

Module B2

Special Issues: TB, Women, Children and Post-Exposure Prophylaxis

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Session 1: Management of Tuberculosis and Other HIV-related Infections and Conditions in Relation to ARV Therapy

In this session, participants learn about the management of tuberculosis and other HIV-related infections and conditions, such as opportunistic infections, hepatitis and the immune reconstitution syndrome, in relation to ARV therapy.

Session 2: ARV Therapy in Women and Pregnancy

Participants learn about the choice of ARV drugs in women of childbearing age and ARV therapy during pregnancy. The session also addresses how to manage drugs in preventing mother-to-child transmission (PMTCT) and the use and limitations of ARV therapy as a preventive measure.

Session 3: ARV Therapy in Infants and Children

Participants learn about the natural course of HIV disease in children, how it differs from adults, how to make a diagnosis, the WHO clinical classification system for diagnosis and classification, and ART therapy for children.

Session 4: Post-Exposure Prophylaxis (PEP)

Participants learn about occupational exposure to HIV, how to manage it, HIV post-exposure prophylaxis (PEP) and drug selection for PEP.

SESSION 1 Management of Tuberculosis and other HIV-Related Infections and Conditions in Relation to ART

PURPOSE

In this session, participants will learn about the management of tuberculosis and other HIV-related infections and conditions, such as opportunistic infections, hepatitis, and the immune reconstitution syndrome, in relation to ARV therapy.

OBJECTIVES:

By the end of this session, participants will be able to:

1. Describe the relationship between TB and HIV coinfection.
2. Discuss how to manage and treat people with TB and HIV coinfection in their local situation, and discuss national guidelines for the treatment and management of TB and HIV coinfection.
3. Describe the problems and management of ARVs in patients with other HIV-related infections and conditions, such as OIs and hepatitis.
4. Describe the immune reconstitution syndrome and how to manage it.

TIME:

40-60 minutes

PREPARATION:

Develop a case study for this session based on your own experience in managing patients on ARV therapy, with TB and HIV coinfection or other HIV-related infections.

Step 1.	Explain the purpose and objectives of the session (see above). (1-2 minutes)
Step 2.	Present the information on TB and coinfection: 1 below, and ask participants if they have any questions or issues about the treatment protocols. (10 minutes)
Step 3.	Ask participants if there are any adherence issues in their local situation and how can these be managed. Discuss the section of the national TB control guidelines that addresses compliance with TB treatment. (10 minutes) Total time: 22 minutes

1. People with TB and HIV coinfection

- a. WHO recommends that people with both TB and HIV complete their TB therapy before beginning ARV treatment, unless there is high risk of HIV disease progression and death during the period of TB treatment (that is, a CD4 count $<200/\text{mm}^3$ or the presence of disseminated TB).
- b. In cases where a person needs concurrent TB and HIV treatment, first-line treatment options include ZDV/3TC or d4T/3TC, plus either an NNRTI or ABC.
 - If an NNRTI-based regimen is used, EFZ would be the preferred drug since its potential to aggravate hepatotoxicity of TB treatment appears less than with NVP. However, you need to increase the dosage to 800mg/day.
 - Except for SQV/r, PIs are not recommended during TB treatment with rifampicin because of its interactions with the latter drug.

Table B2, 1.1: Antiretroviral Therapy for Individuals with Tuberculosis Coinfection

CD4 cell count	Recommended regimen	Comments
CD4 $< 200 \text{ mm}^3$	Start TB treatment. Start ART as soon as TB treatment is tolerated (between 2 weeks and 2 months). ^a EFV-containing regimens. ^{b, c, d}	Recommend ART. EFV is contraindicated in pregnant women or women of childbearing potential without effective contraception.
CD4 200-350/ mm^3	Start TB treatment. Start one of regimens below after the initiation phase (start earlier if severely compromised). EFV- containing regimens ^b or NVP-containing regimens in case of rifampicin-free continuation phase TB treatment regimen	Consider ART.
CD4 $< 350/\text{mm}^3$	Start TB treatment.	Defer ART. ^e
CD4 not available	Start TB treatment.	Consider ART. ^{a, f}

a Timing of ART initiation should be based on clinical judgment in relation to other signs of immunodeficiency. For extrapulmonary TB, ART should be started as soon as TB treatment is tolerated, irrespective of CD4 cell count.

b Alternatives to the EFV portion of the regimen include: SQV/RTV (400/400 mg bid) SQV/r (1600/200 mg qd in sgc), LPV/RTV (400/400 mg bid) and ABC.

c NVP (200 mg qd for two weeks followed by 200 mg bid) may be used in place of EFV in absence of other options. NPV-containing regimens include: d4T/3TC/NVP or ZDV/3TC/NVP.

d EFV- containing regimens include d4T/3TC/EFV or ZDV/3TC/EFV.

e Unless non-TB Stage IV conditions are present (Table A). Otherwise start ART upon completion of TB treatment.

f If no other signs of immunodeficiency are present and patient is improving on TB treatment, ART should be started upon completion of TB treatment.

Step 4. Present the information below: 2-4. Ask participants if they have any questions or concerns about these issues.
(15 minutes)

2. Other opportunistic infections and hepatitis

- a. Patients who develop other OIs should be treated with ARVs.
- b. In contrast to the situation with TB, drug interactions with standard ARV regimens do not pose a significant problem.
- c. Consider prompt initiation of ART when OIs occur for which treatment is not available or for which it is sub-optimal because improvement of the immune system may enhance recovery.
- d. Patients coinfecting with hepatitis B or C can be treated safely with several ARV regimens.
 - Avoid regimens with ddI/d4T in patients known to have active hepatitis because of the possibility of additive hepatotoxicity.
 - 3TC and TDF (see comment below) are both active against hepatitis B and may even protect against new infections. Patients receiving 3TC or TDF who are known to have hepatitis B and experience ARV regimen failure may wish to continue these medications when the ARV regimen is switched.

Comment: Tenofovir (TDF), a relatively new NRTI (approved for use in the U.S. by the FDA in October 2001), is active against most NRTI resistant strains.

3. Immune reconstitution syndrome

- a. Mechanism: For many OIs, including TB, there can be a transient worsening of infection 2-3 weeks after initiating ART. This is called the *immune reconstitution syndrome*. Initiation of ART can unmask previously undiagnosed infections by augmenting the inflammatory response.
- b. Clinical presentation: Fevers, lymphadenopathy, worsening pulmonary lesions and expanding lesions of the central nervous system
- c. Management: Reactions are self-limiting, although the patient may require a brief course of corticosteroids to reduce inflammation of CNS or severe respiratory symptoms

Do not interrupt ART if immune reconstitution syndrome occurs.

4. ART and antimicrobial prophylaxis

ART is the most effective approach to reducing incidence of OIs, but you should complement it with antimicrobial prophylaxis.

On the basis of observations made in developing countries, patients responding to ART with sustained elevation in CD4 cell counts above 200 cells/mm for 3-6 months may be able to discontinue prophylaxis for some OIs.

Step 5. If you have prepared a case study, present it to the whole group and discuss their answers.
(15 minutes)

SESSION 2 ART in Women, During Pregnancy, and for Preventing Mother-to-Child Transmission**PURPOSE**

In this session, participants will learn about the choice of ARV drugs in women of childbearing age and ARV therapy during pregnancy. The session also addresses how to manage drugs in preventing mother-to-child transmission (PMTCT) and the use and limitations of ARV therapy as a preventive measure.

OBJECTIVES:

By the end of this session, participants will be able to:

1. Discuss specific considerations affecting the use of ARVs in women.
2. Describe how ART is used for PMTCT.
3. Describe the various regimens used during pregnancy, intrapartum and postpartum, including short course ART.
4. Discuss the relationship between ART and breast feeding, and WHO recommendations.
5. Discuss national guidelines for HIV and infant feeding as they relate to ARV therapy.

TIME:

60-90 minutes

- | | |
|---------|--|
| Step 1. | Explain the purpose and objectives of the session (see above).
(2 minutes) |
| Step 2. | Present choice of ARV drugs in nonpregnant women, and ARV therapy and MTCT: 1-2 below.
(10 minutes) |

- a. Choice of ARV drugs in nonpregnant women of childbearing age
- b. Women who are receiving ART should have access to effective contraceptive methods to reduce the likelihood of unintended pregnancy.
- c. Avoid drugs with potential toxicity to the developing fetus, such as EFZ, in women who may become pregnant.
- d. ARV therapy and MTCT

Preventing prenatal transmission

 - You can achieve significant reduction of MTCT by using ARV therapy.

Studies conducted in 1994 in industrialized countries showed that administering AZT to women from the 14th week of pregnancy, and to the newborn during labor, decreased the risk of MTCT by nearly 70 percent in the absence of breast feeding.

A shorter AZT alone regimen, starting from the 36th week of pregnancy, was shown to reduce the risk of transmission of HIV at six months by 50 percent in a nonbreast feeding population and by 37 percent in those breast feeding.

A short course of NVP (HVNET 012) has been shown to reduce the risk of transmission; it is the most commonly used protocol because of its demonstrated efficacy in clinical trials in reducing MTCT by 47 percent, its low cost and its ease of use in MTCT programs. The regimen is:

Intrapartum short course: 200 mg at start of labor or at hospital intrapartum

Postpartum mother who did not receive intrapartum dose: 200 mg stat

Postpartum infant: 2mg/kg syrup within 48-72 hours

Other trials of short course ARV regimens using a combination of AZT and lamivudine also substantially decrease the risk of transmission (PETRA).
 - Women on treatment with ARVs for HIV infection have very low transmission if viral load is <1000 copies/ml.
- e. Women first diagnosed with HIV infection during pregnancy
 - Women in the first trimester may consider delaying initiation of ART.
 - Consider severity of maternal HIV disease and potential benefits and risks of delaying ART until after the first trimester
 - For women who are severely ill, the benefit of early initiation may outweigh the theoretical risk to the fetus; in these cases, we recommend initiating with drugs such as AZT, 3TC, NVP or NFV.
- f. HIV-infected women on ART who become pregnant
 - Options are:
 - Suspend therapy temporarily during first trimester
 - Continue same therapy
 - Change to a different regimen
 - Issues to consider:
 - Gestation of the pregnancy
 - Severity of maternal disease
 - Tolerance of regimen in pregnancy
 - Potential for adverse fetal effects

The fetus is most susceptible to potential teratogenic effects of drugs during the first 10 weeks of gestation, and the risks of ART to the fetus during this period are unknown.

g. ART and breast feeding

- Current WHO/UNAIDS/UNICEF guidelines recommend that you fully inform women with HIV infection about both the risks and benefits of breast feeding and support them in their decision about feeding practices.
- Safe alternatives may not be available in some resource-limited settings (for example, an unsafe or inadequate water supply may be the only source available for mixing formulas), in which case, exclusive breast feeding for the first six months of life is recommended.
- Women who require ART and are breast feeding should continue their ART regimen.
- The efficacy of potent ART for mothers used solely to prevent postnatal transmission of HIV through breast milk is unknown, but studies are under way.

h. Approaches to HIV-infected women who received short-course ARV prophylaxis to reduce MTCT and require treatment postpartum:

- Short-course ARV regimens do not fully suppress viral replication and may be associated with development of ARV drug resistance.
The Ugandan HIVNET 012 study of single dose intrapartum/newborn NVP for prevention of MTCT found that 19 percent of the women developed resistance to the drug. This was associated with delivery, HIV viral load and CD4 cell count.
- Based on current information and pending further research, prior administration of short-course AZT/3TC or single dose NVP for preventing MTCT should not preclude using these agents as part of a combination ARV drug regimen initiated for treating these women.

i. Adherence to therapy in pregnancy and postpartum

- Adherence may be more difficult in pregnant and postpartum women than in nonpregnant women.
- Obstacles to adherence may include:
 - Morning sickness and GI upset, which can be compounded by ARV-associated nausea
 - Fears that ARV drugs might harm the fetus
- To reduce the potential for resistance to emerge, if for any reason, you need to discontinue therapy during pregnancy, stop and restart all drugs together.
- Physical changes of the postpartum period, coupled with the stresses and demands of caring for a newborn infant, may make adherence to treatment especially difficult after birth.
You need to provide additional support for maintaining adherence to therapy during the ante- and postpartum periods.

- Step 3. Ask participants to break into small groups and discuss the following questions. Give them 10 minutes for the task.
- a. What are the country-specific obstacles to providing ARV therapy to women of childbearing age? Pregnant women?
 - b. What are some country-specific issues around MTCT?
 - c. What are the solutions to these problems?
- (10 minutes)
- Step 4. Ask the groups to reconvene and report on their discussion.
- (15 minutes)
- Step 5. Discuss national guidelines on using ARV therapy in women of childbearing age, during pregnancy and MTCT. (10 minutes)
- Step 6. Ask participants to break into small groups and discuss the following case study using the questions as a guide. You may also choose to do this exercise with the whole group, depending on how many participants you have.
- Bring the larger group back together and discuss their answers. See answers to questions below.
- (Total time: 30 minutes)

CASE STUDY

A young woman has been newly diagnosed with both HIV and TB (identified in the antenatal clinic). She is 14 weeks pregnant. Her lab results show a CD4 count of 150 and a VL of 62,000.

- 1) *What antiretroviral therapy (if any) would you prescribe?*
- 2) *What TB therapy (if any) would you prescribe?*
- 3) *What would you do if this pregnant woman has a CD4 count of 5?*

Give your reasons.

Answers

Examining interaction between TB, ARVs and pregnancy.

1. Examine possible regimen for teratogenicity and significant drug interaction.
2. This is a difficult question. If you have to use ARVs with TB treatment in pregnancy, use nevirapine or ritonavir boosted saquinavir with ZDV and 3TC .

SESSION 3 ART in Infants and Children

PURPOSE

In this session, participants will learn about the natural course of HIV disease in children, how it differs from adults, how to make a diagnosis, the WHO clinical classification system for diagnosis and classification and ART therapy for children.

OBJECTIVES:

By the end of this session, participants will be able to:

1. Describe the natural course of HIV disease in children.
2. Discuss the WHO clinical classification system and how to make a diagnosis of HIV in children.
3. Describe when and how to provide ART.
4. Discuss national guidelines for ARV therapy in children.

TIME:

1 hour and 15 minutes

Note: If participants are mostly pediatricians, you may need to go into greater depth about the challenges of adherence in children and available drug formulations.

- Step 1. Explain the purpose and objectives of the session (see above).
(2 minutes)
- Step 2. Explain the natural course of HIV disease in children and how to make a diagnosis: 1 and 2 below.
(10 minutes)

1. The natural course of HIV disease in children

- HIV RNA levels in perinatally-infected infants are generally low at birth (<10,000 copies/ml), increase to high values by age two months and then decrease slowly after the first two years.
- CD4 cell count and percentage values in healthy infants who are not infected are considerably higher than those observed in uninfected adults and decline slowly to adult values by the age of six years.
- Although the CD4 absolute number that identifies a specific level of immune suppression changes with age, the CD4 percentage that defines each immunologic category does not. Thus, a change in CD4 *percentage*, not the *number*, may be a better marker for identifying disease progression in children.
- CD4 cell values can be associated with considerable variation because of minor infections and are therefore best measured when patients are clinically stable.

Table B2, 3.1: HIV Pediatric Classification System Immune Categories Based on Age-Specific CD/Cell Count and Percentage

Immune category	Child's Age					
	<12 months		1-5 years		6-12 years	
	No./ml	percent	No./ml	percent	No./ml	percent
Category 1: No suppression	>1,500	>25 percent	>1,000	>25 percent	>500	>25 percent
Category 2: Moderate suppression	750-1,499	15-24 percent	500-999	15-24 percent	200-499	15-24 percent
Category 3: Severe suppression	<750	<15 percent	<500	<15 percent	<200	<15 percent

Source: CDC 1994

- e. A small proportion of children who are infected early in pregnancy will progress to advanced HIV disease more rapidly because of a disruption of the thymus, where CD4 and CD8 cells are produced. These children have low CD4 and CD8 cell counts; their immune system cannot respond to HIV infection. Thus, infants under six months who present with symptoms of HIV disease usually have a shorter survival period than older children.

2. Diagnosis of HIV disease

- a. Most infants are diagnosed on the basis of symptoms and a positive test of the mother or child.
- Passively transferred maternal HIV antibody may persist for up to 18 months.
 - To establish a definitive serologic diagnosis, repeat the test at 18 months.
 - You can use viral diagnostic assays—PCR—to detect HIV in children younger than 18 months, but because of their complexity and cost, these tests are not readily available everywhere.
- b. Pattern of disease and management often differs for children of various age groups
- Some HIV-related conditions are less frequent in children; for example, TB, cryptococcal meningitis, Kaposi's sarcoma
 - Other conditions, such as lymphocytic interstitial pneumonitis (LIP), are usually found only in children or will express themselves differently, as, for example, the condition of HIV encephalopathy
 - You need to adapt drug dosages to the child's weight or surface area (in the case of ARVs)
 - Management of some diseases, such as oral and skin manifestations, is similar for children and adults.
- c. WHO systems for diagnosis and classification
- WHO staging system for HIV infection and disease in children

Clinical Stage I

1. Asymptomatic
2. Generalized lymphadenopathy

Clinical Stage II

3. Unexplained chronic diarrhea
4. Severe persistent or recurrent lymphadenopathy
5. Weight loss or failure to thrive
6. Persistent fever
7. Recurrent severe bacterial infections

Clinical Stage III

8. AIDS-defining opportunistic infections
 9. Severe failure to thrive
 10. Progressive encephalopathy
 11. Malignancy
 12. Recurrent septicemia or meningitis
- You should suspect children presenting with any three of the following signs or conditions of having HIV infection:
 - Two or more chest infections requiring antibiotics (pneumonia) in the past two months
 - One or more episode of persistent diarrhea OR two or more episodes of acute diarrhea in the past two months
 - A parent with tuberculosis
 - Oral candidiasis (thrush)

- Enlarged lymph nodes in two or more sites
- Growth faltering (weight curve flat or falling for two consecutive months)
- Weight-for-age below the third percentile (using international growth reference standards)

CDC classification system for HIV infection in children less than 13 years of age

CDC definition of HIV infection in children: 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 and who is HIV positive by ELISA and a confirmatory test

Step 3. Describe the WHO guidelines for initiating ART in children. Review the WHO recommended first-line and second-line regimens, as well as information on formulations and storage: **3. a-f** below.
(10 minutes)

3. ART therapy for children

a. WHO recommendations for initiating ART in children

Table B2, 3.2: WHO Recommendations for Initiating ART in Children

CD4 Testing	Age	HIV Diagnostic Testing	Recommendations for Initiating Treatment
If CD 4 testing is available	<18 months	Positive HIV virologic test ¹	<ul style="list-style-type: none"> • WHO Pediatric Stage III (AIDS irrespective of CD4 cell percentages²) • WHO Pediatric Stage I disease (asymptomatic) or Stage II disease with CD4 percentage <20 percent
		HIV virologic testing not available, but infant is HIV seropositive or born to HIV-infected mother <i>Note: You must repeat HIV antibody test at age 18 months to obtain definitive diagnosis of HIV infection.</i>	<ul style="list-style-type: none"> • WHO Pediatric Stage III disease (AIDS) with CD4 cell percentage <20 percent
	≥18 months	HIV antibody seropositive	<ul style="list-style-type: none"> • WHO Pediatric Stage III disease (AIDS) irrespective of CD4 cell percentage² • WHO Pediatric Stage I disease (asymptomatic) or Stage II disease with CD4 percentage <15 percent³
If CD 4 testing is not available	<18 months	Positive HIV virologic test	•WHO Pediatric Stage III ²
		HIV virologic test not available, but infant is HIV seropositive or born to known HIV-infected mother	•Treatment not recommended ⁴
	≥18 months	HIV antibody seropositive	• WHO Pediatric Stage III ²

1 HIV DNA PCR or HIV RNA or immune complex p24 antigen assays

2 You can also consider initiation of ARV for children who have advanced WHO Pediatric Stage II disease, including severe recurrent or persistent oral candidiasis outside the neonatal period, weight loss, fevers or recurrent severe bacterial infections irrespective of CD4 count.

3 Factor the rate of decline in CD4 percentage (if measurement available) into the decision making.

4 Many of the clinical symptoms in the WHO Pediatric Stage II and III disease classification are not specific for HIV infection and significantly overlap those seen in children without HIV infection in resource-limited settings. Generally, in the absence of virologic testing and CD4 cell assay availability, do not consider HIV-exposed infants <18 months of age for ART, regardless of symptoms.

b. WHO recommended ARV regimens in children

Table B2, 3.3

First-Line Regimen ¹	Comments
ZDV/3TC ² plus ABC	Preferred, if concomitant anti-TB therapy being received
ZDV/3TC ² plus NNRTI	NNRTI choice: <ul style="list-style-type: none"> • If <3 years or <10 kg give NVP • If ≥3 years or ≥10 kg give NVP or EFV
<p>1 Country-specific considerations and preferences should determine which regimen or regimens to make available.</p> <p>2 ZDV/3TC is the first-choice dual NRTI regimen for children, as there has been the most clinical experience with this regimen. You can substitute other dual NRTI components, including ZDV/ddl, d4T/3TC, d4T/ddl, and ddl/3TC. Never use ZDV/d4T together because of proven antagonism.</p>	

Table B2, 3.4

Second-Line Regimens (in relation to first-line regimens)		
First-line	Second-line	Alternative Second-line
ZDV/3TC ² plus ABC	d4T/ddl plus LPV/r ¹ or NFV or an NNRTI	D4T/ddl plus an NNRTI ² plus either LPV/r or NFV
ZDV/3TC ² plus NNRTI	d4T/ddl plus LPV/r ¹ or NFV	
<p>1 For children who can swallow capsules and for whom the current capsule formulations allow appropriate weight- or body-surface-area-calculated dosing, additional options include SQV/r and IDV/r.</p> <p>2 NNRTI choice: If <3 years or <10 kg: NVP; if ≥3 years or ≥10 kg: NVP or EFV</p>		

- c. Monitoring drug levels in young children, especially below the age of two years, may be useful because of the wide variability in the metabolism of protease inhibitors and NNRTIs in this age group.
- d. ARV liquid formulations
- ZDV 10 mg/ml (syrup, large volume)
 - 3TC 10 mg/ml (syrup)
 - ddI 10 mg/ml (powder, suspension)
 - D4T 1 mg/ml (syrup, large volume)
 - ABC 20 mg/ml (syrup)
 - EFV 30 mg/ml (open capsules)
 - NVP 10 mg/ml (suspension)
 - NFV (suspension; powder, but best to crush tablets)
- e. Storing ARVs in the refrigerator
- Ritonavir
 - ddI suspension
 - d4T solution
 - Lopinavir/ritonavir capsules and solution
- f. Storing ARVs in glass jars
- ZDV syrup
 - d4T syrup

- Step 4. Discuss national guidelines and/or the use of ART in children in the local situations.
(15 minutes)
- Step 5. Present the following case studies for discussion.
(30 minutes)

CASE STUDY

Case 1

A child age 3 comes into your clinic. Her lab results show CD4 percentage below 10 percent. You decide to prescribe ARVs for her.

- a. List three possible regimens for this child.
- b. What are the challenges in delivering ART to children?

Case 2

What ARV combination would you give to a 7-year-old who had previously failed stavudine, didanosine, and nevirapine?

ANSWERS

Answers: See section 3. ART Therapy for Children in the trainer's notes.

Issues for discussion: Adherence is a major issue in giving ART to children. Some suggestions are:

Use available syrup formulations.

Investigate the use of lower doses of tablet formulation as a child grows.

For example:

- AZT – Syrup. Large volumes 10mg/ml
- 3TC – Syrup. Use within one month 10mg/ml
- Stavudine – Syrup. Large volume 1mg/ml; keep refrigerated
- Didanosine – Suspension 10mg/ml. Must shake well; keep refrigerated
- Lower strength Tabs 25mg, 50mg
- Abacavir – Syrup 20mg/ml
- Nevirapine – Suspension 10mg/ml
- Efavirenz 30mg/ml or low strength Capsule 50mg, 100mg
- Lopinavir/ritonavir (kaletra) Suspension, refrigerated. Can be stored for two months; has a bitter taste

SESSION 4 Post-Exposure Prophylaxis (PEP)

PURPOSE

In this session, participants will learn about occupational exposure to HIV, how to manage it, HIV post exposure prophylaxis (PEP), and drug selection for PEP.

OBJECTIVES:

By the end of this session, the participants will be able to:

1. Discuss issues and concerns that health care workers might have about working with HIV-infected persons.
2. Describe how to manage occupational exposure to HIV effectively.
3. Discuss the various PEP regimens and when to use which.
4. Describe ways of helping health care workers overcome their fears and biases about working with HIV infected persons.
5. Discuss national guidelines with regard to PEP.
6. Discuss post-sexual-exposure prophylaxis.

TIME:

1 hour and 30 minutes

- Step 1. Explain the purpose and objectives of the session (see above).
(2 minutes)
- Step 2. Ask participants if health care workers (HCWs) and care providers in their local situation have any issues or concerns about contracting HIV while caring for HIV-infected persons. List these on a flip chart. Ask if there are any known cases of HCWs contracting HIV while caring for HIV-infected patients. If local data is available, present this now. Ask if there is a barrier to PEP because of resistance to HIV testing prior to PEP. Discuss.
(10 minutes)
- Step 3. Present the information in 1a below.
(2 minutes)
- Step 4. Present the information in 1b on how to manage occupational and nonoccupational exposure. Is such management feasible in your local situation? What are the barriers to management?
(5 minutes)
- Step 5. Present information in 1c on nonoccupational exposure to HIV.
(10 minutes)

1. Occupational exposures

- a. Relative risk of viral transmission with sharps injury from infected source
- | | |
|---|--------------------------|
| • Hepatitis B virus (HbsAG positive + unvaccinated HCW) | 37 percent to 62 percent |
| Source HbsAG positive | 23 percent to 37 percent |
| Source HbsAG negative | 1.8 percent |
| • HIV | 0.3 percent |
- b. Management of occupational blood exposure
- Immediate care: wash wounds with soap and water; flush mucous membranes with water
 - Risk assessment: type of fluid and type of exposure
 - Evaluate source: test source for HIV serology (rapid test, if available)
 - Exposed person: initiate PEP as quickly as possible (see below)
 - Follow-up: HIV exposure (source positive HIV serology or acute HIV with positive HIV RNA)
 - HIV serology at baseline, 1.5, 3 and 6 months
 - Reevaluate and adjust regimen at 72 hours, if taking PEP
 - Monitor for drug toxicity
- c. Nonoccupational HIV exposure
- You need to learn the relative risk of HIV infection as depicted on the table on the next page.

Table B2, 4.1

Exposure	Risk/10,000 Exposures
Needle sharing	67
Percutaneous (occupational exposure)	30
Receptive anal intercourse	10 to 30
Receptive vaginal intercourse	8 to 20
Insertive vaginal sex	3 to 9
Insertive anal sex	3

Am J Med 1999; 106:324; Ann Intern Med 1996;125:497; J Acquir Immune Defic Syndr 1992;5:1116; N Engl J Med 1997;336:1072.

- Some states in the U.S. have policies for PEP after sexual exposure (Massachusetts, New York and California); policies also exist in France, Italy, Spain, Switzerland, Australia and at the UN, including WHO. The U.S. Public Health Service does not recommend for or against prophylaxis after nonoccupational exposure because of lack of data.
- It is biologically possible for PEP medications, taken soon after exposure, to prevent HIV infection.
- There is limited evidence available to suggest that prophylactic use of antiretroviral medications is efficacious.
- In particular, one study of PEP following occupational exposure to HIV showed an 81 percent reduction in risk of seroconversion when medications were started, on average, four hours after exposure. Here is one example of a policy guideline (from the San Francisco Department of Health, the state of California, in the U.S.). It recommends:
In cases where PEP is appropriate, offer it to the survivor as soon as possible. In no case offer it after 72 hours following the assault. When deciding whether to offer PEP, consider if any of the following factors were present during the assault: presence of blood; survivor or assailant with a sexually transmitted disease, with inflammation such as gonorrhea, chlamydia, herpes, syphilis, bacterial vaginosis, trichomoniasis, and the like; significant trauma to survivor; ejaculation by assailant; multiple assailants or multiple penetrations by assailant(s).
- When deciding whether to offer PEP, categorize the act of assault into one of the following three categories:
 1. Acts with measurable risk of HIV transmission, including anal penetration, vaginal penetration and injection with a contaminated needle
 2. Acts with possible risk of HIV transmission, including oral penetration with ejaculation, unknown act, contact with other mucous membrane, victim biting assailant and assailant with bloody mouth biting victim
 3. Acts with no risk of HIV transmission, including kissing; digital or object penetration of vagina, mouth or anus; and ejaculation on intact skin
- The simplest regimen that meets the goals of providing two nucleoside analog antiretrovirals (one of which is zidovudine) is zidovudine (300mg) together with lamivudine (150mg) in a combination pill (combivir) to be taken twice a day for 28 days. Dosing of combivir is twice a day rather than every 12 hours; it can be taken with or without food, although taking with food can reduce some of the gastrointestinal side effects. Alternative combinations include lamivudine plus stavudine (40 mg stavudine twice a day for a person weighing \geq 60 kg; 30 mg twice a day for a person weighing $<$ 60 kg; 150 mg lamivudine twice a day for body weight \geq 50 kg; 2mg/kg of body weight twice a day for $<$ 50 kg). Then we recommend treatment for four weeks with combivir (AZT 300 mg bid /3TC 150 mg bid) or d4T (40 mg bid) + ddI (400 mg qd).

- If a protease inhibitor is to be added, consider adding nelfinavir (1250 mg bid with meals) or IDV (800 mg tid on empty stomach) or IDV + RTV or LPV/r (400/100 mg bid) if source has viral load >50,000 c/ml, advanced HIV disease or source has been treated with one or both NRTIs. Be sure to consider PEP medications as one important part of the larger post-assault treatment program. Specialized counseling is another critical aspect of the post-assault treatment.

Step 6. Present the information on HIV PEP: 2 below and discuss any issues or concerns participants may have, given their local situation.
(10 minutes)

2. HIV PEP

- Through June 2000, there were 56 confirmed transmissions (in the U.S.) from an infected source to a HCW. All involved blood, bloody body fluids or high titer viral cultures; 48 of the 56 exposures were sharps injuries; 5 were mucous membranes/nonintact skin exposures; and 2 had both types of exposure.
- Potential sources of transmission (no confirmed cases with occupational exposures): semen, vaginal secretions, tissue or cerebrospinal, peritoneal, pericardial, synovial or amniotic fluid.
- Start PEP as soon as possible; if delay exceeds 36 hours, we suggest expert consultation.
- Continue prophylaxis for four weeks, if tolerated.
- Reevaluate exposed person within 72 hours, as additional information about the source becomes available—serologic status, VL, current treatment, any resistance test results or other factors that would modify recommendations.
- Use HIV EIA to monitor for seroconversion; perform this test at baseline and at 6 weeks, 3 months, and 6 months post exposure. We do not recommend VL tests for screening in the HCW unless there is an illness compatible with acute retroviral syndrome.
- If you give PEP, monitor the HCW for drug toxicity at baseline and at 2 weeks with CBC, renal function tests and hepatic function tests. For those receiving IDV, also do urinalysis.
- Ask HCWs to commit to behavioral measures, for example, sexual abstinence or condom use, for several weeks to 2 months. The greatest risk is during the first 6 to 12 weeks following exposure.
- Treat female HCWs with known or possible pregnancy as you would anyone else, except for selection of drugs. The care provider should discuss the drug benefits and risks with the HCW. Avoid EFV and the combination d4T and ddI.

Step 7. Present the following information on drug selection for PEP: 3 below.
(10 minutes)

3. Drug selection for PEP

a. Recommended regimens for PEP

- Base decisions in part on information about the source of exposure (that is, the HIV-infected patient). Is the patient on ART? What has been his or her response to therapy (including VL at the time of exposure and history of HIV resistance testing)? Health care workers often resist serology, but it is important because of the inadequacy of the PEP regimen for an HIV-positive HCW.
- Do not let decisions delay initiation of PEP; you can make modifications after obtaining the information.
- **Two drug combinations**
 - AZT + 3TC
 - 3TC + d4T
 - d4T + ddI
- **Three drug combinations**
 - Two nucleosides (above list) + IDV, NFV, EFV, ABC, RTV, FTV, APV, DLV or LPV/RTV
Preferred: NFV, EFV, ABC + LPV/RTV

b. Specific recommendations based on type of injury or exposure

- HIV PEP for percutaneous injuries (see table below)

Table B2, 4.2

Exposure	Status of Source		
	Low risk ¹	High risk ¹	Unknown
Not severe: solid needle, superficial	2 drug PEP ²	3 drug PEP ²	Usually none; consider 2 drug PEP ³
Severe: large bore needle, deep injury, visible blood on device, needle in patient artery/vein	3 drug PEP ²	3 drug PEP ²	Usually none; consider 2 drug PEP ³

1 Low risk: asymptomatic HIV or VL <1500c/mL. High risk: symptomatic HIV, AIDS, acute seroconversion, high VL or WHO Stage IV, if viral load not available

2 Concern for drug resistance: initiate prophylaxis without delay and consult an expert

3 Consider two-drug PEP if source is high risk for HIV exposure from unknown source, when HIV-infected source is likely

- HIV PEP for mucous membranes and nonintact skin exposures, for example, dermatitis, abrasion, wound (see table below)

Table B2, 4.3

Exposure	Status of Source		
	Low risk ¹	High risk ¹	Unknown
Small volume (drops)	Consider two-drug PEP	Two-drug PEP	Usually no PEP; consider two-drug PEP ²
Large volume (major blood splash)	Two-drug PEP	Three-drug PEP	Usually no PEP; consider two-drug PEP ²

¹ Low risk: asymptomatic HIV or VL <1500c/mL. High risk: symptomatic HIV/AIDS, acute seroconversion, high VL.

² Consider if source has high risk factors or exposures from unknown source where HIV-infected source is likely.

- Step 8. Ask participants to “brainstorm” a plan of action to help HCWs in their local situation overcome their fears and biases in caring for HIV-infected people.
(10 minutes)
- Step 9. Discuss the feasibility of providing PEP to HCWs in their local situation using the following questions:
(10 minutes)
- Is there a system in place for providing PEP?
 - If so, what is it?
 - If not, what can be done to put one in place?
 - Are there any national guidelines for PEP?
- Step 10. Discuss the case studies given below.
(15 minutes)

CASE STUDIES

In the following cases, assess if the risk is low, moderate or high.

Case 1

A nurse is setting an IV line in a patient and accidentally pricks herself. The patient is a known injecting-drug user, but his HIV status is unknown.

Case 2

A nurse suffers a deep wound when someone passes her a bloodstained instrument during orthopedic surgery on an HIV-positive hemophiliac.

ANSWERS

Case 1

You need to take a history from the nurse and examine the patient who is an IV drug user. You can assess what needs to be done, depending on the risk assessment and the HIV test result.

Case 2

The risk is high.

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