regions move into the mainstream community, it will be young women who are at highest risk of infection.

**Global Actions**

At the United Nations Special Session on HIV/AIDS in 2001, governments from around the globe agreed upon goals and strategies to address the needs of children orphaned and made vulnerable by HIV/AIDS. These strategies include:

- Strengthening the capacity of families to care for children by prolonging the lives of parents and providing families with economic and other support.
- Supporting local community actions to help children.
- Ensuring that children receive essential services such as health care, education, nutrition, and psychosocial support.
- Ensuring that governments develop policies and laws that protect vulnerable children.
- Raising awareness within societies to support children and families affected by HIV/AIDS.\textsuperscript{13}

Every child's situation is unique. Interventions will be most successful when children's gender and sociocultural environment are taken into account. Actions on behalf of orphans and vulnerable children must be guided by child-focused principles. Any action should be in the best interest of the child and be non-discriminatory. The child's view should be taken into account, and the child should be encouraged to be an active participant in the process.

**Adolescents**

The world's adolescents represent an important population that deserves special attention. As antiretroviral treatment becomes more widely available, HIV-infected children are growing up into young adults. This transition brings critical decisions and turning points for which proper guidance is often needed.

**Disclosure**

Adolescents deal with disclosure issues on multiple levels, including finding out their parents are HIV-positive, finding out they themselves are HIV-positive, and deciding to disclose their HIV-positive status to others. Parents who wait to disclose their own HIV-positive status until their children are teens often experience negative consequences; teenagers in such situations report more risky behaviors and negative effects on family relationships.\textsuperscript{15} Regarding adolescents' own HIV status, the American Academy of Pediatrics states that adolescents should know their diagnosis in all cases. That way teens are fully informed of their health status and can make informed decisions regarding their actions and life choices.\textsuperscript{7}

Youth living with HIV (YLH) also face the decision of whom else to tell about their diagnosis. Studies show that a majority of youth have disclosed to their families, and many have disclosed to close friends.\textsuperscript{16} Disclosing to others is associated with positive outcomes. However, stigma surrounding HIV/AIDS makes people more cautious about disclosure. As a form of stigma management, YLH often are selective about when and whom they tell. They thus protect themselves against negative reactions and social isolation. Teens who are able to find a good circle of support, including people who are aware and accepting of their diagnosis, have greater self-esteem and more positive outcomes.

Once HIV-positive youth begin sexual activity, they enter a realm where they have responsibilities toward their sexual partners. Whether it should be mandatory for HIV-positive people to disclose their status to sexual partners is widely debated. No matter what the law requires, partners need to have the confidence and trust to disclose their status. Some youth do not disclose to sexual partners, especially in casual sexual encounters. But many youth feel a moral obligation to disclose their HIV status so their partners are aware of
the risk of transmission. YLH should be supported through these decisions and provided with alternatives to direct disclosure. For example, if a program to anonymously notify sexual partners exists in the area, it can be used in these situations. Disclosing disease status can be very stressful, especially if the HIV-positive adolescents have deep feelings for their partners and are fearful of rejection. Strong support is needed at this time and should be offered before, during, and after disclosure. This support should be offered to the partner as well.

Medical Independence
For adolescents living with a chronic illness, the beginning of the transition to adulthood brings an important shift to medical independence. For vertically infected orphans who may have been in charge of their own health care for years, this transition may still require a change in providers or settings, from pediatric to adult health care. For youth who were infected horizontally and had no prior health conditions, health care may be a new arena. Either way, YLH need assistance in taking charge of their medical care. Tasks they must learn to handle include managing their medications, scheduling their appointments, and discussing their health concerns directly with their health care providers. To perform many of these tasks, teens must understand their condition and feel comfortable discussing it with their health care providers. HIV education will help them feel more confident in these discussions. Some youth will feel unsure as to which health information is important to share with their providers. To assist them, a health-history summary can document the pertinent aspects of their medical past and help them make a more positive transition. Health-history forms should include a list of medications (past and present), prior surgeries, laboratory work, and any recurrent or major illnesses. For teens who are switching to a new provider, additional support is needed to ensure a smooth transition. For example, someone from the pediatric office might accompany adolescents to their first few visits with their new providers.

Self-Esteem and Identity
The adolescent years are a time when identity is developed and children decide what kind of person they wish to be, one of the most important developmental stages prior to adulthood. Healthy youth pass through three stages during this transition. Early adolescence focuses on a shift in attachments, from parents to peer groups. During middle adolescence, youth work on their self-image and begin to develop
abstract reasoning. Late adolescence is when youth begin to feel comfortable with who they are becoming. They also gain awareness of others and their relationships. Adolescents with HIV/AIDS may have difficulty passing through these three stages.

If the disease is fairly advanced, the youth may have a delay in physical development, including a delay in pubescent changes. Consequently, HIV-positive youth may appear younger and smaller than other adolescents because they have not begun the physical process of becoming adults. They may also experience physical changes as a result of their illness, including wasting and opportunistic infections that may cause noticeable physical symptoms. If youth feel different from their peers, they have a harder time bonding with them. This has an adverse effect on these adolescents’ attachments, making it difficult for them to separate from their parents. These changes may also contribute to a negative sense of self-image for these adolescents. They may feel unable to identify with their peers or singled out from other teens due to stigma.

Adolescence is also a time of exploration. Exploring who they are helps youth in their identity development. The stress of having a chronic illness may prevent some YLH from wanting to participate in psychological exploration. This is especially true if they are in denial or are having trouble accepting their HIV status. Developing an identity is a difficult task for any young person, a task that requires guidance and support. This is especially true of young people living with HIV.

Sexuality
Sexuality is an important topic for adolescents, who are at the age when sexual exploration begins. Their drive to explore their sexuality makes adolescents a pivotal population in the HIV/AIDS epidemic. Many youth are poorly educated about sex. This lack of education and the likelihood that they will not practice safer sex leaves teens at high risk of contracting and transmitting HIV. Youth are also engaging in sexual exploration at younger ages than in the past. This is of great concern, because younger groups are even less likely to be educated about sexual protection.

A study conducted in 1999 showed that if youth perceived themselves as more mature than their chronological age, they were more likely to engage in sex earlier than their peers. Their desire to transition into adulthood also was a major factor in their remaining sexually active after their first sexual encounter. This is important in the discussion of HIV-positive youth because of the increasing number of families headed by young adults. With the absence of parental figures, often due to AIDS, youth are being placed in caregiver roles at much younger ages. Many care for younger siblings, and some are sole providers for their families. With these responsibilities, youth may feel greater autonomy and may wish to participate in other adult behaviors besides caretaking, such as sexual intercourse.

An important group within the adolescent population is the non-heterosexual youth, i.e. homosexual and bisexual youth. These youth face the additional stressor of “coming out” to their friends and family about their sexual orientation. This is a daunting task, given the large amount of public stigma and discrimination toward homosexuals and bisexuals. These teens feel different from their peers and experience the “gay-related stress” of growing up homosexual or bisexual in a hostile environment. Symptoms of gay-related stress can include anxiety about disclosing they are gay and fears that someone will inadvertently find out about their sexual orientation. These youth must learn to integrate their homosexuality into their greater identity. This is a difficult process if their home environment is not accepting of their sexual orientation. Stress increases if the teen is HIV-positive because of the additional stigma carried by the disease. Young homosexual men are at increased risk of becoming infected with HIV.
and of transmitting the disease. This makes homosexual youth an important population to reach with HIV education and support. Only education and support will help them achieve positive psychological outcomes and provide them with the tools to protect themselves and others.

**Risky Behaviors**

Many youth, regardless of HIV status, engage in risky behaviors during their adolescent years. The most common risky behaviors include unprotected sexual intercourse and the use of illegal substances. Many youth engage in unprotected sex even if they are aware of their HIV-positive status. This puts them at risk of contracting sexually transmitted infections, including reinfecion with different strains of HIV. Unprotected sexual intercourse also puts their partners at risk of contracting HIV. Studies have shown that females are more likely to use protection than males. However, in many places females are not in a position of power to protect themselves during sexual intercourse.

Substance use and abuse are common risky behaviors among today’s youth. A growing number of young people use tobacco products and consume alcohol on a regular basis. Marijuana is the next-most-popular drug. Tobacco, alcohol, and marijuana are sometimes called “gateway drugs” because of some evidence that they may lead some users to experiment with other drugs. Hard drugs, such as cocaine and heroin, are used less frequently, but their presence in the adolescent scene is growing. Youth who begin using substances early tend to use more substances more frequently as time goes on. Substance use and abuse are serious problems for YLH. These substances can cause a decline in immune-system function, which may strengthen the virus. In teens on HAART, the substances can have adverse effects and interactions with the medications that can make them very ill. Like many antiretrovirals, many illegal substances are processed through the liver. Combining the two may lengthen the time that illegal substances stay in the bloodstream, increasing toxicity and the chance of overdose. Educating teens on these adverse side effects may guide them to make safer life choices.

Adolescents with HIV must feel supported and gain the education they need to protect their health. This education can and should come from multiple sources, including family, school, church, and community groups. Regardless of their HIV status, youth are at the experimentation stage of their development. But the manner in which they experiment can be protective of themselves and all others.

**Conclusion**

Education and support are the tools that help children and adolescents with HIV survive into psychologically healthy adulthood. Support can help children recover from the devastating loss of parents and loved ones. With proper support, children with HIV/AIDS can progress through the appropriate developmental stages and grow alongside their peers. Through education, children and adolescents can learn to care for themselves and protect themselves and those around them. They can also extend this education a step to educate others and help reduce the stigma that still makes life harder than necessary for many people with HIV. Through the many changes and challenges of childhood and adolescence, the support of family, friends, communities, and health care professionals is essential to the well-being of tomorrow’s adults.
Review Questions

1. What are stages that families dealing with chronic illness pass through?

2. What is stigma management, and what are some examples of its use?

3. Why are young women at increased risk of HIV infection?

4. How does a 3- to 5-year-old child understand death?

5. Name some ways to assist adolescents in their transition from pediatric to adult health care.

Exam Questions

1. Internalized stigma occurs when:
   a. A person sees stigma in others
   b. A person believes society’s negativity about his or her disease or status
   c. A person chooses to associate with something that is stigmatized
   d. None of the above

2. Challenges involved in living with chronic illness are:
   a. Behavioral
   b. Emotional
   c. Cognitive
   d. All of the above

3. Care for grieving children should include:
   a. Discussions at their developmental level
   b. Made-up stories of what happened to their dead loved ones
   c. Support as they fulfill their roles in grieving rituals
   d. a and c
Case Study #1

Thomas is an 18-year-old with HIV infection. He has been coming to your pediatric practice for many years. Now he must transfer to an adult clinic for financial reasons. Thomas is nervous about his transition and has come to you for help.

Questions:
1. How can you help Thomas feel more comfortable in this transition?
2. If you use a health-history summary, what should it include?
3. What can be included in Thomas’ education regarding his condition?

Answers: Thomas is going through a transition that is common among teenagers. There are a few things that can be done to assist him. First, a worker from the pediatric office can accompany Thomas on his first visits with his new provider to make him feel more comfortable. Second, role-playing can help Thomas practice questions to ask his new provider. Third, a health-history summary can help smooth Thomas’ transition. This summary should list medications (past and present), prior surgeries, lab work, and any major or recurrent illnesses. Thomas also needs to be educated about his health status. If he has previously been educated about his HIV, this is a good opportunity to refresh his knowledge. Things that can be discussed include the types of lab tests performed and what they look for, how his medications affect his body and how they impact the virus, possible side effects of his medications, and how he can protect himself and others with universal precautions. (For further details, see the section on adolescents’ medical independence above.

Case Study #2

Emily is a 6-year-old HIV-positive girl who is developmentally appropriate for her age. Her father died three days ago, and her mother has been gone for several years. Emily will be staying with her paternal grandparents, but they have no room for her younger sister, who will have to live elsewhere. Emily is unsure about what happened to her father, and her family has avoided speaking with her directly about his death.

Questions:
1. At the age of 6, what does Emily understand about death?
2. What are some additional stressors Emily is experiencing that could be compounding the loss of her father?
3. What are some things you would discuss with Emily’s grandparents now that they have custody?

Answers: Developmentally, Emily is at the beginning stages of comprehending death. At the age of 6, she is probably curious about what has happened to her father and where he has gone. She may believe that her father is simply in a different location and will return sometime in the future. In Emily’s mind, her father is still alive and functioning – just somewhere away from her. She is also experiencing other losses that may be compounding the loss of her father. Emily’s mother has already died, so she now has no living parents. Emily is moving away from her home to live in a different environment with her paternal grandparents. She is also about to be separated from her younger sister. Although Emily may be too young to understand death in the absolute sense, she needs to be talked to regarding her father’s passing. Her family has avoided discussing his death with her, and this could add to Emily’s confusion and sense of loss. Emily may also begin to sense a feeling of secrecy within the family, which may prevent her from asking her grandparents questions. Now that Emily’s grandparents are caring for her full time, it is important to make sure they
understand all that is involved in her care. They should be educated about HIV, including routes of transmission, the importance of clinic visits and medications, laboratory work and what the lab results mean, and how HIV will affect their daily care of Emily. They should be supported through this process and should be allowed to ask questions. The grandparents should be assured that they are not alone in this situation and that they can expect support from the clinic staff. (Please see the section on death and bereavement on Page 298 for further details.)

Case Study #3

Constance is a 15-year-old living with HIV. Her mother died two years ago, and Constance has been caring for her two younger siblings since then. She has conveyed to you that she has been having sexual intercourse for the past three months. Constance says she is in love with her partner but is unsure of his faithfulness. Constance reports that she and her partner always use condoms, but lately he has been asking for sex without them. She has not disclosed her status to him for fear he will reject her.

Questions:

1. What behavior is Constance performing through her non-disclosure?
2. What are some stressors that Constance is experiencing in her life?
3. In what way would you educate and support Constance?

Answers: Constance is engaging in stigma management by not disclosing her HIV-positive status to her partner. She is limiting whom she tells because she fears negative reactions and rejection. Constance is experiencing multiple stressors in her life. She is probably still dealing with her mother’s death two years ago. She is the sole caregiver for two younger siblings, a huge task for a 15-year-old. She is also worried about the faithfulness of her partner and is dealing with pressure from him to have sex without a condom. Constance is living with the secret of her HIV status. She needs support and education during this time in her life. A clinic worker who has a close relationship with Constance should have an informal one-on-one counseling session with her regarding her reasons for not disclosing her HIV status. Invite Constance to bring her boyfriend to the clinic and to disclose her status with clinic staff present. That way the staff can provide support to Constance and help answer the boyfriend’s questions and provide him with thorough explanations about HIV. Also give Constance a chance to role-play with someone at the clinic how she would like to disclose to her boyfriend. This will allow her to practice what she wants to say during her disclosure. There are a number of other things that can be done, and each will be specific to the individual situation. However, in each situation, be sure to provide as much support and education to the adolescent as possible.
References


Objectives

The purposes of this module are to:

1. Examine the psychosocial issues involved in the impact of HIV/AIDS.
2. Evaluate and identify means of reducing the personal and socioeconomic effects of HIV/AIDS.
3. Identify and describe appropriate resources for care and support.
4. Identify the ways in which caring for people with HIV/AIDS affects health care providers.
5. Identify sources of stigma and discrimination and discuss ways of reducing their negative effects on patients and health care workers.

Key Points

1. Stigma affects all aspects of caring for people with HIV/AIDS.
2. HIV has profound psychosocial effects on the HIV-infected person, the family, the community, and the society at large.
3. Denial of HIV and depression are common responses to HIV infection.
4. Emotional and spiritual care are important components of providing care for people with HIV.
5. Health care providers are affected by the stressors of caring for patients with HIV and need to develop resources for personal and occupational support.

Overview

HIV/AIDS has many physical effects, but perhaps some of its most profound effects are on the psychological, social, and economic health of the HIV-positive person, his or her loved ones, and the community. Since the beginning of the epidemic, stigma and fear have surrounded many of those who live with and die from HIV/AIDS, as well as those who love and care for them. The magnitude of these psychosocial effects makes them central to HIV-prevention efforts, care for people with HIV, and the response of communities to the massive losses of people in their most productive years of life. This lecture will examine the effects of stigma on care for people with HIV; the effects of HIV on the individual, family, group, community, and society; and potential interventions on each of these levels.
Stigma, Discrimination, and HIV

Probably the single most important factor in producing and extending the negative psychosocial impact of HIV and AIDS is stigma. Consequently, actions to reduce or protect against stigma may be the most significant step that can be taken to improve the psychosocial well-being of people with HIV/AIDS. Stigma can be defined as “an act of identifying, labeling, or attributing undesirable qualities targeted towards those who are perceived as being shamefully different and deviant from the social ideal” and as “an attribute that is significantly discrediting (and is) used to set the affected persons or groups apart from the normalized social order.”

Discrimination can be defined as “an action or treatment based on the stigma and directed toward the stigmatized” and as “sanction, harassment, scapegoating, and violence based on infection or association with HIV/AIDS.”

Stated more simply, stigma is the attitude, and discrimination is the act. Acting through discrimination, denial, and shame, stigmatization is an impediment to HIV prevention and treatment efforts. A broader definition of stigma argues that the concept can be understood only in relation to notions of power and domination. Power and control exerted over the devalued group create social inequality and result in the social exclusion of people with the stigmatized disease.

People with HIV/AIDS are stigmatized and discriminated against for many reasons, including:

- HIV is a slow, incurable disease that eventually results in suffering and death.
- Many people regard HIV as a death sentence.
- The public often poorly understands how HIV is transmitted and is irrationally afraid of acquiring HIV from people infected with it.
- HIV transmission is often associated with violations of social mores regarding proper sexual relationships, so people with HIV are associated with having done something “bad.” For example, in some cultures, people believe that a woman becomes infected with HIV because she has violated the mourning period after her husband died.
- Therapeutic protocols are lacking for anti-HIV medications that could control the spread of the epidemic and prolong lives.

Stigma prevents people from talking about and acknowledging HIV as a major cause of illness and death. Stigma prevents HIV-infected people from seeking counseling, obtaining medical and psychosocial care, and taking preventive measures to avoid infecting others. Prevention behaviors are also stigmatized, and people are reluctant to introduce behaviors that could associate them with the virus, such as use of condoms, certain medications, and infant formula when appropriate. A woman with HIV might want her partner to use a condom but might be reluctant to ask because of the stigma associated with the suggestion of HIV risk.

If one family member exhibits signs and symptoms of HIV, the entire family may face rejection and even violence from the community. The loss of social support results in isolation for the family, which may also fear loss of employment, denial of school admission, or denial of adequate housing. Stigma can attach to children of HIV-infected parents and to orphans whose parents died of AIDS. Globally, the AIDS epidemic has robbed 15 million children (12 million in sub-Saharan Africa) of one or both parents. Children may be ostracized at school if it is known that they have an HIV-infected family member, and HIV-infected children may be denied school services for fear that they might spread the virus through casual contact.

Stigma and discrimination also occur in the health care setting. Sometimes HIV-infected patients are denied appropriate care or are segregated from the general hospital population. Health care workers may selectively use universal precautions only with HIV-infected patients. Reasons may include a lack of medical resources, but health care workers’ ignorance...
and stigmatization of HIV can also be factors. A survey of 1000 physicians and nurses in West Africa in 2002 found that 20 percent of them felt that HIV-infected patients had behaved immorally and deserved their fate. Oftentimes health care workers who help patients with HIV may also be stigmatized because of their association with the virus.

Statistics indicate that close to 75 percent of the global HIV/AIDS caseload occurs in Africa. As in other places, stigma associated with HIV/AIDS in Africa involves attributions of other stigmatized behavior, such as homosexual acts among young men. Homosexuality is highly stigmatized and is even illegal in many parts of Africa and Asia. HIV/AIDS is also often blamed on outside forces, such as foreigners or the devil. Stigma may even lead to violence against those blamed for introducing the disease. In 2003, schoolchildren in Ghana staged a demonstration to demand that all tourists be required to get HIV tests. Sex workers, an integral part of the spread of HIV, are stigmatized in most societies. Stigma and discrimination prevent sex workers from playing a bigger role in the fight against HIV/AIDS.

Anal sex is also widely stigmatized, independent of its association with HIV infection. It has been shown to be a more common practice in Africa than previously thought: In a 2004 survey in South Africa, male-male sex accounted for 7 percent of sexual practices, and heterosexual anal intercourse is not uncommon as a form of birth control. Stigma may cause people not to talk about risk behaviors and risk reduction. By association with HIV, stigma may also attach to HIV-prevention methods, such as the use of condoms, and thus prevent HIV risk reduction among the uninfected.

Social dislocation carries with it not only additional risks of infection but also the stigma associated with being a foreigner or outsider. A significant number of refugees may have contracted HIV in their own countries before seeking refuge elsewhere. Warring groups in Sudan, Congo, Uganda, and Rwanda have raped thousands of women and girls, putting them at high risk of contracting HIV. Among an estimated 250,000 rape survivors, it is estimated that up to 67 percent are living with HIV.

Sex education may also be stigmatized, perhaps in the belief that it can contribute to sexual activity. As a result, young people may lack information to prevent the spread of HIV. Research shows that a significant number of girls in Africa contract HIV during their first sexual encounter. Remarkably, 8 percent of women surveyed reported having sex before the age of 13, and 15 percent said they had sex before their first menstrual period. Only 27 percent reported using a condom during their first sexual experience. In areas of high HIV prevalence, infection during early sexual encounters is likely.

Most routes of HIV transmission are not exclusively associated with “immoral” behaviors. But such behaviors are attributed to those infected, thus doubly stigmatizing them – through infection and through attribution. Prevention efforts are also stigmatized through their association with HIV; the attribution is that those trying to protect themselves must be infected. Stigma is thus associated not only with psychosocial distress, but also with a reduction in prevention efforts and practices. The need to minimize the effects of stigmatization in order to improve prevention and treatment efforts cannot be overemphasized. Since HIV/AIDS stigma is a social and cultural phenomenon of the entire community and not simply the result of individual actions, attempts to reduce stigma must address the community rather than focus on individuals.

Health care professionals must be aware of the stigma faced by their HIV-positive patients and must be scrupulous in protecting their patients’ confidentiality. At the same time, providers can take steps to reduce the effects of stigma on their patients. By promoting disclosure of a positive HIV test result to the patient’s family or spouse, they can help build a support system for the patient and educate family members about
HIV. They should provide supportive counseling to patients, caregivers, and fellow health care providers to reduce the stressful effects of stigma. Lastly, all providers should regularly examine their personal values as they relate to caring for people with HIV/AIDS.

**Psychosocial Effects of HIV on the Individual**

Even if stigma is minimized, an incurable and often fatal disease requires enormous psychosocial adjustments. People diagnosed with HIV experience many of the emotional responses identified in people facing a terminal illness. They commonly go through an initial stage of denial, in which they do not acknowledge having the disease or deny its likely consequences. HIV threatens a person's life, goals, expectations, and significant relationships; no wonder that many people are reluctant to admit their diagnosis or their risk of infection. It is not uncommon for people who subject themselves to high-risk situations or behaviors to deny that they are at risk of HIV infection. They often avoid testing, and if they are tested, they avoid following up on results, as if avoiding a clinical diagnosis might prevent the disease. In order to battle HIV successfully, people must have some level of acceptance of the disease so that they can seek counseling, social support, and medical care.

**Stages of Reactions to HIV-Positive Status**

When people discover they have HIV or AIDS, their reactions tend to follow a series of stages, although these are not invariable and some people may skip several stages. The stages are similar to the Kübler-Ross stages of response to dying. The first stage is shock, denial, and anger; people may feel guilty about their infection or angry at those they believe infected them. The second stage is withdrawal; they recognize the stigma associated with HIV/AIDS and may be uncertain or apprehensive about how others will react. Third is a “bargaining” stage; they may tell carefully selected significant others about their HIV. Fourth, people may look for others in the same situation to obtain peer support and discuss problems. In some cases, a fifth stage of seeing themselves as special or different may occur, followed by altruistic behavior or acceptance of their infected status. However, the more stigmatized HIV/AIDS is, the less likely the patient will progress beyond confiding in carefully selected others. When disease symptoms occur, new psychological issues arise.

**Psychological Issues Through the Progression of HIV/AIDS**

The issues facing HIV-positive people vary in accordance with the disease process, including whether the disease is symptomatic. In a study following 80 homosexual men with HIV/AIDS for 15 years, Nilsson Schönnesson and Ross noted common themes that emerged at different points in the disease process. They found that HIV is a threat not only to people's physical survival, but also to their psychological survival. Early in the disease, people often see themselves as being “persecuted” by the virus – an external, alien, bad object. At later stages, physical and psychological anxieties and fears about death are common.

As the disease progresses, control (or power) issues emerge as patients face increasing loss of physical control. Self-efficacy and active involvement in their health can increase people's sense of being in control and reduce their risk of feeling helpless. But hope may alternate with despair. Nilsson Schönnesson and Ross found that existential issues invariably emerged in response to threats to physical and psychological survival. Patients' sense of the meaning of life may be shattered, and they will need to reconstruct new meanings that incorporate HIV. For some, this may include personal and spiritual growth, with HIV as an impetus to do something with their life or for
their family. Existential isolation – a fear of being rejected or abandoned – may lead to anxiety and depression. For many, the existential issues involve spirituality, often a rediscovery of religion if the person has a history of religiosity. For such people, religious belief systems may be a major source of psychosocial support and consolation.

At the beginning of the disease process, issues of death tend to be dealt with indirectly, as fears of psychological death. At the severe symptomatic stage of AIDS, patients experience these issues as much more direct concerns related to physical death. Views of the persecutory nature of HIV change over time. Initial bewilderment turns to fear as the disease becomes more severe. Denial is most typical in the early stages of infection. Control issues are more salient in the asymptomatic and mild symptomatic stages, and helplessness and hopelessness are most concentrated in the severe symptomatic and terminal phases of AIDS. Thus, HIV disease can be characterized as producing four major psychological concerns: existential and spiritual issues; a perception of HIV as a threat or persecutor; feelings of vulnerability and loss of control; and death-related concerns. These concerns emerged from a longitudinal study of a Western, gay population, but it is likely that the same issues and stages of dealing with HIV would emerge in non-Western countries.

Depression is common among people with HIV, especially as they adjust to the fact that they are no longer the healthy people they once thought they were. Adjustment to HIV is affected by the lack of hope that comes from a person’s inability to access or benefit from treatment and the anticipated rejection and need for secrecy because of HIV-associated stigma. Depression is increased by internalized shame regarding previous risk behaviors and by fear that others will find out about their risk behaviors and HIV infection. Seeing many others become ill and experience alienation before succumbing to AIDS increases fear and depression. One common issue is the equation of HIV with AIDS and of AIDS with death. People faced with this may have a variety of reactions. They may become depressed and hopeless and feel that there is no reason to seek care for what is considered a terminal illness. Others may deny that they have the illness because they feel “too healthy” to have HIV.

Psychosocial support is an important part of providing health care to people with HIV. Professional counselors, social workers, health care workers, ministers of religion, trained volunteers, friends, and family play crucial roles in providing psychosocial support. One of the first steps in providing adequate assistance for people with HIV is to make sure the helper is thoroughly aware of and comfortable with the facts about HIV transmission. If helpers feel personally at risk from HIV-infected patients, they will convey those feelings to the patients, who will feel even more isolated than before. Counselors need to educate themselves about HIV to adequately counsel people with HIV. Individual and supportive counseling can help patients come to terms with their HIV diagnosis and with how it will affect all aspects of their lives. Patient education should include information about how HIV is transmitted and should give the patient some idea of common physical and emotional responses to HIV. This type of education can help patients anticipate and plan for these experiences.

Group counseling can also play an important role by allowing individuals with HIV to share experiences with one another. However, this is usually not a good idea until the person has been able to accept the diagnosis enough to come to the group and communicate honestly. Group support can help patients cope with their emotional responses to HIV based on accurate information, shared experiences, empathetic listening, and assistance with problem-solving. Counseling and support can help people with HIV share their feelings about secrecy and stigma and consider how these influence their emotional and physical health. Counseling and support can also
help people consider how their own behaviors can promote health and well-being, such as seeking resources for adequate nutrition, shelter, proper medical follow-up, adequate sleep, and management of stress and anxiety.

Supporting the spiritual needs of HIV-infected people and their families is a critical component of good care and support. Patients with AIDS report significantly lower levels of spiritual well-being than patients with cancer and other terminal illnesses. They also report greater feelings of loneliness, fewer support systems, and less satisfaction with the support systems they have. Support from spiritual leaders who are significant to the patient helps the patient and family cope with the existential and intrapersonal questions raised by a life-threatening illness and with regrets the person may feel about past actions, relationships, or experiences. Traditional healers, often the first care providers sought out by patients, can also be a source of support. When traditional healers and other medical providers work together and have a shared understanding of the goals of care, patients with HIV benefit. Hope can be engendered in terminally ill patients by controlling symptoms, encouraging relationships, assisting the patients with practical needs, affirming their value, and helping them review their life experiences and personal worth in a positive way.

HIV is an illness that affects the whole family.
Psychosocial Effects of HIV on the Family

HIV is an illness that affects the whole family, not only the infected individual. When one member of a family has HIV, often there are others who are as yet undiagnosed. When HIV infects one partner in a relationship, both partners are affected. The infection may indicate that sex or other risk behavior has occurred outside the relationship, but even if the infection predated the relationship, both partners will be involved in the emotional trauma of the discovery. Ideally, the couple should openly discuss sensitive matters such as condom use, sexual fidelity, and childbearing. This does not always happen. Regardless of his or her own risk behavior, the undiagnosed partner may express anger and violence toward the person who has been diagnosed. The diagnosis of HIV infection in a child usually indicates the presence of the virus in the mother. The father and other siblings may carry the infection as well.

Cultural, social, biological, and economic pressures make women more vulnerable to HIV infection than men. In some areas, the high prevalence of rape puts some women at risk of acquiring HIV. In others, teenagers are pressed into sexual relationships with older men who may be infected with HIV. Women are often economically dependent on men and unable to negotiate safer-sex practices, including condom use. Women are usually the primary caregivers for their families and may have little support from others when they are ill themselves. As more people receive care for HIV/AIDS in their own homes or the homes of others, health care workers must keep in mind that HIV-infected women are likely to care for everyone else in the family, often to the detriment of their own health. Households led by women also face greater economic difficulties and have fewer supports.

Strengthening the family structure is especially important because of the tremendous stress that HIV puts on family systems. Besides caring for ill relatives and for orphans, families are often beset by economic and social problems as well as the grief that accompanies the loss of family and friends. They may benefit from group or family counseling, including counseling about their desire to have a family, perhaps the need to prevent unwanted pregnancies, and negotiation of risk-reduction practices such as condom use. Individuals may need training in assertiveness and how to communicate their needs. It is also important not to forget the more basic needs the family is facing: food, shelter, and dwindling finances.

A common issue in counseling is who should be told of a person’s HIV status and how and when the matter should be communicated. One approach is to educate the infected person about how HIV progresses. While the person is still asymptomatic, he or she should consider whom to tell about the infection before the illness begins to manifest itself. A counselor can help the patient identify family members and friends who are supportive and will be open to education regarding HIV. A related issue is disclosure to a sexual partner or spouse. Partner-notification programs may help patients who want to tell their partners but do not feel comfortable doing so. Some patients may opt not to tell people with whom they live because they fear losing their home and family support. The reaction of a partner or other family member could be violent. At times, it may be possible to give alternative explanations for changed behavior, such as wanting to use condoms to avoid pregnancy. In societies where a man’s virility and a woman’s worth are measured by how many children they have, this may be more difficult.

Socioeconomic Effects of HIV/AIDS

HIV/AIDS affects the economic well-being of families, businesses, and societies in many ways. When people become ill and die, society loses not only those people but also their productive potential. They no longer hold jobs, manufacture goods, provide services, or
support their families. Families lose their breadwinners; the nation loses people who contribute to the well-being of society.\textsuperscript{12,13}

As families use their time and money to care for ill members, their energies are diverted from working to provide income or farming to provide food. Not only the present but also the future is affected, as family members discontinue education because of the financial needs of the family. Even burying the dead makes life more difficult for families and society. Funerals are costly, and people miss days from work to attend the rituals. The epidemic’s high death toll is producing cultural changes. In some communities with high rates of HIV, cemeteries have become overcrowded, creating pressure to adapt to practices not previously sanctioned by religious and cultural authorities, such as cremation. Funerals are a visible, potentially numbing reminder to all that a deadly disease threatens their survival.

HIV threatens workplace productivity due to deaths, absenteeism because of illness and funeral attendance, and lower productivity of sick or newly hired replacement workers. Other increased costs to the business sector include expenses for insurance and medical care for sick employees, which must be weighed against the cost of having to train new employees if more experienced employees become sick because of inadequate health care.

At the societal level, economic growth in many nations is lagging because so many skilled and experienced workers have died of AIDS.\textsuperscript{12,13} High unemployment and high rates of infection among skilled workers bode ill for countries’ ability to keep social supports intact. Studies of teachers and health care workers, for example, indicate that many in those professions have been infected with HIV. Society faces the challenges of having a great number of its productive members sick or dying, leaving few people to care for children and the elderly. In many countries, the number of people affected by HIV/AIDS is overburdening health-care and social-support resources.

The impact of HIV/AIDS on broader indicators of development, such as life expectancy, has been profound. In the 1950s, a child born in southern Africa had a life expectancy of 44 years. By the early 1990s, that had risen to almost 60 years. But life expectancy is expected to drop to 45 years between 2005 and 2010 because of the toll AIDS has taken.\textsuperscript{12,13} Poor households are being pushed deeper into poverty. The effects of the AIDS epidemic will be felt for generations, because so many children are being deprived of adequate nurturing, nutrition, education, and good role models.

In sub-Saharan African countries such as Malawi, Mozambique, Tanzania, Uganda, and Zambia, determinants of long-term growth show sharp declines as a result of the AIDS pandemic. In South Africa, the gross domestic product (GDP) is projected to decline by 17 percent between 2002 and 2010.\textsuperscript{14}

Frail economies, weak institutions, declining standards of living, and reduced social and governmental capacities indicate that the impact of HIV/AIDS on the future of African societies will be devastating. The decimation of countries’ most productive segment, with the resultant undermining of their tax base and their ability to finance such critical infrastructure as health and education, are certain to hamper sustained economic, cultural, and societal development.

The scale of the setback to human development by HIV/AIDS is confirmed by a United Nations Development Programme study carried out between 1980 and 1992. The average loss of human development progress due to AIDS was estimated at 10 years in Zambia, eight years in Tanzania, seven years in Rwanda, six years in the Central African Republic, and three to five years in Burundi, Kenya, Malawi, Uganda, and Zimbabwe.\textsuperscript{15} Since the severity of the AIDS epidemic in sub-Saharan Africa has increased significantly since 1992, subsequent losses in human development are likely even greater. Reduced productivity in important sectors of the economy feeds into economic instability, which in turn
can undermine a country’s political stability. Civil unrest and war create social dislocation, refugees, and rape, fueling a vicious cycle whose hallmark is an increased incidence of HIV/AIDS.

**Effects of HIV on the Societal Level**

HIV places enormous and varied stresses on the political, cultural, and religious fabric of society. Among issues that become critical are the availability of health care, social supports for orphans and caregivers, legal rights and responsibilities of people with HIV, and the response of religious and cultural systems to the needs of their members who are infected with or affected by HIV/AIDS. Political instability may be exacerbated by growing frustration with the government’s inability to stop or slow the epidemic or to respond effectively to the needs created by it. Increased poverty and social inequality may encourage conflict and crime. How these critical issues are resolved will determine society’s survival and viability.

The effects will be most obvious in the area of health care as the need for services increases. Providing treatment for HIV/AIDS and the illnesses that accompany the infection is expensive. Often governments must choose between providing treatment and funding prevention programs. The choices are not easy.

Education systems face shortages as teachers become ill and die. A rare public-sector assessment commissioned by the Government of the Kingdom of Swaziland estimated that the country would have to train 13,000 teachers between 2003 and 2011, compared to 5,093 if no AIDS epidemic existed. Schools also have to deal with significant numbers of infected and affected children with psychological, social, and economic problems caused by the epidemic. Enrollment rates in institutions of higher education may drop because fewer children live to adulthood.

**Societal Interventions**

Because of the complex effects of HIV/AIDS on the individual, the family, the community, and the society, interventions on many levels are needed to mitigate the impact of the epidemic. Some interventions are targeted at individuals with or at risk of HIV, while others are aimed at the larger community. Their objective is prevention of HIV and reduction of societal factors that increase the risk of infection. Protecting the human rights of vulnerable members of society, who are often hardest hit by any health problem, is another important step in mitigating the effects of HIV. Destigmatization of HIV and legal protection from discrimination and physical harm of people with HIV are important because of the broad effects that stigma and fear have on prevention and treatment efforts.

Role modeling is an effective way to encourage behavior change, as in the case of HIV testing in Siaya, Kenya. When three members of parliament took the lead by offering to be tested in public, a large number of people joined them. The three MPs later called on fellow legislators and civic leaders to follow suit and take the lead in motivating other districts to join in this voluntary counseling and testing initiative. Leading figures who discuss their HIV infection in public may also make a major contribution to reducing stigma.

Many projects try to help patients and families with basic needs and income generation. Reduction of poverty and improvement of the overall health of the population are important objectives in the fight against HIV/AIDS. Considerable work is being done at the local level by non-governmental organizations (NGOs) and community-based organizations (CBOs), often in conjunction with the government. Approaches range from institutionalized care to home-based care for terminally ill patients to training for lay counselors. To be successful, home-care interventions must be supported with structured programs from the health-
service delivery system. Poor families without such basic resources as clean water and adequate food are likely to need extra training and resources to care for a sick family member at home. Health care providers should assess each family’s needs for support when making a home-care plan. Many families may benefit from very simple support, such as a friendly visit, a referral for food assistance, latex gloves, or advice to improve caregiving skills. Families also need contact information, such as phone numbers or addresses, in the event of a problem or emergency.

On a larger scale, public and private-industry policies regarding HIV and HIV prevention should be evaluated on an ongoing basis to examine their effects on the lives and health of the population. Advocacy for policies ensuring confidentiality of HIV status, access to medical care, and protection from discrimination are likely to help more people with HIV meet their physical and social needs. Education and advocacy within religious and cultural groups, and support from these groups, help patients and families living with HIV. Governments and NGOs must devote resources to advocacy for increased attention to HIV prevention and the need for medications, medical care, and psychosocial and cultural support for individuals, families, and communities living with the virus.

**Prevention of Transmission**

People who find out they have HIV may feel powerless against the virus. But they are not powerless to prevent its spread. The pandemic’s growth depends on an infected person who transmits the infection and an uninfected person who receives it. To slow the epidemic, people who are infected must be educated to avoid transmitting it. Thus, on diagnosis and during subsequent visits, prevention information needs to be provided and reinforced. As part of this reinforcement, a health care provider might emphasize that despite their infection, patients still have some control over where the epidemic goes in their community and a responsibility not to become another link in the chain of transmission. This will need to be balanced against the stigma of being identified as being HIV-infected, e.g. through condom use.

**The ABC Prevention Approach**

Uganda has significantly reduced the transmission of HIV by using the ABC approach: **Abstinence, Be faithful, use Condoms.** This harm-reduction approach provides each person with several strategies for preventing HIV transmission to themselves and others.

Abstinence from intercourse is likely to be most useful with adolescents, who may be encouraged to delay intercourse, and in situations where families or partners are separated by work or travel.

Being faithful (staying with one sexual partner) will prevent HIV transmission if both partners have the same HIV status (both negative or both positive with the same strain of HIV), which can be known only through testing. If only one partner is faithful, the activities of the unfaithful partner may put the faithful one at risk. Where there is a high prevalence of HIV in the population, even one or two additional partners may make infection likely.

Using condoms consistently and properly prevents HIV transmission and significantly reduces transmission of other sexually transmitted infections (STIs) such as syphilis, gonorrhea, and chlamydia. Because having an STI greatly increases the risk of contracting HIV (via infected membranes and sores), both condom use and treatment of any STIs are important.

It must be emphasized that people must be given all relevant information and allowed to make their own choices as to which prevention method is most appropriate. What works for one person will not always work for another, and what works at one point in life may not work for the same person later on. Regardless of their own points of view, health workers are ethically bound not to withhold ANY information from patients that might prevent
transmission of HIV or other STIs. The benefits and drawbacks of each approach should be explained. We can give our patients the tools in the form of information, and it is up to them to use the most appropriate ones at the most appropriate times.

**Situational Approaches to Prevention**

Sometimes health care providers assume that patients have more individual power to practice prevention than they actually have. For example, someone may have the power to practice prevention in one situation but not in others. One useful approach is to ask patients to list the situations in which they can successfully use any of the ABC approaches and the situations in which they cannot. Issues of power and stigma will often be the determinants of prevention, with the weakest person in the situation having the least power. Ask patients to list “risk situations” rather than “risk behaviors.” Then ask how they might avoid getting into such a risk situation if at all possible, or how they might reduce the risk if the situation is unavoidable. Explore ways in which patients have some power in the situation to control or modify risk.17

**Knowledge, Attitudes, Beliefs, and HIV Prevention**

A common myth among many health professionals is that information about HIV/AIDS is an effective way to prevent HIV transmission. It is true that adequate information is a necessary condition to prevent transmission, but it is often not a sufficient condition. In other words, there needs to be basic information, but by itself information will not always overcome barriers to actually doing preventive activities. The best predictor of whether people will carry out preventive activities is their intention to do so.18 People will have good intentions if they see some value (for themselves, for their family, and for their community) in preventing the spread of HIV, either to themselves or from themselves.

Even with the best intentions, people may come up against barriers to prevention of HIV transmission. These barriers may be situational (low power in a situation, the influence of alcohol or other drugs, potential violence, no condoms, or a need for food, shelter, or money). They may also be emotional (when people are highly attracted to their partner, when they want children, when they are sexually aroused); often, despite what people know, their emotions override their intentions. It is useful to have people describe the situations in which emotions may override their knowledge and judgment, and to identify the “point of no return” beyond which unsafe sex is likely to occur. A helpful concept to introduce is “anticipated regret.” Here you can ask patients to describe how they would feel after putting themselves or others at risk, and how significant others in their family or community might feel about their actions. How might infected patients feel upon learning that they have infected their partner, when that partner gets a positive HIV test? Can they imagine explaining infection to their partner? Seeing risk situations by envisaging one’s regrets afterward can help to balance the emotional pressures at critical times.17

**Knowledge and Myths**

Increasing knowledge about HIV transmission and prevention (or treatment) cannot occur where the mythology about HIV/AIDS is actively contradictory. Myths will often constitute “folk epidemiology” – a description of beliefs and explanations about HIV. These will underlie all aspects of HIV/AIDS – the stigma, HIV transmission beliefs, HIV treatment beliefs, and the way people cope with HIV. Cultures will differ on these myths and beliefs, but it is critical that health workers be able to list the most prevalent myths. Attempting to deal with HIV/AIDS while ignoring the folk epidemiology will almost always be a failure. Health care personnel need to be able to credibly refute myths that are in direct contradiction to appropriate psychosocial approaches to HIV/AIDS, or that stigmatize such approaches, while reinforcing those that are supportive of optimal psychosocial care and prevention. Myths that have been reported include:

- That people who look healthy cannot have HIV
- That there are medical and/or folk cures for HIV
• That religious and cultural rituals can remove HIV/AIDS
• That being a member of certain religions protects against HIV/AIDS
• That HIV/AIDS is a punishment
• That intact condoms will allow transmission of HIV
• That HIV cannot be transmitted from females to males
• That having only one partner will prevent HIV (one partner may put someone at risk, depending on what that one partner has done)
• That HIV infection will not harm a person, and only AIDS is dangerous
• That having sex with a virgin will cure HIV/AIDS
• That HIV does not cause AIDS

All of these myths have the potential to hinder HIV prevention or treatment, and health care providers must be prepared to counter them effectively.

**Spirituality, Religion, and HIV/AIDS**

Existential issues, including spirituality and religious belief, may take on increasing importance to people who get a diagnosis of what is still, despite advances in treatment and health care, a frequently fatal disease. Unfortunately, despite the importance of the spiritual and religious dimensions of life, in some cases officials of some established religions seek to stigmatize, rather than help, people with HIV. This is despite the fact that without exception, the major religions of the world strongly emphasize the importance of caring for the sick and suffering and clearly recognize the obligation of their adherents to support personally and charitably those suffering from disease.

The health care worker also has a special obligation to help the sick live and die with respect and dignity. Whether the health care worker personally has a spiritual or religious belief or not, the patient has an absolute right to be cared for and respected. Stigma, which is a problem in the mind of judgmental others, not inherent in the disease, can be significantly lessened if the patient’s spiritual and religious beliefs are supported. This can be done by recognizing that the spiritual and religious needs of patients may be as important for their mental health and comfort as more widely recognized psychological and social supports. Particularly when medical interventions are of limited effectiveness, the health worker may sometimes, if requested by the patient, support or facilitate (but never impose) ways of meeting the patient’s religious or spiritual needs. Sometimes the consolations of

*Addressing spiritual and religious needs can be important for patients’ mental health.*
traditional spirituality or religion may make a significant difference to psychosocial adjustment and mental health. Such existential issues should not be overlooked in caring for the total needs of the person with HIV disease.

**Psychosocial Impacts of HIV/AIDS on Health Care Professionals**

Eventually, health care professionals who have lost many patients to HIV/AIDS begin to suffer because they have inadequate time to grieve or deal with their losses. Like their patients, they display many of the symptoms of the stages of grief (denial, anger, guilt, bargaining, depression, acceptance). However, as they experience loss after loss, the stages become intermingled. They haven’t worked through one loss before another occurs. Loss of multiple patients can lead to complicated and ongoing grief and can prevent the health care worker from processing the thoughts, feelings, and responses to patients in healthy and helpful ways. Over time, the unacknowledged sadness, anger, and guilt can become compressed and result in cynicism and decreased ability to invest emotionally in patients. It is painful to acknowledge the feelings associated with seeing patients suffer and die, so the professional becomes more hardened and expresses less sensitivity and sympathy for the needs of the next patient.

Symptoms of AIDS-related burnout may be physical (exhaustion, headaches, back pain, sleeplessness, malaise, and gastrointestinal disturbances) as well as behavioral (becoming easily irritated and angry, increased alcohol/drug use, marital/relationship problems, inflexibility in problem-solving, impulsivity and acting out, and withdrawal from non-colleagues). Cognitive and emotional symptoms may include emotional numbness or hypersensitivity, over-identification with patients, grief and sadness, pessimism and hopelessness, cynicism, indecision and inattention, and depression.

Environmental factors contribute to the stress of health care professionals who care for people with HIV/AIDS. Providers suffer stigma similar to that of their patients and are often unable to talk with family and friends about their work with patients suffering from an often unmentionable disease. In addition, HIV counselors must face their own fears about being HIV-infected as they encounter patients who may have risk behaviors similar to their own. In a study of HIV counselors in Zambia, 72 percent worried about their HIV status, but less than one-fourth had been tested for HIV. Half of the counselors said they did not want to be tested because they did not want to deal with the hopelessness of a positive result or they thought it pointless because there is no cure and only limited treatment. This would seem to have a detrimental effect on the ability to counsel effectively or encourage others to seek testing.

Health care providers working with HIV patients see many patients with complicated family situations and seemingly unlimited needs. Frequently, there are insufficient resources, such as medication and supplies, to meet the needs of such patients. A high caseload combined with inadequate staffing makes it difficult to provide sufficient counseling to the patient.

Caregivers are acutely aware of personal limitations and powerlessness to fix the patient’s situation. The provider should remember the power he or she does have – to provide the medical treatments that are necessary and available, to try to comfort patients when they are suffering, to provide hope and humor in a potentially devastating situation, and to be a positive influence in the lives of patients and caregivers.

Health care providers can help one another by creating a supportive environment in which they feel free to express their feelings. This reduces the isolation and emotional pain that can affect an individual’s ability to provide sensitive care. Formal support groups for health care providers can not only reduce feelings of isolation, but they can also lead to new ways to cope with the stress of work. In these settings, it is often more important to discuss how the person feels...
about and responds to difficult situations, and to
develop new ways to think about and respond to
them, than to discuss in detail the situation itself.
Informal discussions are also helpful because they
can occur directly after a stressful experience. The
goal should be for the person to express feelings, to
see things in a new light, and to develop new skills
and strategies for coping. Humor is also an effective
way of coping with stress.

The health care provider will need to evaluate the
effects of stress on his or her life on an ongoing basis.
Adequate rest, exercise, and nutrition are important
for the promotion of health for the caregiver as well
as the patient. Relaxation techniques such as
progressive relaxation and breathing exercises can
help the stressed professional to detach from stressful
situations to address them more effectively. At various
times, the health care provider may need to re-
examine the stressors and positive factors in his or her
life to find balance and positive physical and mental
health to continue the important work of caring for
patients with HIV/AIDS.

**Discrimination and Human-Rights Issues Among Health Workers**

Discrimination against people with HIV may occur
at all levels of the community, including to and from
health workers. Almost invariably, this is because of a
# Psychological Assessment

<table>
<thead>
<tr>
<th>Patient Information</th>
<th>Support System</th>
<th>Disclosure and Risk Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Counselor:</strong></td>
<td><strong>Education level:</strong></td>
<td><strong>Does the emergency contact know the patient’s HIV status?</strong></td>
</tr>
<tr>
<td><strong>Date:</strong></td>
<td><strong>Patient diagnosis date/year:</strong></td>
<td><strong>Patient’s primary language:</strong></td>
</tr>
<tr>
<td><strong>Referral source:</strong></td>
<td><strong>Understanding of HIV:</strong></td>
<td><strong>Patient lives with:</strong></td>
</tr>
<tr>
<td><strong>Name:</strong></td>
<td><strong>Patient’s support system:</strong></td>
<td><strong>Financial situation:</strong></td>
</tr>
<tr>
<td><strong>ID #:</strong></td>
<td><strong>Who is aware of the patient’s diagnosis?</strong></td>
<td><strong>Who else are important people in the patient’s support system?</strong></td>
</tr>
<tr>
<td><strong>Address:</strong></td>
<td><strong>Who else are important people in the patient’s support system?</strong></td>
<td><strong>Discussion of disclosure issues/partner notification:</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Spiritual beliefs/background:</strong></td>
<td><strong>Discussion of risk factors/risk reduction plan:</strong></td>
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<tr>
<td><strong>Phone number:</strong></td>
<td><strong>Patient employed?</strong></td>
<td><strong>Transportation:</strong></td>
</tr>
<tr>
<td><strong>Alternate phone number:</strong></td>
<td><strong>Housing situation:</strong></td>
<td></td>
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<tr>
<td><strong>Emergency contact:</strong></td>
<td><strong>Financial situation:</strong></td>
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<tr>
<td><strong>Phone #/Address:</strong></td>
<td><strong>Patient employed?</strong></td>
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**PSYCHOSOCIAL ASPECTS OF HIV/AIDS: ADULTS**

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325
Psychological Assessment - Continued

Current issues:
1. 

2. 

3. 

4. 

5. 

Assessment
Assessment of depression/suicidal thoughts: 

Patient’s beliefs that will influence reaction/treatment:

Positive coping skills:

Barriers to coping:

General assessment:

Acuity level: 

Acuity descriptions:
1. Minimal: information sharing, brief contact; agency referral; patient/family alert, cooperative, able to follow through; minimal barriers
2. Mild: Some assistance necessary for follow-through; limited psychosocial counseling; coping skills evident
3. Moderate: Counselor makes most contacts for follow-through; patient/family unable to complete tasks; limited coping skills; high stress level; limited family support; psychosocial dysfunction evident
4. Severe: Patient/family resistance hinders process; non-compliance; depressed, hostile, dysfunctional; extremely limited coping skills; extremely limited family support.
5. Counselor involvement beyond Level 4; multiple psychological problems; psychiatric referral; legal/abuse intervention; patient/family at risk to self or others.

Interventions/referrals:
1. 

2. 

3. 

4. 

5. 

Follow up with:
Date:
Additional comments:
## Review Questions

1. Find out which agencies provide services for patients with HIV in the area. Create a report on the resources available to patients with HIV, either in general or based on subcategories, such as in-home services, psychosocial services, services for orphans, etc.

2. Interview a counselor who works with HIV-infected patients.

3. If possible, sit in on an open group for people affected by HIV.

4. Write an essay regarding your own experience with people with HIV and how that has affected you.
References


Additional Resources for Reading and Research

Books

Web sites

Acknowledgment
This material is based on a chapter originally authored by Leslie Raneri, M.S.S.W., A.C.S.W.
HIV/AIDS AND PSYCHOSOCIAL INTERVENTIONS

Andrea K. Rigamonti, L.C.S.W.

Objectives

The purposes of this module are to:

1. Identify common themes in the lives of people infected with HIV.
2. Review characteristics of effective health care professionals.
3. Analyze elements of a therapeutic relationship.
4. Teach useful intervention skills.
5. Explain techniques used in solution-based therapy.
6. Address the benefits of disclosure to children.

Key Points

1. People infected and affected by HIV/AIDS often have complex psychosocial issues that benefit from psychosocial interventions.
2. All health care professionals need to be able to assess patients’ needs and provide basic psychosocial support. Patients needing additional support can be referred to trained mental health professionals.
3. Effective health care professionals demonstrate acceptance, empathy, unconditional positive regard, and respect for patients.
4. It is ultimately the genuine relationship between the professional and the patient that creates growth and positive change in the patient’s life.
5. Intervention skills are best developed through practice.
6. Health care professionals should offer to help patients disclose their HIV status to loved ones.
7. Children infected and affected by HIV/AIDS need developmentally appropriate psychosocial interventions to help them cope.

Overview

No one knew that Sheila had HIV except her husband and the health care professionals providing her care. She did not disclose her status to her family or friends for fear they would reject her. Sheila had a 10-year-old daughter, Jenny, who was infected perinatally.

Her son, Matthew, was 12 years old and HIV-negative. When Sheila’s husband died of AIDS, she turned to her health care professionals for support. She believed they would understand her feelings and keep her issues confidential.

HIV/AIDS is distinct from other chronic and potentially life-threatening illnesses because of the societal stigma associated with it. People with HIV often keep their illness a secret to protect themselves from stigma and discrimination. But trying to cope alone also keeps them from receiving significant social support from loved ones.

There are common themes and feelings that are expressed by people coping with HIV. They often experience tremendous feelings of distress, anxiety, and depression, especially after receiving a test result indicating they are HIV-positive. They may feel emotionally overwhelmed at times and emotionally numbed at other times. Hopelessness and uncertainty
about the future are other prominent themes for people with HIV. They may feel uncertainty about how to avoid infecting others, how to take care of their health, whether to continue in a job or relationship, and whether to disclose their status to others. A fundamental question for people with HIV, often not stated explicitly, is whether to prepare to die or continue directing their focus toward living.

People with chronic or life-threatening illnesses are also likely to experience multiple instances of loss and grief in their lives. In Sheila’s case, she was grieving the loss of her husband, her self-image as a healthy person, and the expectations she’d had for the future. Health care professionals who understand the grief process are more likely to help their patients cope with loss effectively.

Grief theorist Dr. Elisabeth Kubler-Ross described five stages of grief that patients experience after learning they have a life-threatening illness or have lost a loved one. The first stage is denial. After getting a positive test result, patients are likely to react with shock and disbelief. “No, not me” is their initial response. This is a healthy stage and is a means of initially protecting themselves. The next stage is anger or resentment. “Why me?” is the question asked now. Blame directed against others is often a part of this stage. Their outcry should be accepted as part of a natural step in the healing process. The third stage is bargaining: “Yes, me, but …” or “If you just give me five years, I will. …” Bargaining is a last effort at overcoming death by “earning” longer life. The fourth stage is depression. Now the person says, “Yes, me” with the courage to acknowledge that the loss is happening. Depression occurs after the full impact of imminent loss strikes. Eventually comes the stage of acceptance, when patients are realistic about their loss and prepare for it.³

Feelings of isolation are common when people with HIV have not disclosed their status to loved ones. Sheila felt distant from her friends and family, particularly her children. Lately Jenny and Matt had been asking questions that she avoided answering. They wanted to know what caused their father to die and why she and Jenny had to go to the doctor and take medicine. Keeping secrets from them was a tremendous burden for Sheila. Jenny had also become less willing to take her medications, saying she felt fine and did not need them. Sheila knew how important it was for Jenny to be adherent to her medications, and she wondered whether disclosing to her would be beneficial.

**Characteristics Developed by Effective Health Care Professionals**

Sheila wanted guidance from a professional and chose to speak to her doctor because he was attentive, had a real interest in helping her, and did not rush through her appointment. She was willing to bring her concerns to her doctor because she found him to be genuine, compassionate, sensitive, supportive, and encouraging. Effective health care professionals have developed personal qualities that enable them to connect with their patients, empathize with their feelings, and respond therapeutically. These characteristics include the following:

**Trustworthy** – “I have spread my dreams under your feet. Tread softly, because you tread on my dreams.”
– Author unknown

Unlike a friend or neighbor, health care professionals must keep sacred their patients’ confidentiality. They should explain to patients the legal guidelines regarding confidentiality and any circumstances under which it may need to be broken.

**Self-Aware** – Effective health care professionals are aware of their own attitudes, values, and beliefs. In addition, they show openness and respect for the values and beliefs of others.

**Accepting and Non-Judgmental** – “If you judge people, you have no time to love them.” – Mother Teresa
Effective professionals recognize the worth and dignity of all people and show unconditional positive regard for their patients.

**Ethical** – “A strong code of ethics is as reliable as a compass.” — Author unknown
Being ethical includes being honest with patients and making decisions in their best interest. Professionalism and ethical behavior helps patients feel safe and secure in your care.

**Empathetic** – Empathy is the capacity for understanding the feelings, thoughts, and experiences of another person without having them explicitly communicated.

**Knowledgeable** – Health care professionals need to be well-informed about HIV and able to communicate their knowledge to patients in terms they can understand.

**Culturally Competent** – Culturally competent health care professionals respect the culture and religion of patients and accept that their patients’ practices may differ from their own. Effective health care professionals are careful not to impose their personal values and beliefs on patients.

**Therapeutic Relationships**
It is ultimately the genuine relationship between the professional and the patient that creates positive change and growth in the patient’s life. A therapeutic relationship tends to develop through the following stages:

**Connecting**
One way to connect with patients is to greet them by name and take a few extra minutes to talk informally at the beginning of the appointment. This builds trust and rapport in the relationship. Lighthearted humor also encourages patients to relax and feel comfortable.

**Identifying Patient Concerns**
Next, the provider can ask about the patient’s concerns. Sheila’s doctor understood her main concern to be Jenny’s recent resistance to taking medications. He asked her to describe when the problem seemed to begin, what solutions had been tried, and what seemed to make the situation better. During this conversation, Sheila revealed that Jenny had persistently been asking her what the medications were for.

**Exploring Options**
Once patients’ needs and concerns have been identified, their options can be explored. Sheila and her doctor discussed the option of disclosing to Jenny and telling her the purpose of her medications. The doctor understood Sheila’s ambivalent feelings but expressed his confidence in her ability to talk to Jenny. He also offered to help her disclose to Jenny that she had HIV and to answer any questions Jenny had.

**Implementing Solutions**
Sheila felt empowered by her doctor and decided to disclose to Jenny with her doctor’s help at his office the following week. At the end of the appointment, the doctor validated her decision and summarized their plan to disclose to Jenny.

**Counseling Skills**
“People may not remember exactly what you did or what you said, but they will always remember how you made them feel.” — Author unknown
All health care professionals caring for people with HIV need to be able to assess patients’ needs and provide psychosocial support. Psychosocial support addresses the ongoing psychological and social problems of HIV-infected patients and their partners, families, and caregivers. With psychosocial support, people living with HIV are able to respond better to the stresses of being infected and are less likely to experience serious mental health problems. Psychosocial support also empowers patients to create positive changes, make informed decisions, find solutions to their problems, and improve their quality of life.
Patients who need additional support can be referred to trained mental health specialists for individual, group, or family counseling.

The ability to provide psychosocial support can be practiced and improved. The more a health professional practices counseling skills, the easier and more comfortable it becomes to use them. Counseling skills described here are active listening, asking effective questions, reflecting feelings, giving constructive feedback, validating, and empowering.

**Active Listening** – “The first duty of love is to listen.” – Theologian Paul Tillich

Effective health care professionals use both verbal and nonverbal communication to demonstrate that they are actively listening to their patients. They show attention by using eye contact, leaning forward, nodding, and encouraging patients to continue talking. A pleasant voice tone can also convey concern and warmth to patients. Providers should try to minimize distractions and interruptions and give their complete attention to patients. Psychosocial support is ideally provided in a place that is quiet and private, especially if sensitive information is being discussed.

**Asking Effective Questions** – Both open-ended and closed-ended questions can be effective when talking to patients, depending on the circumstances. Open-ended questions can be used to gather general information and to help patients clarify their thoughts and feelings. Examples of open-ended questions used by Sheila’s doctor are, “How do you feel about disclosing to Jenny next week?” and “What are your concerns about Jenny missing her medications?” Closed-ended questions are often used to obtain specific information, often with a yes-or-no answer. An example of a closed-ended question is, “Have you told anyone else that Jenny has HIV?”

**Reflecting Feelings** – Effective health care professionals listen for feelings that may not be explicitly expressed. Sheila was telling her doctor that she did not know how to disclose to Jenny and Matt. Her shoulders were tense, and her voice was trembling slightly. Even though Sheila did not explicitly say she was feeling nervous, her doctor recognized that she probably was. He normalized her feelings by saying that many caregivers feel apprehensive about disclosing to their children but tend to feel relieved afterward. It is helpful to let patients know that their reactions to the situations they are coping with are normal.

**Constructive Feedback** – Providing feedback in a constructive manner helps patients reflect on their words or actions. Feedback needs to be expressed in a way that is helpful and specific. Constructive-feedback statements can be made in the form of “I” statements. “I” statements describe a specific emotional reaction to a specific behavior for a specific reason. The format is, “I feel (specific feeling) when you (specific behavior) because (specific reason).” For example, the doctor could tell Sheila, “I feel concerned when you keep your concerns to yourself because no one is able to help you” or “When you take your medicine every day, I feel proud of you, because you’re keeping yourself healthy and strong.” Direct feedback should be gentle and appropriate to the level of involvement the health care professional has with the patient.

**Validating** – “Kind words can be short and easy to speak, but their echoes are truly endless.” – Mother Teresa

Remember to assess and express patients’ strengths. Sheila’s doctor validated how open she was in communicating her feelings and how apparent it was that she loved her children. He also validated her for keeping her viral load undetectable and choosing a healthy lifestyle. All patients have strengths that can be validated if the health care professional takes the time to discover them.

**Empowering** – “Psychotherapy is not about happiness; it is about power. I cannot guarantee you will leave happier; you will leave more competent.” – M. Scott Peck, M.D.

Many patients with HIV have goals they would like to fulfill, but they need more confidence to pursue...
them. Sheila had always dreamed of being a nurse, but she was not sure whether she could succeed in nursing school. Her doctor reminded her how motivated, bright, and compassionate she was. He helped her reframe her experience of having HIV into a positive one, saying she could use her experiences to help others with HIV. Her doctor’s belief in her abilities made the difference between her choosing to go to nursing school and giving in to feelings of helplessness and hopelessness.

**Using Solution-Focused Interventions**

“We are creatures of hope and invention, both of which belie the idea that things cannot be changed.”

– Novelist Tom Clancy

There are a variety of therapeutic models that health care professionals can use to help patients. One therapeutic model is solution-focused therapy. In solution-focused therapy, the professional’s role is to help patients use their inherent strengths, resources, and skills to find their own solutions to problems. The solution-focused professional emphasizes hope, encouragement, patient strengths, and possibilities. A central question that a solution-focused professional would ask a patient is: “What things are you currently doing in your life that you want to see continue?”

Techniques used in solution-focused therapy include the miracle question, identification of exceptions to the problem, and scaling questions. The miracle question is: “Suppose one night when you were asleep, there was a miracle, and this problem was solved. How would you know? What would be different?” This technique allows patients to speculate on what life might be like when the problem is solved.

The exception question encourages patients to remember times in the past when they did not have the problem. Instead of pronouncing the importance of an exception, it is important to be curious about it, ask how the person makes sense of it, wonder how the person was able to do it, and speculate about what kind of difference it might make in the future.

Scaling questions are useful for encouraging patients to move toward a goal. For example, a provider may ask a depressed patient, “On a scale of 1 to 10, with 1 being extremely depressed and 10 being very content, how are you feeling?” If the patient answers with the number 4, the provider can then ask, “What do you think you need to do to move from a 4 to a 5?” In this way, the provider and the patient can recognize and nurture small steps toward the patient’s goal. Once a small change is accomplished, patients can feel more confident about tackling new challenges and accomplishing additional goals.

Solution-based therapy also uses the power of suggestion. For example, the professional may ask the patient, “What do you think will happen to your health when you take your medicine every day?” The professional uses the word “when” instead of “if” to imply that the patient has the ability to make a positive change and achieve his or her goals.

Solution-focused therapy asserts that people want to change and improve their lives. In fact, it is believed that if patients ever demonstrate resistance, it is really their way of cooperating by teaching the professional the best way to help them. Therefore, patients are approached from a position of cooperation and collaboration, instead of from a belief that they may be resistant to treatment.

**Special Considerations for Children With HIV**

“Silence about a thing magnifies it. It grows and festers in silence, becoming malignant.” – Playwright Tennessee Williams

Caregivers and health care professionals often find it difficult to reveal a child’s HIV-positive status to the child. Caregivers with good intentions try to “protect” children from the truth about their illness. Sheila initially thought that telling Jenny she had HIV would
cause her to give up her will to live. Caregivers are also afraid that the children will tell others they have HIV and experience discrimination. In addition, caregivers often fear the hard questions they cannot face answering, such as how the child got the disease and whether he or she is going to die.

**Phases of Disclosure**

Social worker Mary Tasker has identified four phases of disclosure that caregivers pass through as they decide to tell a child that he or she is HIV-positive:

- **Secrecy Phase** – The caregiver vows not to disclose the status of the child to anyone and experiences feelings of isolation and loneliness.

- **Exploratory Phase** – The caregiver continues to maintain secrecy, but the secret is guarded with less intensity. The caregiver may feel ambivalent about keeping a secret from the child.

- **Readiness Phase** – The caregiver begins to activate plans to tell the child. The caregiver considers ways to disclose to the child and may tell other adults about the child’s status.

- **Disclosure Phase** – The caregiver tells the child that he or she has HIV. This can be done privately between caregiver and child. Optimally, caregivers can disclose alongside knowledgeable professionals.

**Benefits of Disclosure**

Many caregivers would like to know when they should disclose to children and what they should tell them. Disclosure is not a one-time event, but rather an ongoing process. As the child matures and asks more questions, developmentally appropriate information about HIV should be given.

One natural time to tell a child that he or she has HIV is at the time of diagnosis, when the caregivers are also finding out. Other natural opportunities arise when children ask questions about why they take medicine or go to the doctor more often than their friends do. Disclosure can also occur when medications need to change or the child has to be admitted to the hospital. It is critical at these times that adults tell the truth.

Young children often come up with explanations to bits and pieces of medical information they overhear from adults. The “explanations” they make up may be much more frightening than the truth. Disclosure gives children “permission” to talk openly about HIV, ask questions, and learn accurate information from adults. Disclosure also helps children face reality and start learning how to cope with HIV. Knowing their diagnosis may also motivate some children to take their medications more consistently. Once Jenny was told she had HIV, she said, “If I’d known all along what my medicines were for, I would have taken them.”

Oftentimes, children seem to accept disclosure better than caregivers expect. In fact, several preliminary disclosure studies reveal that children informed about their HIV diagnosis have higher self-esteem than infected children who are unaware of their status. Children will model their attitudes and feelings about HIV on the reactions and feelings expressed by their caregivers and clinicians.

Infected adolescents need to be disclosed to so they can make responsible and informed decisions about relationships and sexuality. They need comprehensive information about how HIV is transmitted, their treatment options, medication resistance, and prevention of mother-to-child transmission. Children and adolescents alike need additional comfort, assurance, and nurturance after disclosure.

**Psychosocial Interventions With Children**

“There stands no man as tall as he who kneels to help a child.” – Author unknown

Children’s thoughts, feelings, and behaviors are all affected by the grief they feel when they learn that they or a loved one has HIV/AIDS.
There are a variety of ways to help children infected or affected by HIV cope with their feelings:

- Give children the opportunity to talk openly about their feelings and experiences.
- Reassure children about their safety and security.
- Keep children's routines as normal as possible. This provides some comfort and stability in their lives.
- Let children keep pictures of their loved one or an object belonging to their loved one.
- Encourage children to write a letter to their loved one expressing their feelings.
- Allow children to participate in cultural or religious burial ceremonies.
- Help children identify supportive family members and friends.
- Refer children to a peer-support group or community program where they can feel a sense of belonging.
- Make periodic phone calls or home visits to check on children.
- Help children express themselves through various art forms, such as drawing, painting, music, dance, and writing in a journal.
- If needed, refer children for continuing psychosocial support with a trained mental health care professional.

**Conclusion**

“Love cures people—both the ones who give it and the ones who receive it.” – Dr. Karl Menninger

People infected and affected by HIV/AIDS need ongoing care and support. This includes providing patients with support and validation, mobilizing resources for coping, providing educational information, and helping them solve pressing situational demands. Psychosocial support may be most essential when patients are encountering a crisis in life, such as after being diagnosed with HIV or experiencing a significant loss.

There is no perfect way to provide psychosocial support, and there are many ways to provide it well. Trust in your inner wisdom to know how to best serve the needs of your patients. Lastly, remember that most of the time, patients already have the solutions to their problems. However, they need professionals who will listen to them, reaffirm their positive choices, and support them as they make their way through life.
Review Questions

1. Julie, who is HIV-positive, tells you she has met a new boyfriend and is having sex with him but has not yet told him her diagnosis. She says they use condoms most of the time. What would you say to Julie? What would you educate her about?

2. Diana was diagnosed with HIV during her pregnancy and has just delivered her baby. She lives with her husband and her in-laws. It is typical in her culture to breastfeed a baby. What are your beliefs about breastfeeding in general? What are your beliefs about women with HIV and breastfeeding? What would you educate Diana about?

3. John is an inquisitive and mature 9-year-old who was perinatally infected with HIV. The day before his doctor’s appointment, he asks his grandmother why he has to go to the doctor. His grandmother tells you that she would like you to disclose to John. Is John ready to be disclosed to? Why or why not? Who do you think should disclose to John? What would you tell John?

Exam Questions

1. Which of the following best describes solution-focused therapy?
   a. Telling patients what they must do to solve their problems
   b. Referring patients to specialists
   c. Empowering patients to use their strengths to find solutions
   d. Giving patients literature written by experts

2. Which statement is NOT true about disclosure to children?
   a. Most HIV-positive children are better off not knowing their status.
   b. Disclosure is optimally done together by caregivers and knowledgeable professionals.
   c. Information about HIV needs to be given over time in a developmentally appropriate manner.
   d. Adults should answer children’s questions about HIV honestly.

Answers: 1c, 2a
Counseling Skills Exercises

Reflecting Feelings:
Have participants reflect the underlying feeling of the patient using sentences beginning with “It sounds as if you’re feeling. …”

1. “My parents finally told me I had HIV. Whew, now we can all talk about it openly.”
   Example: It sounds as if you’re feeling relieved that you can talk to your parents about HIV now.
2. “No one knows I have HIV or understands what I am going through.”
3. “I do not know what will happen to my children if I get sicker.”

Use of Questions:
Have participants ask closed-ended and open-ended questions based on these patients’ statements.

1. “I need help telling my daughter she has HIV.”
   Open-ended example: How do you feel about telling her?
   Closed-ended example: When do you want to tell her?
2. “I forget to take my medications sometimes.”
3. “I am not feeling so good these days.”

Constructive Feedback:
Have participants give constructive feedback responses, based on this format: “I feel (specific feeling) when you (specific behavior) because (specific reason).”

1. A teenage female patient is having sex with a much older man who you know has had several other partners.
   Example: “I feel concerned when you have sex with older men because you are putting yourself at risk for HIV and other STDs.”
2. A patient returns for her second follow-up medical appointment, which is a surprise because she said she would not come back for care.
3. A patient says she needs to talk to her husband before being tested for HIV. She is seven months’ pregnant and has several risk factors for HIV.
References


Additional Resources for Reading and Research


The purposes of this module are to:

1. Describe the benefits of HIV-prevention counseling.
2. Describe specific skills that promote effective prevention counseling.
3. Discuss appropriate techniques for use during HIV-prevention counseling, health education, and supportive counseling.
4. Provide case studies to practice prevention-counseling skills.

HIV-prevention counseling plays a role in education about HIV transmission and risk-reduction behaviors.

Using a prevention-counseling assessment will help counselors and health care professionals promote optimal support and guidance of patients seeking HIV testing.

An organized approach to prevention counseling is essential to provide effective support to patients receiving HIV results.

HIV/AIDS is a uniquely stigmatized disease. Stigma affects every aspect of medical and social care for
people infected with HIV or at risk of infection. It is rare for the diagnosis of a disease to result in the possible loss of home, family, and religious or cultural supports, as well as the infected person’s feeling of connection with the community, but this is a real threat with a diagnosis of HIV/AIDS. Stigma may prevent people at risk of HIV infection from identifying their symptoms or risk factors at an early stage, because acknowledging personal risk of HIV forces them to face their own preconceptions about people with HIV and to associate those attitudes with themselves.1 Stigma may prevent people who have received positive test results from accepting them, seeking appropriate treatment, and implementing risk-reduction strategies to prevent transmission to others. One of the aims of HIV-prevention counseling is to reduce internalized stigma by providing information about HIV in a neutral, non-judgmental manner. Health care professionals should extend the reduction of stigma by treating people at risk of HIV infection with respect and compassion in all encounters.

HIV-prevention counseling helps patients and health care professionals identify risk factors and symptoms that may indicate HIV infection. It helps patients begin to anticipate a possible HIV-positive result and consider how they would respond to such a result. During the initial session, a patient can begin to think of a safe person he or she will tell about the HIV test. If the patient is able to talk with someone about being at risk of HIV infection, that patient will also be better prepared to talk to that person if the test is positive. If couples are tested at the same time, they avoid the potentially difficult situation in which only one partner is tested and then must reveal his or her diagnosis to the other. In addition, by involving a trusted person in the decision to test, the person being tested will have someone with whom to discuss the test results.

HIV-prevention counseling is an effective public-health intervention because it promotes the health of HIV-infected people and plays a role in reducing HIV transmission. Client-centered interventions, education regarding transmission factors, and risk-reduction techniques are the main focus of HIV-prevention counseling. A randomized trial conducted in Kenya, Tanzania, and Trinidad showed that people who received voluntary counseling and testing were significantly more likely to reduce unprotected intercourse with non-primary partners than those who received only health-education sessions.2 Couples in which one or both partners were HIV-infected showed a reduction in unprotected intercourse with their primary partner after counseling and testing. Analysis shows that voluntary counseling and testing for HIV can reduce HIV transmission and is cost-effective, especially among women presenting individually for testing and men and women presenting as a couple.3

Informed Decision-Making

Before being tested for HIV, the patient should make an informed decision to test. One of the factors that should be addressed is what legal and social consequences would result from a positive test result. Are test results reported to public health or government officials? If so, what are the consequences? Are significant others or relatives routinely notified of the results, along with the patient? It is important for health care professionals to understand the legal and procedural reporting policies in their institutions.

Patients may consider the advantages and disadvantages of testing and of knowing a positive result, but often they focus mainly on the disadvantages of testing. Health care professionals may be able to help their patients by making a chart of the advantages and disadvantages of testing and of knowing one’s HIV status, compared to the advantages and disadvantages of not knowing one’s HIV status. Advantages may include the ability to seek medical care to prevent complications of HIV/AIDS, to prevent transmission to others, and to make healthy lifestyle changes. There is also value in knowing the cause of symptoms one is experiencing. Disadvantages may include increased
fear of illness and death, fears related to family relations and parenting, guilt and anger about past decisions or relationships, and the stigma associated with HIV/AIDS. The patient should be informed as to whether testing is voluntary or involuntary, confidential (with a name) or anonymous (without name or identifier); whether he or she is able to refuse testing; and what consequences, if any, will result from refusing the test.

**Health Education**

Health education about the etiology and transmission of HIV is an important part of HIV-prevention counseling. Most patients associate HIV with death and know little about what HIV is or how it affects the body. Health care providers can help reduce stigma and fear by explaining that HIV is a virus that enters the body and causes the immune system, which fights infections, gradually to become less effective, which makes people with HIV more susceptible to infections than people without HIV. Health care providers can further explain that HIV is transmitted only in a few ways, namely through sexual contact, exchange of blood (e.g. through contaminated needles or cutting instruments), and from a mother to her child during pregnancy, childbirth, or breastfeeding. Knowing this will help an HIV-positive person think more clearly about HIV transmission, rather than associating transmission with having done something "bad." It may also alleviate the HIV-infected person's concerns about the possibility of transmitting the virus to others during daily activities. For example, a mother need not fear that by being around her children, she is putting them at risk of HIV infection.

**Group Health Education**

Some facilities use a group setting for teaching about general aspects of HIV testing, HIV risk factors, and risk reduction. In a study of individual versus group health education for pregnant women in Burkina Faso, group counseling was generally more effective in increasing knowledge about HIV infection. This may have been due to the interaction among patients and counselor as well as the possibility for patients to learn from answers to questions they may not have been willing to ask themselves. Patients in the groups were also given individual HIV-risk assessments. Group health education may be a time- and cost-effective tool for increasing HIV/AIDS knowledge and reducing high-risk behavior. In group-level interventions, confidentiality should always be emphasized and reiterated, especially if individuals reveal their HIV status.
Couple and Family Counseling

When it is culturally appropriate and legal, counseling a couple together so that they can decide together to be tested and to return for results is often an effective strategy. When only one partner is tested and is diagnosed with HIV, that person often experiences feelings of shame and fear about notifying the partner. Some women may want to involve their families in the decision to receive testing. One reason to encourage family involvement is to prevent potential problems with treatment adherence. If a woman is diagnosed with HIV/AIDS, she may not receive support from her partner. For example, he may not understand steps taken to prevent transmission, such as using infant formula. A male partner who is not involved in an initial decision to be tested may never be tested once the woman is diagnosed because he fears that he, too, is HIV-infected. Ideally, the spouse or partner should be included in initial HIV-prevention counseling discussions. The counselor will need to listen carefully to each person and help resolve conflict. Close attention must be paid to the cultural and family dynamics between the two partners, which will provide information about counseling techniques that may be helpful. For example, in some families, the counselor will need to show respect to the husband by speaking to him first or by not looking directly at him, which may be interpreted as a lack of respect. Considerations of culturally appropriate communication styles should not prevent the counselor from including the woman in the session. It may be difficult to obtain an accurate assessment of individual risks when the couple is counseled together, because either person may be reluctant to be honest about risk factors in the presence of the other. Additionally, gender roles should be considered when discussing sexual risk behaviors. Some patients may feel less or more comfortable discussing sensitive sexual and risk-reduction issues with counselors of the opposite sex.

Discussing Reasons to Test

For patients who are seeking HIV testing voluntarily, a discussion of the reasons for testing will focus primarily on risk factors. However, many patients may be identified for testing because of symptoms indicative of HIV or because they have sought medical care for a related medical need, such as pregnancy or a sexually transmitted infection (STI). In such cases, health care providers will need to discuss the connections between the reasons the patients are being seen for medical care and the reasons for and benefits of testing.

Sometimes a patient may identify as a perceived risk an activity or factor that is not associated with HIV infection. For example, the patient may be concerned about casual contact with a “risky” person, or the patient may fear that he or she is bewitched. The health care provider should respond respectfully to the patient’s beliefs and provide education about the known ways in which HIV is transmitted. At times, patients may not feel comfortable talking about particular risky behaviors in which they have participated. In such cases, patients should be supported in being tested. Some patients may display anxious behavior and seek repeated testing, despite repeated negative test results. These patients may need help in identifying their fears of infection, more in-depth discussion of risk reduction, and/or increased education about HIV transmission and testing.

Increasing the Odds That Patients Return for Results

Often individuals may come for testing but not return for results. It is important for health care providers to reinforce the importance of returning for results. Providers should aid patients in setting up a plan for the return visit and prepare them for the anxiety they may experience during the waiting period. Patients are often anxious and depressed in the time between being tested and receiving results, so strategies for reducing anxiety and stress are important. Counselors should help patients decide when they will return for results, whom they will tell about the test, and who may come with them when they return for results.
A study conducted in Ethiopia evaluated attendance for follow-up of HIV test results. Increased attendance of result counseling was related to greater knowledge and understanding of HIV infection and to the belief that good medical care will improve the course of HIV infection. Education about HIV and the positive effects of medical follow-up for HIV-infected patients should be discussed during initial HIV-prevention counseling, since this increases the likelihood that tested patients will return for results and follow-up counseling.

In a study of pregnant women, a positive test result was associated with failure to return for post-test counseling, suggesting that those who are most afraid of HIV-positive results may fail to return for them. Fear of violence from partners and feelings of lack of control over past and current risk factors also have been associated with failure to return for results. Likewise, feelings of fatalism may keep a patient from returning for results. Providing a sense of realistic hope is important. By using culturally appropriate counseling skills, counselors can help patients discuss the difficult subject of HIV testing and plan for the consequences of test results.

Discussing risk behaviors and fears is uncomfortable. Therefore the counselor will need to use good listening skills and supportive discussion to elicit the concerns surrounding the patient’s decision to be tested. Risk-reduction messages should be targeted to the patient’s particular risk factors and behavioral and psychosocial profile.

Follow-Up Counseling

Since the counselor will be the one providing the test results to the patient, it is important for the counselor to examine his or her own reactions to those results. The counselor should obtain the results and take time to review them alone or with a supervisor prior to delivering the results to the patient. If the counselor is shocked or distressed, that reaction will affect how he or she delivers the news of a positive or negative test. It is important to enter the counseling session focused on the patient’s needs and concerns. A quiet and confidential place to discuss results is essential. If possible, the same person who did the initial prevention counseling should provide follow-up counseling, because the patient has already developed a relationship with that counselor.

Assessment of Patient’s Knowledge About HIV Testing

Before giving test results, the counselor should assess the patient’s knowledge about the HIV testing he or she underwent. Most patients will have had initial prevention counseling and will know what HIV is and which risk factors place one at risk of HIV infection. However, some may have consented in haste or declined in-depth discussion of HIV and risk factors prior to testing. Other patients may have been tested without their knowledge because of insurance reasons, blood screening, a concern by the medical provider, or other reasons. Under most circumstances, it is considered unethical to test people without their knowledge, and doing so is illegal in some countries. Unfortunately, however, some people are tested without their knowledge or consent. Such patients may not be knowledgeable about HIV or prepared to
receive HIV results. They may be angry at having been tested or in shock because they are getting unsolicited test results. Counselors will need to use their listening skills and help patients express their emotions and thoughts about the testing process and results.

**Assessment of Patient’s Readiness to Receive Test Results**

Prior to giving test results, it is important for the counselor to assess the patient’s readiness to receive them. The counselor should go over what was discussed during the initial session of prevention counseling, including the meaning of a positive or negative test result and the patient’s understanding of the process and outcome of testing. The counselor should assess how the patient thinks he or she is likely to respond to a positive test result. Many patients may be anxious about receiving test results. If the patient is not ready to receive the test result, the counselor should help the patient reduce anxiety and consider delaying the giving of the test result until after a break or even until a follow-up appointment. However, the counselor will need to weigh the benefits of a delay against the risk that the patient may not return for the test result.

**Giving HIV Test Results**

If the patient is ready to receive the test result, the counselor should clearly and directly state the result using a neutral and calm tone of voice.

**Reactions of Patients to HIV Test Results**

People receiving a positive HIV test result have a variety of reactions, ranging from lack of emotion to profound and disruptive reactions resulting from anger and fear. The counselor must remain calm and comforting, even if he or she feels uncomfortable with the patient’s reactions. It may not be possible to provide the patient with HIV education about risk-reduction practices right after he or she has been diagnosed. A follow-up appointment may need to be scheduled to cover important topics and to offer ongoing supportive counseling. Some common issues that may need to be addressed are discussed in the module on psychosocial issues. The counselor should not set a separate time for discussion of these topics just because he or she wishes to avoid the intense emotions of the patient. Instead, the separate appointment should be set only if it will benefit the patient. Skillful counseling can provide support the patient needs. Listening skills, positive use of silence, and appropriate touch can help patients experiencing the immediate shock of an HIV-positive diagnosis.

Since denial is a prominent feature of patients’ response to a diagnosis of HIV infection, the patient should be shown a copy of the test result with his or her name on it. Many patients will want the test repeated, either at the same medical clinic or somewhere else. Patients with a positive test result should be provided with referrals to medical providers and social-support networks or counseling.

**Follow-Up**

During a follow-up counseling session, the counselor may focus primarily on crisis intervention and supportive listening. As in the initial prevention-counseling session, the counselor should reinforce the ways in which HIV is and is not transmitted and the benefits of medical follow-up for HIV-positive patients.

Regardless of their test results, patients should be provided with information on reducing their personal risk of HIV infection or HIV transmission to others. Prevention messages should be tailored to the person’s risk factors and willingness and ability to change risk behaviors or situations. Practical information and assistance should be provided, and motivational factors that might prevent the use of risk-reduction practices should be discussed.
# HIV Prevention Counseling Guidelines

## Before prevention counseling
- Obtain the patient’s identifying information as determined by the testing site.
- Take the patient to a quiet, designated counseling space to discuss testing and ensure confidentiality.

## Assess the patient’s risk factors and provide education
- Ask the patient’s reasons for seeking testing at this time or discuss the reasons the patient is being targeted to discuss HIV testing.
- Discuss confidentiality of testing.
- Ask if the patient has had a previous HIV test.
- Ask if the patient has had any signs or symptoms he or she fears are associated with HIV.
- Ask if the patient has ever had another sexually transmitted disease, and if so, ask when that was and what the circumstances were.
- Provide education about HIV risk factors and about risk reduction based on risk factors the patient has identified.

## Assess the patient’s coping and support
- With whom does the patient live? Who is a positive support in the patient’s life?
- What current life stressors is the patient experiencing?
- What other losses has the patient experienced, and how did he or she cope?
- Does the patient have a history of medical or psychiatric problems?
- Does the patient have a history of suicidal thoughts or attempts? Is the patient currently having thoughts about suicide? Has the patient attempted suicide?
- What experience has the patient had with people with HIV/AIDS?
- What individual strengths does the patient have that help him or her cope with difficulties?
- What are some family and cultural strengths that help the patient cope with difficulties?
- What social networks (church, community organizations, etc.) help the patient cope with difficulties?

## Anticipation of results
- Ask the patient what result he or she anticipates and why.
- Ask the patient what he or she will do if the result is different from the one he or she anticipates, either positive or negative.
- Ask the patient what relationships or situations may change if the test is positive.
- Ask the patient what relationships or situations may change if the test is negative.

## Discuss the benefits of testing
- The patient is able to seek medical intervention to prevent complications of opportunistic infections and to improve the course of the disease.
- The patient can reduce the risk of transmission to others, including children.
- The patient can make healthy lifestyle changes to improve his or her life.
- The patient can be proactive in seeking help for signs and symptoms.

## Discussion of HIV antibody tests
- HIV antibody tests look for antibodies to HIV, which in adults and in many children means that the person has HIV.
- There is a window period during which an HIV-positive person can test negative because he or she has not yet developed antibodies. This period is usually no more than three months.
- Antibody screening and confirmatory testing are both performed before positive diagnosis.

## Discuss medical-treatment options if test results are positive
- The patient may receive referrals to health care providers, referrals for support, and counseling and testing for other family members.
- Emphasize the positive effects of medical follow-up for HIV-positive patients.

## Ensure the person is making an informed decision to test
- Does the patient understand the documenting requirements of the site? Yes No
HIV-Prevention Counseling Guidelines Continued

1. Sexual risk factors
   Assess
   • Has the patient had sex?
   • Does the patient have a known infected sexual contact?
   • Has the patient had any other sexually transmitted diseases?
   • Does the patient have a history of non-consensual sex or sex for survival needs or drugs?

   Educate about the ABCs
   • Abstinence.
   • Be faithful.
   • Condom use – discuss techniques of proper use and negotiation of condom use.
   • Risk reduction – minimizing exchange of body fluids, using lubrication, and decreasing the number of partners.

2. Drug-use risk factors
   Assess
   • Does the patient have a history of drug use?
   • What types of drugs does he or she use? How often? By what method (inhalation, injection, ingestion, topical application)?

   Educate
   • Changing method of use, e.g. from injection to inhalation or ingestion.
   • Changing frequency of use, e.g. from daily to less frequently.
   • Acquiring clean needles or cleaning needles with bleach and water.
   • Drug treatment to stop using drugs.

   Emphasize the need for follow-up of results
   • Schedule a follow-up appointment for test results.
   • Discuss what the patient will do to reduce anxiety and stress while waiting for results.
   • Help the patient envision coming back for results.
   • Ask if anyone will come with the patient for results.
   • Discuss day, time, and place to return for results.
   • Emphasize the benefits of returning for results and the courage it took to come in for testing.

3. Medical/traditional practices with contaminated instruments or blood
   Assess
   • Has the patient ever had a blood transfusion?
   • Does the patient have a history of medical procedures with potentially contaminated instruments or needles?
   • Does the patient have a history of traditional practices with potentially contaminated razors or exchange of blood?

   Educate
   • Use personally owned razors. Clean razors.
   • Take universal precautions.

4. Mother/child transmission
   Assess
   • Does the child have an HIV-positive mother?
   • Does the child have a mother who died of unknown causes?
   • Is the woman pregnant or considering pregnancy?

   Educate
   • Educate mother about perinatal transmission and risk reduction for future pregnancies.
   • Educate mother about the risk of breastfeeding.
   • Educate HIV-positive woman considering pregnancy about the risk of transmitting HIV to her infant and about treatment to reduce that risk.

5. Other risk factors
   Assess
   • Does the patient identify other risk factors for HIV?

   Educate
   • Correct misconceptions about transmission.
**HIV Follow-Up Counseling Guidelines**

**Before prevention counseling**
- Obtain the patient's identifying information as determined by the testing site.
- Take the patient to a quiet, designated counseling space to discuss testing and ensure confidentiality.

**General guidelines**
- Make time to review all test results, either alone or with a supervisor, prior to delivering the results.
- Confirm the patient's identity with the information acquired during the initial session.
- Greet the patient and take him or her to the room in which the results will be discussed.
- Assess his or her emotional and physical state of anxiety.
- Ask if the patient has told anyone that he or she has been tested and is coming for results.
- Did the patient receive initial HIV-prevention counseling?
- Assess the patient's level of HIV knowledge and awareness that he or she was tested for HIV.
- Discuss with the patient whether he or she is ready to receive the HIV test result. If the patient is not ready to receive the result at this time, discuss strategies to reduce anxiety and schedule a follow-up appointment.
- If the patient is ready to receive them, give the test results directly.
- Observe and assess the patient's initial reactions to the test results.

**When the HIV test is negative**
- Clarify that the test did not detect HIV antibodies and that this means the patient either does not have HIV or has not yet developed HIV antibodies.
- Listen to the patient's thoughts and fears about the test results.
- Congratulate the patient on the test results.
- Discuss risk-reduction methods.
- Discuss the current risk situations of the patient and help develop strategies to prevent infection.

**When the HIV test is inconclusive**
- Clarify what the result means.
  - The test needs to be repeated.
  - It is not possible to assess a positive or negative result until the repeat testing is performed.
- Complete repeat testing.
- Reinforce risk-reduction behaviors or abstinence until the test results are back.
- Help the patient think of what he or she will do to reduce stress and anxiety.
- Help the patient think of personal coping strategies.
- Provide referrals for individual or group support.
- Reinforce the importance of returning for the test results.

**When the HIV test is positive**
- Clarify that the test detected HIV antibodies, and a confirmatory test was done. In an adult, a positive test that has been confirmed usually means that the person is HIV-infected.
- Acknowledge the patient's shock or other reactions.
- Listen to the patient's thoughts and fears about the test results.
- Avoid speculation on the patient's prognosis.
- Explain in lay terms what HIV is and how it affects the immune system.
- Review routes of transmission and how to prevent transmission to others.
- Discuss the importance of informing current and previous partners.
- Discuss fears about disclosing the diagnosis.
  - Who might be a safe and positive person to talk to?
  - Discuss the possibility of waiting to tell others if it's uncertain how they might respond.
  - Discuss safety concerns related to possible violent reactions or people who may not keep the diagnosis confidential.
- Listen to the patient.
  - Be willing to listen to feelings about HIV.
  - Ask about fears of illness and death.
  - Listen for expressions of guilt, rejection, fatalism, and spiritual beliefs.
HIV Follow-Up Counseling Guidelines Continued

- Help the patient recognize positive coping skills used in earlier times of crisis or in other areas of life.
- Anticipate previous negative coping responses or difficult social networks.
  - Encourage the patient to seek help if he or she becomes severely depressed or anxious.
  - Advise the patient to talk to someone if he or she has thoughts of suicide.
- Assess the patient for current thoughts of suicide.
- Prepare the patient to anticipate emotional ups and downs.
- Prepare the patient to interpret common symptoms of HIV. Not all symptoms or problems are related to being HIV-infected.
- Provide information on support networks and groups.

- Discuss the importance of receiving medical follow-up.
- Provide referrals for medical care and treatment.
- For women, discuss considerations regarding childbearing and contraception.
- Discuss healthy lifestyle adjustments the patient can make.
- Provide the patient with a sense of realistic hope.
  - There is currently no cure for HIV.
  - However, treatments are available that can prolong health and life.
  - Emphasize that the patient should continue to pursue goals, e.g. at work or school.
  - Encourage the patient to anticipate other goals he or she might want to accomplish.
  - Provide encouragement and appropriate follow-up. Schedule follow-up counseling.
### HIV-Prevention Counseling Assessment

<table>
<thead>
<tr>
<th>Patient's identifying information obtained?</th>
<th>Yes</th>
<th>No</th>
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<tr>
<th>Reasons for seeking testing:</th>
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<tr>
<th>Previous HIV test?</th>
<th>Date and result:</th>
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<table>
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<tr>
<th>Signs/symptoms of HIV:</th>
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<tr>
<th>Understanding of HIV risk factors: Discuss and mark patient’s risk factor(s)</th>
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</table>

#### Sexual risk factors
- [ ] Has had sex
- [ ] Known HIV-infected sexual contact: |

- [ ] Other STIs: |

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<tr>
<th>When:</th>
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- [ ] History of non-consensual sex or exchange of sex for survival needs/drugs?
- [ ] Use of condoms as preventative strategy?
  - [ ] Always
  - [ ] Sometimes
  - [ ] Never

#### Drug-use risk factors
- [ ] Type of drug, frequency, and method |

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- [ ] History of medical/traditional practices with contaminated instruments? |

- [ ] History of blood transfusion? When and where? |

#### Mother/child risk factors
- [ ] Child of a known HIV-positive mother? |

- [ ] Child of a mother who died of unknown causes? |

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<tr>
<th>Other risk factors identified by the client:</th>
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<tr>
<th>Assessment of coping and support</th>
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<tr>
<th>With whom does the patient live?</th>
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<tr>
<th>Current stressors:</th>
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<tr>
<th>Previous experiences of loss:</th>
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</table>

- [ ] History of mental illness
- [ ] History of suicidal thoughts or attempts
- [ ] Current suicidal thoughts or attempts
- [ ] Experiences with people with HIV/AIDS

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<tr>
<th>Individual strengths:</th>
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<th>Family strengths:</th>
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<tr>
<th>Social network strengths:</th>
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<tr>
<th>What result does patient anticipate?</th>
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<tr>
<th>What will the patient do if the test result is different?</th>
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<tr>
<th>What situations or relationships will change if result is positive?</th>
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</table>

<table>
<thead>
<tr>
<th>What situations or relationships will change if result is negative?</th>
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</table>

- [ ] Understanding of the benefits of returning for results
- [ ] Understanding that good medical care will improve the course of HIV infection

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<tr>
<th>Follow-up appointment date:</th>
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<table>
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<tr>
<th>Patient agrees to return</th>
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<tr>
<th>What will the patient do until he or she receives the result of the test?</th>
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<tr>
<th>Notes on session:</th>
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<tr>
<th>Signature:</th>
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## HIV Follow-Up Counseling Assessment

- **Patient's identifying information obtained?**
  - Did the patient tell anyone about the testing and about coming for results?  Yes  No
  - Did the patient receive initial HIV-prevention counseling?  Yes  No
  - Does the patient understand HIV risk factors and that he or she was tested for HIV?  Yes  No
  - Is the patient ready to receive the HIV test result?  Yes  No
  - If not, follow-up appointment date: ____________________

### Patient's test result

- **Negative test**
  - Patient understands test did not detect antibodies.
  - Current risk situations discussed: ____________________
  - Risk-reduction methods discussed: ____________________
  - Follow-up testing needed? Date: ____________________

- **Inconclusive test**
  - Patient understands test result was ambiguous and test must be repeated.
  - Current risk situations discussed: ____________________
  - Risk-reduction methods discussed: ____________________
  - Strategies for reducing anxiety reinforced.
  - Discussed importance of returning for result.
  - Follow-up testing done?  Yes  No
  - Follow-up appointment date: ____________________

- **Positive test**
  - Patient understands the test detected antibodies and a confirmatory test was done. This means the person is HIV-infected.
  - Patient understands what HIV is and what it does to the immune system.
  - Patient understands that medical follow-up can improve the course of HIV infection.
  - Partner notification discussed.
  - Disclosure-related concerns discussed.
  - Fears and concerns discussed.
  - Patient understands he or she will experience emotional ups and downs and may interpret symptoms as being HIV-related when that is not always the case.

### Additional notes

- Risk factors reviewed. Patient’s risk factors: ____________________
- Risk-reduction techniques discussed: ____________________
- Assessment of depression/suicidal thoughts: ____________________
- Patient’s support system: ____________________
- Patient’s beliefs that will influence reaction/treatment: ____________________
- Positive coping skills: ____________________
- Referrals to support groups/counseling: ____________________
- Referrals to medical providers: ____________________
- Reinforced hope and family relationships.
- Follow-up date set: ____________________

### Patient's reaction to results:

### Notes on session:

### Signature:

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HIV PREVENTION COUNSELING

Review Questions and Role Plays

1. Mary, who is 14, has told you that she has been having a sexual relationship with a 30-year-old man and has had other sexual relationships.
   - What would you be thinking and feeling about this situation? How might your thoughts and feelings potentially interfere with your ability to communicate with Mary?
   - What important information would you discuss with Mary about the risks of HIV and other sexually transmitted infections?
   - How would you bring up the need for HIV testing with Mary?
   - What information would you want to know about Mary’s home situation and relationship with her sexual partners to help you provide prevention counseling and support to her?
   - What referrals might you want to make?
   - What risk-reduction strategies would you discuss with Mary?

Mary agrees to be tested for HIV but does not want to discuss this with her mother.
   - What information would you want to know about Mary’s relationship with her mother?
   - How might you talk to Mary about thinking of someone else whom she could tell about being tested for HIV?
   - How would you help her make that decision?

Mary’s test comes back inconclusive.
   - What information would you present to her, and how?
   - What would you tell her to do while awaiting a repeat test?

Upon repeat testing, Mary’s test is positive for HIV. She misses her first scheduled appointment for the test result.
   - What would you be thinking and feeling in this situation?
   - How would you go about contacting her to bring her back to the clinic to discuss the test result?

Mary comes back in for her HIV result. She is visibly anxious.
   - How would you connect with Mary during this return appointment?
   - What would you want to know about what Mary recalls from the initial prevention counseling session and about her thoughts and experiences since she first came for testing?
   - What would you want to review with Mary prior to giving her the test result?

Mary says she’s not sure if she wants to know her result.
   - What would you discuss with her about her feelings about receiving the test result and the pros and cons of knowing the result of the test?
   - Do you feel patients have a right not to know their test results?

Mary says she is ready to learn her test result. When you tell her, she begins to cry. She says she has a close friend who recently died of AIDS.
   - How might you provide support to Mary?
   - What would be the most important information to convey to Mary at this time?
   - What strengths would you try to build in Mary at this time?
   - What referrals might you make?
   - How would you ensure follow-up for Mary?

2. The Dlaminis have been married for five years. Last month, after their 8-month-old child died of severe pneumonia, a physician recommended that the Dlaminis both be tested for HIV. They agreed to be tested and now have returned for their results. You
have the results, which show that one of the Dlaminis is positive and the other is negative.

• Would you tell the couple their results together? Why or why not?
• If the woman is positive, does that change how you would handle the situation? What if it is the husband?
• What issues would you discuss with the person whose test is negative? What recommendations might you make? Would this be different if the couple were not married? Would it be different if you did not know the partner’s status?
• How would you tell the person who is positive? What would you counsel that person about the partner? Would your counsel be different if the positive partner is male or female? Why or why not?

References