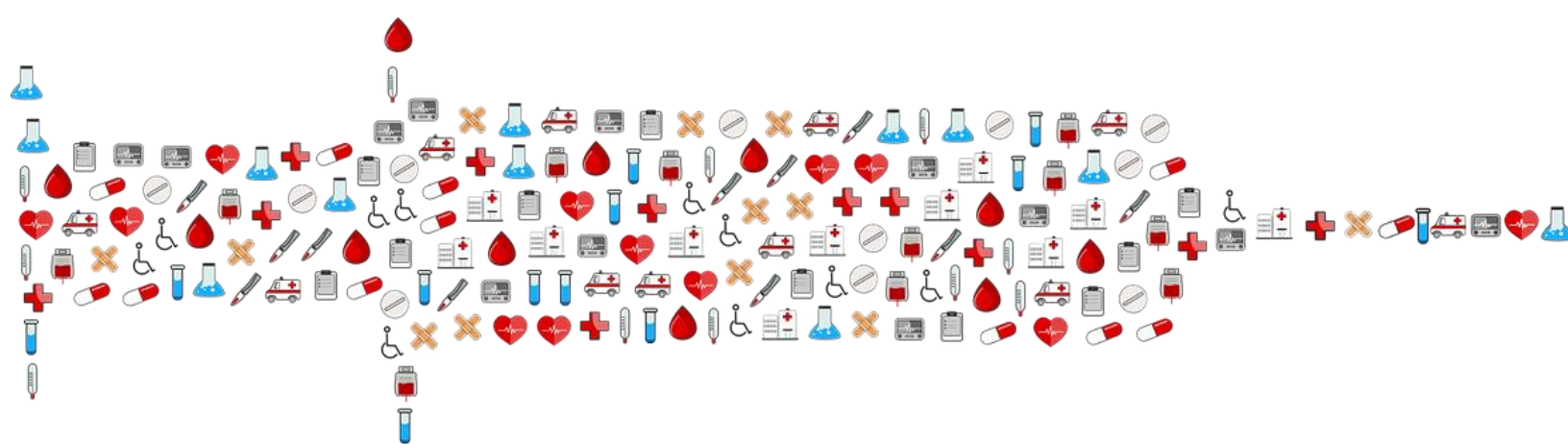


Health Care Maintenance and Disease Prevention When Working with HIV Patients



Introduction

HIV/AIDS clinical care has improved dramatically over the decades, given the availability of new medications and a better understanding of how best to use antiretrovirals and deliver primary care to persons living with HIV/AIDS. Positive change on such a massive scale, however, brings with it new demands on clinicians.

Along with innovations in HIV drug therapies, HIV/AIDS care has become more complex than ever before due to increasing comorbidities that are attributable to HIV treatment and the aging of the HIV-infected population in the United States. Patient needs also have expanded across a broad spectrum of medical, psychological, behavioral, and social issues. Notably, significant numbers of infected individuals are identified and enter care late in the course of their HIV disease, confronting clinicians with complex and immediate care challenges.

Since the early days of the epidemic, clinicians have received training in HIV/AIDS clinical care through the AIDS Education and Training Centers (AETCs) Program – the clinical training arm of the Ryan White HIV/AIDS Program that is administered by the Health Resources and Services Administration (HRSA) and its HIV/AIDS Bureau (HAB). The AETC network conducts more than 14,000 training events each year with approximately 143,000 health care providers in attendance.

The *Guide for HIV/AIDS Clinical Care* is a pillar of the Ryan White HIV/AIDS Program's mission to continuously improve HIV/AIDS clinical care. The *Guide* was first published in 1993 as a collaborative effort of several regional AETCs. It was subsequently updated and expanded in 2006 and 2011. The version before you incorporates many new insights, but the time-tested format has been retained – easy access to crucial facts for a busy clinician.

The developers of the *Guide* strive to be responsive to how HIV/AIDS clinical care is provided today.

- With more routine HIV testing in medical settings, a large number of individuals are entering care via primary care sites that have relatively limited experience managing HIV/AIDS disease.
- A notable proportion of HIV/AIDS primary care in the United States is provided by advanced practice nurses and physician assistants.
- Shortages in the health care work force are worsening. Experienced staff members are aging and retiring, a limited number of new clinicians are entering primary care and specializing in HIV/AIDS care, and fewer clinicians are available in geographic areas with limited resources.

As a result, front line primary care providers may be less familiar with management of HIV/AIDS disease, as outlined in U.S. Department of Health and Human Services treatment guidelines (available at aidsinfo.nih.gov) and clinical practices presented in this *Guide*.

By presenting best practices in the clinical management of HIV/AIDS disease, the *Guide* can help us continue the remarkable advances in HIV/AIDS care that have made the Ryan White HIV/AIDS Program a model for health care delivery for our Nation and for the world.

Abbreviations for Dosing Terminology

BID = twice daily

BIW = twice weekly

IM = intramuscular (injection), intramuscularly

IV = intravenous (injection), intravenously

PO = oral, orally

Q2H, Q4H, etc. = every 2 hours, every 4 hours, etc.

QAM = every morning

QH = every hour

QHS = every night at bedtime

QID = four times daily

QOD = every other day

QPM = every evening

TID = three times daily

TIW = three times weekly



Occupational Postexposure Prophylaxis

Background

Health care personnel (HCP) and other individuals working in medical, public safety, sanitation, and laboratory settings are at risk of occupational exposure to HIV. Although avoiding exposure to HIV is the only reliable way of preventing HIV infection, postexposure prophylaxis (PEP), can reduce the risk of HIV infection in exposed HCP. PEP is defined as antiretroviral (ARV) therapy that is initiated soon after exposure to HIV with the intention of preventing HIV infection.

This chapter examines the general issues involved with PEP in occupational settings. The information is based on 2013 U.S. Public Health Service (USPHS) guidelines for occupational PEP (see “References,” below). For information on PEP for *nonoccupational* HIV exposures (such as sexual exposure), see chapter *Nonoccupational Postexposure Prophylaxis*. Note that other bloodborne pathogens, particularly hepatitis B virus (HBV) and hepatitis C virus (HCV), also may be transmitted through occupational exposure; it is important to consider these potential infections when assessing occupational exposures. For information on the management of occupational exposures to HBV and HCV, refer to the 2001 USPHS PEP guidelines (see “References,” below). In addition, the National Clinicians’ Post-Exposure Prophylaxis Hotline (PEPline) is available for telephone consultation at 888-HIV-4911 (888-448-4911).

The risk of HIV infection after exposure depends on several factors that are related to the exposure itself and to the source patient (see below). To make sound PEP recommendations, the clinician must assess the risk of HIV infection from the particular exposure. After this, the clinician and the exposed worker must discuss the possible benefit of PEP (given the risk of HIV transmission from the injury) in relation to the willingness of the exposed worker to adhere to a 28-day course of ARV medicines, the potential toxicity of the regimen, and drug interactions. HCP who are pregnant at the time of their exposure must weigh the risk of fetal exposure to HIV against the potential teratogenic and other risks of the ARV drugs (it should be noted that pregnancy is not a contraindication to PEP, and that a number of ARVs are recommended for use during pregnancy, based on safety and efficacy data) (see chapter *Reducing Perinatal HIV Transmission*).

The efficacy of PEP is related to the specific PEP regimen, the timing of PEP, and the exposed worker’s level of adherence to the PEP regimen. PEP is most likely to be effective if it is started within hours of an exposure, and outcomes may be compromised as the time from exposure increases. Nevertheless, it may be reasonable to offer PEP up to 72 hours after exposure. Adherence to PEP is strongly affected by factors such as the tolerability of the ARVs, the number of pills in the regimen, and the frequency of dosing. As current guidelines emphasize, it is very important to select a PEP regimen that is expected to be tolerated and that is convenient to take; any side effects or adherence difficulties should be managed promptly. The guidelines recommend the use of 3 (or more) PEP drugs for all exposures. Although the optimal duration of PEP is not known; studies support ARV treatment for 28 days.

In the work setting, HIV infection may occur through percutaneous injuries (e.g., needlesticks) or mucocutaneous exposures (e.g., mucous membrane or nonintact skin exposure) to blood or other potentially infectious body fluids. The risk of HIV seroconversion after occupational exposure with an HIV-contaminated hollow-bore needle is best described as 0.3%, on average. Another way of describing this to an exposed HCP is that, without PEP, HIV transmission occurs about

once in 300 instances of needlestick from a known HIV-infected source patient. In a retrospective case-control study of HCP with percutaneous exposure to HIV, the following exposure and source patient factors were associated with an increased risk of HIV transmission:

- Large-gauge (<18-gauge) hollow-bore needle
- Deep injury
- Visible blood on the device
- Procedure with needle in a blood vessel
- Terminal AIDS in the source patient
- High HIV viral load of the source patient

The factor described as “terminal AIDS in the source patient” is considered a surrogate for a source patient with a high HIV viral load (this study was done prior to the routine use of HIV viral load assays); high HIV viral load is known to be a substantial risk factor for HIV transmission. On the other hand, although an undetectable HIV viral load is thought to indicate a low risk of HIV transmission, transmission still is possible, and cases of perinatal and sexual transmission from sources with undetectable serum HIV RNA have been reported.

Compared with percutaneous injury, exposure of infectious body fluids to mucous membranes (e.g., eye or mouth) or to skin with an obvious impairment of integrity (e.g., abrasion or wound) typically involves a lower risk of HIV transmission (the transmission risk for mucous membrane exposure to HIV is approximately 1 in 1,000, and less than 1 in 1,000 for cutaneous exposure). However, mucocutaneous exposures that involve large volumes of blood or other infectious fluid from an HIV-infected patient with a high HIV RNA level or prolonged duration of contact are considered increased-risk exposures.

S: Subjective

An HCP reports possible exposure to HIV through a needlestick injury or mucocutaneous exposure.

Ideally, the HCP should immediately decontaminate the injured or exposed skin with soap and water, or flush the exposed mucous membranes with copious amounts of water or saline. The HCP should report the exposure immediately to appropriate authorities in the health care institution (e.g., the institution's needlestick hotline).

Take a thorough history of the specific exposure, including the type of exposure, the type and amount of body fluid involved, the point of entry or exposure, the time it occurred, the HIV status of the source patient (if known), and HIV risk factors of the source patient (if HIV status is not known).

A: Assessment

Assess potential exposure to HIV (and to HBV and HCV). Consider the HIV status of the source and the characteristics of the exposure in deciding whether PEP should be offered.

The guidelines recommend the use of PEP following percutaneous or mucous membrane exposures to potentially infectious body fluids. They note that PEP should be offered even in the case of an exposure to a source patient with an undetectable HIV viral load. Consult with experts if there is uncertainty about whether a particular exposure poses sufficient risk to warrant PEP.

P: Plan

Laboratory Testing

For the exposed HCP

- Perform a baseline HIV antibody test.
- Test for other infections transmitted through occupational exposure, particularly hepatitis B (HBV surface antigen, surface antibody, core antibody), and hepatitis C (HCV antibody).
- Obtain complete blood count (CBC), creatinine and estimated glomerular filtration rate (GFR), and hepatic transaminases at baseline, before treatment with ARV medications.
- For women who may be pregnant, perform a pregnancy test.

For the source person

- The institution should perform appropriate testing of the source person for bloodborne pathogens (e.g., HIV, HBV, and HCV) if the person's status is unknown.
- The use of rapid or expedited HIV tests makes it possible to render quick decisions about the need for HIV PEP, and the 4th-generation Ag/Ab tests identify most cases of HIV during the window period of acute HIV infection (see chapter *Expedited HIV Testing*).
- Although a positive expedited test result requires confirmation before the individual is diagnosed as HIV infected, for the purposes of PEP, it should be considered a true positive until proven otherwise, and the exposed worker should be counseled accordingly. If, upon further testing, the source patient is determined to be HIV uninfected, PEP should be discontinued. A negative expedited test result is considered reliable unless the source has signs or symptoms of acute HIV (see chapters *Expedited HIV Testing* and *Early HIV Infection*).

- PEP should not be delayed (beyond 1-2 hours) while source patient HIV testing is under way.

Treatment

A regimen consisting of at least 3 ARV drugs is recommended for all occupational HIV exposures (the U.S. guidelines no longer recommend evaluation of the severity of exposure to determine the number of drugs in a PEP regimen). Recommendations for PEP regimens are based on expert opinion and largely follow the principles of HIV treatment regimens, but the PEP guidelines place particular emphasis on optimizing the tolerability and convenience of the regimen to facilitate adherence for 28 days.

Considerations in choosing the medications for a PEP regimen include:

- Possible ARV adverse effects
- Dosing schedule
- Drug-drug interactions with other medications the HCP may be taking
- The likelihood that the source patient's virus is resistant to 1 or more ARV medications

Provide counseling about the potential risks and benefits of PEP drugs, including possible adverse effects, drug-drug interactions, and the importance of close adherence. Recommended regimens are shown in Table 1; select one that is likely to be effective, tolerable, and convenient. Note that although these regimens are potent in treating HIV infection, their efficacy as prophylaxis has not been demonstrated. Consultation with experts is recommended (see "Expert Consultation," below).

These recommendations are drawn from the 2013 guidelines for occupational PEP; consult the most recently updated version of the guidelines for current information.

Table 1. Antiretroviral Regimens for Occupational Postexposure Prophylaxis of HIV Infection

Preferred Regimen	
<ul style="list-style-type: none"> Raltegravir 400 mg BID + tenofovir 300 mg/emtricitabine 200 mg QD (Truvada) 	
Alternative Regimens (combine 1 drug or drug pair from left column with 1 NRTI pair from right column)	
<ul style="list-style-type: none"> Raltegravir 400 mg BID Darunavir 800 mg QD + ritonavir 100 mg QD Etravirine 200 mg BID Rilpivirine 25 mg QD Atazanavir 300 mg QD + ritonavir 100 mg QD Lopinavir/ritonavir 400/100 mg BID 	<div style="text-align: center;">+</div> <ul style="list-style-type: none"> Tenofovir + emtricitabine (Truvada), 1 tablet QD Tenofovir 300 mg QD + lamivudine 300 mg QD Zidovudine + lamivudine (Combivir), 1 tablet BID Zidovudine 300 mg BID + emtricitabine 200 mg QD
OR	
<ul style="list-style-type: none"> Elvitegravir/cobicistat/tenofovir/emtricitabine (Stribild) (complete regimen; no additional NRTIs needed) 	

Adapted from Updated *U.S. Public Health Service Guidelines for the Management of Occupational Exposures to Human Immunodeficiency Virus and Recommendations for Postexposure Prophylaxis* (2013). Available at aidsinfo.nih.gov/guidelines. Accessed December 1, 2013.

Refer to the appendix in the updated PEP guidelines for more complete information on the advantages, and disadvantages of the various ARV agents available for PEP, and to the adult and adolescent ARV treatment guidelines (reference below) for more information about ARV adverse effects and drug-drug interactions.

Certain ARVs generally are not recommended for PEP because of elevated risk of toxicities; these include nevirapine (which is contraindicated as PEP), abacavir (testing for HLA- B*5701 must be done), didanosine, enfuvirtide, and tipranavir. Efavirenz may have a higher rate of significant adverse effects than other listed agents. Additionally, efavirenz should not be used with women who are in the first trimester of pregnancy or who may become pregnant while on PEP, because of possible teratogenicity. Some “alternative” ARVs may be considered for use based on consultation with experts.

If the source person is known or suspected to have infection with HIV that is resistant to ARV medications, seek expert consultation in selecting an appropriate PEP regimen.

However, PEP should not be delayed while consultation is being solicited, and it is possible to adjust regimens based on expert advice.

Begin ARV prophylaxis as soon as possible after the exposure occurs, preferably within a few hours and no later than 72 hours postexposure. Treatment should be continued for 28 days unless the source person is determined to be HIV uninfected.

Provide counseling about the efficacy of PEP, including timely initiation of PEP medications, the importance of adherence to the regimen for 28 days, and management of common adverse effects. Counsel exposed workers to avoid possible transmission of HIV, e.g., by using use latex barriers with their sex partners, avoiding breast feeding if possible, avoiding pregnancy, and avoiding blood/tissue donations, until transmission of HIV infection has been ruled out.

Follow-Up

Exposed workers should be reevaluated within 72 hours after exposure to review any available new information about the exposure and the source person as well as test results. For HCP taking PEP, early reevaluation

offers the opportunity for further education and counseling, including assessment and support of PEP adherence and evaluation and management of any side effects. In addition to health education counseling, many exposed workers need emotional support during their follow-up visits.

For persons on PEP, monitoring for adherence and adverse effects should be conducted again at 2 weeks. Blood testing (e.g., CBC, creatinine and electrolytes, liver function tests, others as indicated) should be done to monitor for PEP toxicity, as indicated by the particular ARV regimen.

PEP is discontinued after 4 weeks, and monitoring for ARV toxicity generally should not be repeated unless there is a need to recheck an abnormal result.

Follow-up HIV antibody testing should be done at 6 weeks, 3 months, and 6 months after the exposure. If a 4th-generation HIV Ag/Ab assay is used, the final HIV test can be done at 4 months rather than 6 months. Follow-up for 12 months is recommended for HCP who acquired hepatitis C via exposure to a source who was coinfecting with HIV and HCV.

Symptoms of acute HIV infection such as fever, rash, and lymphadenopathy (see chapter *Early HIV Infection*) may occur in HCP who are infected with HIV through occupational exposure. Exposed HCP should be counseled about the symptoms of acute HIV infection and instructed to return for reevaluation as soon as possible if symptoms develop. If symptoms consistent with acute HIV appear within 4-6 weeks after an occupational exposure, the HCP should be evaluated immediately; an HIV RNA test should be performed if acute HIV infection is suspected. If an HCP is found to be infected with HIV, that individual should be referred immediately to an HIV specialist for further evaluation and care.

Expert Consultation

Consultation with experts in PEP and in ARVs is recommended for assistance with managing all occupational exposures. This is particularly important if the source person is known or suspected to have ARV-resistant virus or if there are unusual or perplexing elements about the case (e.g., if the exposed HCP is pregnant or breast feeding, has significant medical illness, or takes medications that may interact with PEP ARVs). Consultation on the treatment of occupational exposures to HIV and other bloodborne pathogens is available to the clinician managing the exposed person on the National Clinicians' Post-Exposure Prophylaxis Hotline (PEpline) at 888-HIV-4911 (888-448-4911). This service is available 7 days a week, at no charge (additional information is available on the PEpline website at www.nccc.ucsf.edu).

Prophylaxis Against HBV and HCV

Prophylaxis against HBV is recommended for patients with potential exposure to HBV who do not have immunity against HBV. Give hepatitis B immune globulin (HBIG) as a 0.06 mL/kg IM injection and initiate the vaccination series. For patients who received the vaccination series but did not develop protective antibodies (HBV sAb+), give HBIG at the time of the postexposure workup and initiate revaccination; consider repeat of HBIG in 1 month. For patients with immunity to HBV, no treatment is indicated.

For HCV, no prophylactic treatments are recommended. After potential exposure, perform a baseline HCV antibody test. If the source is known to have HCV infection, consider alanine aminotransferase (ALT) and HCV viral load testing at 4-6 weeks. HCV antibody testing should be repeated at 4-6 months. If HCV seroconversion occurs (indicated by ALT elevation, detectable HCV viral load, or confirmed positive HCV

antibody test result), refer the patient to a hepatitis C expert because early treatment of HCV may be indicated.

Addendum: Workplace Obligations

The health care institution has certain obligations to an exposed employee.* The institution should do the following:

- Evaluate the circumstances of the exposure, the type of fluid, and possible entry points.
- Evaluate the source patient.
- Perform baseline HIV antibody testing of the exposed HCP.
- Counsel the exposed HCP about the possible risks and benefits of PEP.
- Offer or recommend PEP as soon as possible after the exposure, preferably within the first several hours.
- Counsel the HCP about avoiding secondary transmission to others (safer sex and other risk-reduction practices, as indicated).
- Support and maintain the confidentiality of the HCP.
- For an HCP who is taking PEP, monitor for medication toxicity and adherence, and check for drug-drug interactions with other medications the HCP may be taking.
- Repeat HIV testing at 6 weeks, 3 months, and 6 months (if a 4th-generation HIV Ag/Ab assay is used, the final HIV test can be performed at 4 months).
- Report the exposure as required by federal and state regulations (including U.S. Occupational Safety and Health Administration requirements).

The PEP guidelines recommend that health care institutions have a formal mechanism for consultation about occupational HIV exposures, appropriate initial lab testing for source patients and exposed HCP, counseling for exposed HCP, availability of initial PEP regimens (e.g., starter packs), and a mechanism for outpatient follow-up. The protocols should

be readily available to emergency department providers and others who manage exposure incidents.

* Legal issues vary from state to state. In many states, institutions and clinics have no obligation toward nonemployees or students who are exposed to HIV in their settings. In such situations, clinical supervisors or school or university officials often are the first contact for notification. However, everyone working in a health care setting should be familiar with the procedures and financial responsibilities for HIV exposure management to avoid delays in HIV PEP treatment.

Patient Education

- Persons who have possible exposures to HIV in the work setting should contact the PEP service of their employer or a qualified medical provider as soon as possible after the exposure, or they should go to an emergency department. Although PEP may be effective if it is started within 72 hours of exposure, the sooner medications are initiated, the better the chance for preventing HIV transmission.
- PEP medications should be taken as directed for the full 28-day course. Adherence to PEP medications is essential for successful treatment.
- PEP recipients should be advised to contact their providers if they experience uncomfortable side effects. Providers may prescribe medications to alleviate the side effects, or they may prescribe different PEP medications.
- Until HIV infection has been ruled out, exposed workers should be advised to use latex or polyurethane barriers to prevent transmission of HIV to their sex partners, to avoid pregnancy, and to avoid breast feeding if possible.
- Exposed HCP should be counseled about the symptoms of primary HIV infection and instructed to contact their care providers immediately if symptoms develop.

Nonoccupational Postexposure Prophylaxis

Background

Although avoiding exposure to HIV is the only reliable way of preventing HIV infection, postexposure prophylaxis (PEP) can decrease the risk of infection after exposure to HIV. Antiretroviral (ARV) therapy is an important prophylactic intervention for appropriate persons with nonoccupational exposures (e.g., sexual contact; sharing of injection drug needles or other equipment) as well as those with occupational exposures (e.g., needlesticks). The U.S. Department of Health and Human Services (HHS) has developed recommendations for nonoccupational PEP (nPEP) based on data from animal models, perinatal clinical trials, and observational studies. Efficacy of nPEP remains hypothetical, and randomized clinical trials are not possible, but nPEP appears to be safe.

Overall, nPEP is more likely to be effective when the exposure is a single episode and nPEP is initiated in a timely manner. It is not appropriate for cases of multiple sexual exposures or injection drug use (IDU) exposures over time or for exposures that occurred >72 hours before starting nPEP treatment (see Figure 1).

The model for nPEP is derived in part from protocols for occupational PEP (e.g., in terms of risk assessment, pretreatment testing, timing of treatment, treatment regimens, and duration of treatment). (For information on occupational PEP, see chapter *Occupational Postexposure Prophylaxis*.) One significant difference between the protocols is that nPEP protocols should include interventions to reduce the risk of future HIV acquisition. Although exposed individuals usually seek care because they are interested specifically in antiretroviral prophylaxis, the nPEP model takes advantage of a critical opportunity to provide risk-reduction counseling and education.

See chapter *Occupational Postexposure Prophylaxis* for further discussion of evaluating possible benefits and risks of PEP.

S: Subjective

The patient reports potential exposure to HIV through a sexual encounter or the sharing of needles or other equipment for IDU.

Take a thorough history of the specific sexual or drug-use activities, the time the exposure occurred, the HIV status of the source person (if known), and HIV risk factors of the source person (if HIV status is not known). In cases of sexual assault, evidence collection and specific paperwork may be required as well.

O: Objective

Examine for trauma and for signs or symptoms of sexually transmitted diseases (STDs), which may increase the risk of HIV transmission. In injection drug users, examine for abscesses and signs or symptoms of infection. For women who may be pregnant, perform a pregnancy test.

A: Assessment

Assess for potential exposures to HIV and other bloodborne pathogens and for the presence of other STDs. The risk of HIV infection depends on the HIV status of the source and on the characteristics of the exposure (e.g., HIV viral load) and of the exposure (see Figure 1). Note that, although an undetectable HIV viral load is thought to indicate a low risk of HIV transmission, transmission still is possible, and cases of sexual transmission from sources with undetectable serum HIV RNA have been reported.

The estimated risk of HIV exposure will determine whether nPEP should be offered. An algorithm for risk evaluation and treatment decisions is presented in Figure 1.

P: Plan

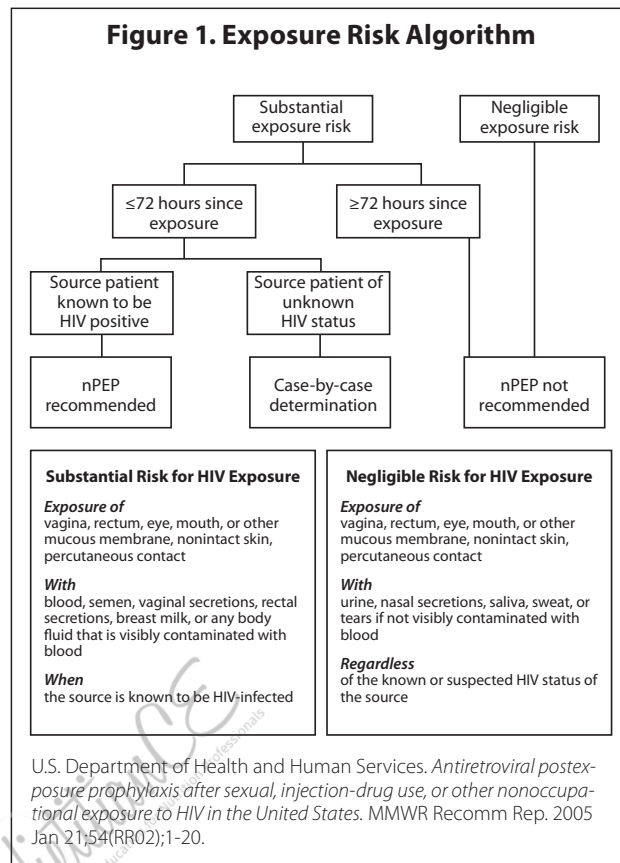
Laboratory Testing

- Perform a baseline HIV antibody test.
- Evaluate and test for other infections transmitted through sexual or IDU exposures, including chlamydia, gonorrhea, syphilis, herpes simplex virus, hepatitis B (HBV surface antigen, surface antibody, and core antibody), and hepatitis C (HCV antibody).
- Obtain complete blood count (CBC), liver function tests (LFTs), and creatinine and estimated glomerular filtration rate (GFR) at baseline before treatment with ARV medications.

Treatment

Follow the algorithm in Figure 1 to determine whether the patient should be offered nPEP medications. If the patient is a candidate for treatment, provide counseling about the potential risks and benefits of nPEP.

Select an nPEP regimen that is likely to be effective but tolerable; consider the potential



adverse effects and drug interactions of ARV agents (Table 1). Adherence to nPEP is strongly affected by factors such as the tolerability of the ARVs, the number of pills in the regimen, and the frequency of dosing. It is very important to select a regimen that is expected to be tolerated and that is convenient to take; any side effects or adherence difficulties should be managed promptly.

In general, the recommendations for nPEP involve 3-drug combination therapy. In some circumstances, more than 3 ARVs may be appropriate (e.g., if the source virus is resistant to ARVs), and in some cases, 2-drug PEP may be considered (e.g., if the HIV status of the source person is unknown, the exposure is thought to be of relatively low risk, or there is a need to minimize possible toxicity); consultation with experts is recommended.

Note that the HHS nPEP guidelines were last updated in 2005 and do not reflect current practice. **The recommendations presented here have been adapted to reflect current nPEP strategies, current guidelines for occupational PEP, and the availability of newer ARVs** (see Table 1). Note that a number of ARVs that were included in “preferred” or “alternative” regimens in the 2005 guidelines are no longer recommended in current practice, based on factors such as higher likelihood of causing adverse effects, greater pill burden, or inconvenient dosing. A number of alternatives to the recommendations listed below are available; consult with an expert. Note that, although these regimens are effective in treating HIV infection, their efficacy as prophylaxis has not been demonstrated.

If the source person is known or suspected to have infection with HIV that is resistant to ARV medications, seek expert consultation in selecting an appropriate nPEP regimen.

Certain ARVs are not currently recommended for PEP, including nevirapine (which is contraindicated for PEP), abacavir (testing for HLA-B*5701 must be done), didanosine, enfuvirtide, and tipranavir. Although the 2005 nPEP guidelines designate it as a preferred agent, efavirenz may have a higher rate of significant adverse effects than other agents listed in Table 1. Additionally, efavirenz should not be used during the first trimester of pregnancy or for women who may become pregnant while taking PEP, because of possible teratogenicity. Refer to the updated occupational PEP guidelines and to the adult and adolescent ARV treatment guidelines for more complete information on the advantages and disadvantages, adverse effects, and drug-drug interactions of the various ARV agents available for PEP (references below). Consider consultation with experts (see “Expert Consultation,” below).

Table 1. Antiretroviral Regimens for Nonoccupational Postexposure Prophylaxis of HIV Infection*

Preferred Regimens	
<ul style="list-style-type: none"> Raltegravir 400 mg BID + tenofovir 300 mg/emtricitabine 200 mg QD (Truvada) 	
Alternative Regimens (combine 1 drug or drug pair from left column with 1 NRTI pair from right column)	
<ul style="list-style-type: none"> Raltegravir 400 mg BID Darunavir 800 mg QD + ritonavir 100 mg QD Etravirine 200 mg BID Rilpivirine 25 mg QD Atazanavir 300 mg QD + ritonavir 100 mg QD Lopinavir/ritonavir 400/100 mg BID 	<div style="text-align: center;">+</div> <ul style="list-style-type: none"> Tenofovir + emtricitabine (Truvada), 1 tablet QD Tenofovir 300 mg QD + lamivudine 300 mg QD Zidovudine + lamivudine (Combivir), 1 tablet BID Zidovudine 300 mg BID + emtricitabine 200 mg QD
OR	
<ul style="list-style-type: none"> Elvitegravir/cobicistat/tenofovir/emtricitabine (Stribild) (complete regimen; no additional NRTIs needed) 	

* Forthcoming HHS guidelines on nPEP may differ from these recommendations; check current recommendations.

Abbreviations: NNRTI = nonnucleoside reverse transcriptase inhibitor; NRTI = nucleoside analogue reverse transcriptase inhibitor; PI = protease inhibitor

Adapted from Kuhar DT, Henderson DK, Struble KA, et al.; U.S. Public Health Service Working Group. *Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to Human Immunodeficiency Virus and Recommendations for Postexposure Prophylaxis*. Infect Control Hosp Epidemiol. 2013 Sep;34(9):875-92; and U.S. Department of Health and Human Services. *Antiretroviral Postexposure Prophylaxis After Sexual, Injection-Drug Use, or Other Nonoccupational Exposure to HIV in the United States—January 21, 2005*. Available at aidsinfo.nih.gov/guidelines. Accessed December 1, 2013.

Once the decision is made to institute nPEP, do the following:

- Begin ARV prophylaxis as soon as possible after the exposure, but always within 72 hours. Treatment should be continued for 28 days, unless the source person is determined to be HIV negative.
- Provide counseling about the efficacy of nPEP, timely initiation of nPEP medications, adherence to the regimen for 28 days, and the importance of preventing additional HIV exposures during this time.
- Counsel exposed patients to use latex barriers with their sex partners until transmission of HIV infection has been ruled out.
- Counsel patients, as appropriate, about ways to reduce risks of future exposure to HIV.
- In cases of sexual assault, refer the patient to a rape counselor.

Follow-Up

Patients should be evaluated within 1 week for review of all test results and further risk-reduction counseling. For patients taking nPEP, this follow-up should include adherence assessment and evaluation of any adverse effects. Side effects should be managed aggressively in order to maximize the likelihood of adherence to nPEP. A 2-week blood screening (CBC, LFTs, and creatinine) should be performed for patients on the 28-day nPEP regimen to monitor for nPEP toxicity.

Follow-up testing for HIV antibody in patients with a negative baseline HIV antibody test should be done at 6 weeks, 3 months, and 6 months after the exposure. If a 4th-generation HIV Ag/Ab assay is used, the final HIV test can be done at 4 months rather than 6 months.

Patients need health education and risk-reduction counseling and emotional support during their follow-up visits. Nonoccupational PEP programs should focus efforts on

risk-reduction counseling rather than the continued use of medicines for prevention. To this end, many programs have case managers, social workers, and health educators as the key providers of follow-up and counseling after an exposure, with referral to clinicians as needed.

If patients develop acute HIV infection or are discovered to be HIV seropositive at follow-up testing, immediately refer to an HIV specialist for evaluation and care (see chapter *Early HIV Infection*).

Expert Consultation

For consultation on the treatment of exposures to HIV (and HBV and HCV), the clinician managing the exposed person can call the National HIV/AIDS Clinicians' Post-Exposure Prophylaxis Hotline (PEPline) at 888-HIV-4911 (888-448-4911). This service is available 7 days a week at no charge. Additional information on the Internet is available at www.ncccf.ucsf.edu. PEPline support may be especially useful in challenging situations, such as when drug-resistant HIV strains are suspected to be involved in the exposure or when the exposed person is pregnant.

Prophylaxis Against HBV and HCV

Prophylaxis against HBV is recommended for patients with potential exposure to HBV who do not have not have immunity against HBV. Give HBV immune globulin (HBIG) as a 0.06 mL/kg IM injection and initiate the vaccination series. For patients who previously received the vaccine series but did not develop protective antibody (HBV sAb+), give HBIG at the time of the postexposure workup and initiate revaccination; consider repeat of HBIG in 1 month. For patients with immunity to HBV (HBV sAb+), no treatment is indicated.

For HCV, no prophylactic treatments are recommended. After potential exposure, perform a baseline HCV antibody test. If the source is known to have HCV infection, consider alanine aminotransferase (ALT)

and HCV viral load testing at 4-6 weeks. HCV antibody testing should be repeated at 4-6 months. If HCV seroconversion occurs (indicated by ALT elevation, detectable HCV viral load, or confirmed positive HCV antibody test result), refer the patient to a hepatitis C specialist because early treatment of acute HCV may be indicated.

Patient Education

- Persons who have possible exposures to HIV should contact a medical provider or go to an emergency room as soon as possible after the potential exposure has occurred. PEP may be effective if it is started within 72 hours of exposure, but the sooner medications are initiated, the better the chance for preventing HIV transmission.
- PEP medications should be taken as directed for a full 28-day course. Adherence to PEP medications is essential for successful treatment.
- If patients are experiencing uncomfortable adverse effects, they should contact their care provider right away. Providers may prescribe medications to alleviate the adverse effects or select other PEP medications.
- Until HIV infection has been ruled out, exposed persons should be advised to use latex barriers to prevent transmission of HIV to their sex partners.
- Exposed persons should be counseled about the symptoms of primary HIV infection and instructed to contact their care provider immediately if symptoms develop.
- The most effective way to prevent HIV infection is to prevent exposure to HIV by practicing safer sex and safer IDU techniques. Use of condoms and other latex or polyurethane barriers and avoidance of needle sharing are successful preventive measures. If patients have questions about access to condoms or clean needles, they should contact their care provider for assistance.

Preventing HIV Transmission/ Prevention with Positives

Background

In recent years, the rate of new HIV infections in the United States has remained stable in the range of 50,000 per year. Antiretroviral therapy (ART) not only improves the health of individuals on treatment but also substantially reduces the risk of transmitting HIV infection. It has become a critical component of efforts to prevent new infections (hence the saying, “treatment is prevention”), but it is not fully effective. Additionally, it remains true that only a minority of persons living with HIV infection in the United States is taking ART and a smaller proportion has maximal suppression of HIV viral load. Thus, behavioral and other risk-reduction interventions remain important aspects of HIV prevention. This chapter will focus primarily on interacting with patients around transmission risk behaviors, with the goal of reducing HIV transmission. This aspect of care is often referred to as “prevention with positives” (PWP).

For many years HIV, prevention efforts have been targeted primarily at HIV-uninfected individuals, but HIV-infected persons also must be a crucial focus for HIV prevention. Helping HIV-infected persons reduce their risks of transmitting HIV to others is an important aspect of medical care for HIV-infected patients. Most people with HIV infection want to prevent others from being infected with HIV, but they may practice sexual or injection-drug behaviors that put others at risk of infection.

Health care providers for HIV-infected patients can play a crucial role in prevention efforts, including but not limited to provision and monitoring of ART. Many HIV-infected individuals report that they want to discuss prevention with their health care providers; however, (according to multiple studies), one third to three fourths of HIV medical providers do not ask their patients about sexual behavior or drug use. Each patient visit presents an opportunity to provide effective prevention interventions, even in busy clinical settings.

It is clear that information alone, especially on subjects such as sexual activity and drug use, cannot be expected to change patients’ behavior. However, health care providers can help patients understand the transmission risk of certain types of behavior and help patients establish personal prevention strategies (sometimes based on a harm-reduction approach) for themselves and their partners. Some patients may have difficulty adhering to their safer sex goals. In these cases, referrals to mental health clinicians or other professional resources such as prevention case management may be helpful.

Patient-education needs are variable and must be customized. Providers must assess the individual patient’s current level of knowledge as part of developing a prevention plan. All the information that a patient needs cannot be covered during a single visit. A patient’s prevention strategy should be reinforced and refined at each visit with the clinician. Clinicians also should ask patients questions to determine life changes (e.g., a new relationship, a breakup, or loss of a job) that may affect the patient’s sexual or substance-use practices. If the patient can read well, printed material can be given to reinforce education in key areas, but it cannot replace a direct conversation with the clinician.

HRSA HAB Performance Measures

Percentage of patients with a diagnosis of HIV who received **HIV risk counseling** in the measurement year

(Adult and Adolescent measure)

Note: The U.S. Department of Health and Human Services is expected to publish guidelines on HIV prevention in the near future; those may contain recommendations that differ from the ones presented here.

National Prevention Intervention Efforts

The U.S. Centers for Disease Control and Prevention (CDC) has developed a prevention approach called High-Impact Prevention that focuses on populations at greatest risk of acquiring or transmitting HIV, using proven, scalable, and cost-effective interventions. Proven interventions include:

- HIV testing and linkage to care
- ART
- Prevention programs for people living with HIV and their partners
- Prevention programs for people at high risk of HIV infection
- Access to condoms and sterile syringes
- Screening and treatment for sexually transmitted diseases (STDs)
- Substance abuse treatment

The CDC has identified a number of evidence-based behavioral prevention interventions aimed at persons with HIV infection that meet criteria for efficacy and scientific rigor. These are conducted on the individual, group, or community level, and a number of them may be implemented in the treatment setting. A Compendium of these interventions can be accessed online at the CDC website (see www.cdc.gov/hiv/prevention/research/compendium/rr/index.html). Training and educational materials for effective intervention models can be found on the CDC-supported Diffusion of Effective Behavioral Interventions (DEBI) website (www.effectiveinterventions.org/en/Home.aspx).

Among the many examples of Prevention Intervention Programs with Demonstrated Efficacy in Treatment Settings on the CDC website are the following:

- **Options/Opciones Program:** The program features brief, 5-10 minute patient-centered discussions between patients and providers at each clinic visit using motivational interviewing techniques. Providers evaluate sexual and drug-use behaviors, assess the patient's readiness to change, and elicit methods from the patient on moving toward and maintaining safer behaviors. The provider and the patient develop an individually tailored plan, which the provider writes out on a prescription pad and gives to the patient.
- **Partnership for Health:** This intervention involves brief, 3-5 minute, one-on-one counseling sessions between the provider and the patient on self-protection, partner-protection, and disclosure. The approach features loss-framed messages that emphasize the risks or negative consequences of risky behavior. The provider then helps the patient develop a plan for risk reduction.
- **Positive Choice – Interactive Video Doctor:** This program involves an approximately 24-minute session during which HIV-infected patients complete the Positive Choice risk assessment on a laptop computer while waiting for scheduled visits with their providers. Based on the risk-assessment results, a video clip appears with the actor-portrayed Video Doctor who delivers interactive risk-reduction messages that are tailored to the patient's gender, risk profile, and readiness to change. The messages are delivered with motivational interviewing principles, using a patient-centered, empathetic and nonjudgmental approach. After the video session, the computer prints out an individualized educational sheet for the patient and an assessment sheet for the patient and the provider to use for follow-up.

The U.S. Preventive Services Task Force (USPSTF) has recommended high-intensity behavioral counseling to prevent STDs (including HIV) in persons at risk of these infections; these approaches also are being used in persons with HIV infection to reduce their risk of transmitting HIV. Effective high-intensity behavioral counseling typically comprises multiple sessions with either groups or individuals. Examples of these are included amongst the models presented on the CDC and DEBI websites.

Strategies for Brief, Effective Interventions by Providers

A number of strategies have been shown to be more effective than providing information alone. Effective and brief provider-initiated interventions often include the following elements:

- **Establish rapport** and provide services in an understanding, nonjudgmental manner. Patient educators, nurses, peer counselors, social workers, and mental health providers may be effective in discussing prevention strategies with patients.
- **Conduct a quick, detailed behavioral risk assessment:**
 - See the key areas of risk assessment and intervention listed in Table 1, below.
 - Assess where the patient's risk behavior lies along the risk continuum (described in chapter *Smoking Cessation*).
 - Correct misinformation and answer questions.
 - Assess the patient's readiness for behavior change (see "Stages of Change model," below).
 - Screen for and treat STDs: a positive STD test result can be a biologic marker of behavioral risk, and STDs may facilitate HIV transmission (see chapter *Initial and Interim Laboratory and Other Tests*).
 - Supply medications, condoms, and lubricant as needed.
- **Assess the patient's readiness for change** and approach any high-risk behavior in a step-wise manner, recognizing when the patient is ready for next steps. Such interventions may be carried out for 5-10 minutes per visit over a series of visits. The "Stages of Change" model and appropriate strategies include the following:
 - **Precontemplation:** The patient is not ready to change; reassess at subsequent visits.
 - **Contemplation:** The patient is considering a change in the future; discuss and help the patient to identify concrete next steps, such as a date for initiating change.
 - **Preparation:** The patient is ready to change soon; discuss a concrete action plan and connect the patient with appropriate resources as needed.
 - **Action:** The patient is actively engaged in changing behavior; continue to discuss and address challenges; offer encouragement.
 - **Maintenance:** The patient has made behavioral changes; continue to discuss and address challenges, offer encouragement and congratulations.
 - **(Relapse):** The patient has relapsed to previous risky behaviors; recognize the triggers and difficulties the patient had with maintenance and offer support and encouragement to try again when the patient is ready.
 - **Customize messages**, as each individual patient's needs are variable.
 - **Understand** that patients often have competing priorities and pressures involving mental health needs, relationships, finances, housing, employment, and other issues that may result in risky sexual and drug-use behaviors.

Prevention with Positives: Key Areas of Assessment and Intervention

These topics should be explored over time. Some sample questions and areas for intervention are presented in Table 1. More detailed discussions of topics follow this table.

Table 1. Components of a Detailed Risk Assessment, with Key Areas for Intervention

Topic	Sample Questions, Assessment, and Plan
General Risk Assessment	<p>Subjective/objective questions to ask:</p> <ol style="list-style-type: none"> 1. What do you know about HIV transmission? 2. What, if anything, are you doing that could result in transmitting HIV to another person? <p>Assessment and plan:</p> <ul style="list-style-type: none"> • Use this as an opportunity to help educate the patient on HIV transmission and to correct misinformation. • Place the patient's behaviors on a risk spectrum and try to prioritize the behaviors that are riskiest or the behaviors that the patient is most willing to address.
Sexual Practices	<p>Subjective/objective questions to ask:</p> <ol style="list-style-type: none"> 1. Tell me about any sexual activity since your last clinic visit. 2. What do you know about the HIV status of each sex partner? 3. Tell me about condom use during any sexual activity. 4. What has made it more difficult for you to use condoms during this sexual encounter or with this partner? 5. Do your sex practices differ with HIV-infected versus HIV-uninfected partners ("sexual positioning")? <p>See below for more on partner notification.</p> <p>Other information:</p> <ul style="list-style-type: none"> • Number of sex partners in the past 6 months • Gender of each partner • Type of relationship with each partner (main, casual, anonymous) • Type of sexual activity engaged with each partner • Safer and less-safe sexual practices with each partner • Substance use, including alcohol, associated with sex • Circumstances of risky sex behaviors (e.g., bars/clubs, anonymous partners, intoxication) <p>Assessment and plan:</p> <ul style="list-style-type: none"> • Assess the patient's level of risk of sexual transmission. • Assess the patient's willingness and ability to use condoms during each sexual encounter, particularly with partners who are HIV uninfected or of unknown HIV serostatus. • Assess the patient's ability to use condoms (male and/or female) and correct any misinformation. See information on how to use condoms below. • Supply the patient with condoms and lubricant. • If the patient is unwilling to use condoms, counsel that risk of transmission can be reduced by screening for and treating STDs, using abundant amounts of lubrication, avoiding concurrent drug use, avoiding the use of spermicides and douching, and by choosing less risky sexual activities. Additionally, serosorting, in which the HIV-infected person has sex only with other HIV-infected individuals, can prevent transmission to uninfected persons (note: this is <i>not</i> an effective strategy for persons who are HIV uninfected or are unsure of their serostatus).

Partner Notification	<p>Subjective/objective questions to ask:</p> <ol style="list-style-type: none"> 1. What are your thoughts and experiences talking with your partner(s) about your HIV infection? This may be one of the hardest things you have to do. 2. (If the patient has not disclosed to main partner[s]): How might you approach this? 3. Are you afraid for your safety if you tell your partner(s)? <p>Assessment and plan: ways to offer help for disclosure</p> <ul style="list-style-type: none"> • Local health departments may have partner services programs that help locate and notify partners in a confidential manner. • Providers and support staff can help disclose to partners with the patient present. • Providers and support staff can help disclose to partners without the patient present.
Antiretroviral Therapy (ART)	<ul style="list-style-type: none"> • ART has been shown to reduce the rate of HIV transmission in serodiscordant heterosexual couples by 96%. In other studies, lower levels of HIV in the blood (in particular, complete suppression of the HIV RNA through ART) have been associated with lower levels of HIV virus in genital secretions and with reductions in the rate of sexual transmission of HIV. • Current HHS guidelines recommend ART for all HIV-infected persons, both for their own health and to reduce risk of HIV transmission. • Close adherence to ART and continuous HIV suppression are likely to be key factors in making this an effective prevention tool; assess and reinforce adherence at every visit. • For a number of reasons, ART alone is not completely effective in preventing transmission; it should be viewed as one important tool in a broader approach to prevention. Be watchful for attitude shifts away from safer sexual and needle-sharing behaviors among patients who believe that ART protects them from transmitting HIV.
STD Screening and Treatment	<ul style="list-style-type: none"> • The presence of an STD suggests behaviors that can increase HIV transmission, and it is detrimental to the patient's health. • Additionally, some STDs may increase the risk of HIV transmission. • Screen all patients at baseline and regularly afterward, depending on their risk factors according to CDC and USPSTF guidelines. For example, screen men who have sex with men (MSM) every 3-6 months if multiple sex partners. • Routinely ask patients if they have symptoms of an STD and educate about the importance of seeking care if symptoms are present. • Depending on risk, it is recommended to screen for the following STDs (see chapters <i>Initial History</i> and <i>Initial and Interim Laboratory and Other Tests</i> for screening questions and lab tests): <ul style="list-style-type: none"> • Syphilis: Serologic test (e.g., RPR, VDRL) • Gonorrhea: For pharyngeal infections, use nucleic acid amplification test (NAAT) or culture of oral swab*; for rectal infections, use NAAT or culture of rectal swab*; for urethral or cervical or vaginal infections, use first-catch urine or urethral (male) or cervical (female) specimen for NAAT, or culture of urethral (male) or cervical (female) specimen • Chlamydia: For rectal infections, use NAAT or culture of rectal swab*; for urethral or cervical infections, use first-catch urine or urethral (men) or cervical or vaginal (women) specimen for NAAT; testing for pharyngeal chlamydial infection is not recommended although the test result often accompanies the GC pharyngeal NAAT result • Trichomonas: Wet mount (insensitive), culture, or NAAT on vaginal secretion • Herpes simplex virus (HSV): Type-specific HSV-2 antibody testing <p>Although hepatitis B and hepatitis C are not known to increase the risk of HIV infection, they may be transmitted sexually, and persons with risk factors (particularly MSM with risky sexual practices) should be screened regularly (see chapter <i>Initial and Interim Laboratory and Other Tests</i>).</p> <p>* NAAT is not yet approved for this indication by the U.S. Food and Drug Administration (FDA), though there is evidence that NAAT can accurately diagnose pharyngeal and rectal gonorrhea and chlamydia infections. Many local public health departments and other laboratories have received Clinical Laboratory Improvement Amendments (CLIA) waivers to perform these tests.</p>

Drug and Alcohol Risk Assessment	<p>Subjective/objective questions to ask:</p> <ol style="list-style-type: none"> 1. Tell me about any drug or alcohol use since your last clinic visit. 2. How do you think your drug or alcohol use affects your sexual behaviors? 3. What are your thoughts about quitting or cutting down on drug and alcohol use, and about separating it from sex? <p>See below for follow-up on needle-sharing practices.</p> <p>Assessment and plan:</p> <ul style="list-style-type: none"> • Assess the patient's level and circumstances of risk to target your intervention. • Emphasize that nasal straws or sniffers (e.g., for cocaine) should not be shared. • Assess the patient's readiness to quit or cut down on drug and alcohol use, and to separate these activities from sex. • Deliver messages tailored to the patient's readiness; for example, educate on the risks of harming oneself or others, facilitate a plan for harm reduction, or refer to rehabilitation/detoxification programs and centers.
Needle-Use Practices	<p>Subjective/objective question to ask:</p> <ol style="list-style-type: none"> 1. Tell me about any needle sharing since your last clinic visit. <p>Assessment and plan:</p> <ul style="list-style-type: none"> • After assessing the patient's risks and readiness, and if the patient is not ready for treatment (e.g., referral to detoxification programs or to buprenorphine and methadone programs for heroin users), the following messages for harm reduction can be offered: <ul style="list-style-type: none"> • Use only sterile needles and syringes, e.g., from pharmacies or syringe service (needle exchange) programs. (Provide information about local syringe service programs. Some are listed on the North American Syringe Exchange Network website at www.nasen.org.) • Never reuse or share needles, syringes, or drug preparation equipment because it leads not only to transmission of HIV, hepatitis B, and hepatitis C, but also to bacterial infections and abscesses. • Use new or disinfected cookers and new cotton filters to prepare drugs. • Clean the skin with a new alcohol swab before injecting. • If equipment must be reused, it should be cleaned properly with bleach or water. • Safely dispose of syringes in a sharps container (which can be a clean detergent or other container), then take them to a needle exchange program or pharmacy for disposal.
Mental Health Assessment	<p>Mental illnesses such as bipolar disorder, depression, and post-traumatic stress disorder can increase the chances of risky sexual and drug-use behaviors. Ask about mental health illnesses directly and pay attention to any symptoms that may indicate a psychiatric illness (e.g., manic episodes, depressive episodes, hallucinations).</p> <p>Subjective/objective questions to ask:</p> <ol style="list-style-type: none"> 1. Tell me about any previous diagnoses or hospitalizations for mental health illnesses. 2. Have you taken any medications for mental health illnesses? 3. Perform a depression screen: see chapter <i>Major Depression and Other Depressive Disorders</i>. <p>Assessment and plan:</p> <p>See section <i>Neuropsychiatric Disorders</i> for more information.</p>

Pregnancy Screening	Subjective/objective questions to ask: For women of childbearing potential: <ol style="list-style-type: none"> 1. Are you currently pregnant or wanting to become pregnant at some point in the future? 2. Have you missed any periods recently? Are you having any symptoms of pregnancy? 3. What are your thoughts and plans about birth control? For men with female sex partners: <ol style="list-style-type: none"> 1. What are your thoughts on having a baby with your partner? What are your thoughts about fathering? 2. What are your thoughts on using birth control with your partner? Assessment and plan: See chapter <i>Health Care of HIV-Infected Women Through the Life Cycle</i> .
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Sexual Transmission and Prevention of HIV

Begin the education process by learning what the patient and his or her immediate family members (if the family is aware of the patient's HIV status) believe about HIV transmission. Also be sure the patient understands how the virus is not transmitted (e.g., via sharing plates and eating utensils or using the same bathrooms) to allay any unnecessary fear.

Advise the patient not to share toothbrushes, razors, douche equipment, or sex toys to avoid transmitting HIV via blood or sexual secretions. This also will help prevent the transmission of other bloodborne or sexually transmitted diseases, including hepatitis C, from coinfecting patients. The patient should not donate blood, plasma, tissue, organs, or semen because these can transmit HIV to the recipient.

There is no reason why a person with HIV cannot have an active, fulfilling, and intimate sex life. However, the patient must be counseled properly about the risk of transmission. This discussion between the provider and patient should be client centered. This means that the provider should let the patient guide the discussion, starting from the patient's current point of knowledge and practice, always addressing any presenting concerns the patient may have prior to proceeding with a discussion about sexual

transmission and risk. The provider should ask open-ended questions, in a nonjudgmental manner, to elicit information about the patient's relationships, sexual behaviors, and current means of reducing transmission risk.

It is important to recognize that not every patient seeks the complete elimination of risk (e.g., via abstinence) but rather a reduction in risk, chosen after the options are discussed with the provider. The clinician may help the patient select and practice behaviors that are likely to be less risky. There are many methods for reducing risk, including the following:

- Disclosing HIV status
- Maintaining maximal suppression of HIV through ART
- Reducing the number of sex partners
- Using condoms, particularly for anal or vaginal intercourse (insertive or receptive)
- Avoiding drug use in conjunction with sex
- Using adequate lubrication to avoid trauma to genital or rectal mucosa

If the patient requires more extensive counseling to support behavioral changes, the provider should refer the patient to support groups or prevention case management to meet those needs. Certainly, if the patient is dealing with a dual or triple diagnosis (including substance abuse or mental illness), a referral to address those needs is indicated.

Partner Notification and Partner Services

A good way to begin a discussion about HIV prevention and transmission is with an inquiry about any previous experiences disclosing to partners. The provider then can ask whether the patient currently has a need to disclose to one or more partners and whether he or she is ready and motivated to share information about HIV status. The provider should prompt patients to consider several questions about disclosure, including how they might approach the discussion, how their partners might react, what information they might offer their partners, whether partners are likely to keep their status confidential, and whether they have any concerns about personal safety (e.g., owing to fear of a violent reaction). If patients fear violence or retaliation or are not ready to share their status but want their partners to know, the provider may offer assistance with partner services, for example through the local health department, through which partners can be notified and linked to services in a confidential manner. As an alternative, patients may want the provider to talk with their partners, and that option can be offered as well. See the CDC website (www.cdc.gov/nchhstp/partners/Partner-Services.html) for information on partner services.

Antiretroviral Therapy

ART that results in maximal HIV suppression is an important means of HIV prevention. In serodiscordant heterosexual couples, one randomized controlled trial showed that ART reduced the risk of sexual transmission of HIV by 96%. Similar study data for MSM, injection drug users, and other HIV risk groups do not exist, but multiple other lines of evidence suggest that effective ART sharply reduces risk of HIV transmission. Thus, ART should be offered to all HIV-infected persons, both to benefit their own health and to reduce risk of HIV transmission to others, as recommended

in HHS guidelines. Support patients' adherence to ARVs in order to optimize the effectiveness of ART as both treatment and prevention.

Note that ART does not eliminate HIV transmission risk. In some individuals, there can be substantial discrepancies between HIV RNA levels in the serum and the sexual fluids. There have been case reports of HIV transmission from HIV-infected individuals who had maximal virologic suppression on ART. Thus, other behavioral and biologic risk-reduction approaches (e.g., screening for and offering interventions or treatment for risky sexual behaviors, substance use, depression, STDs, and other factors listed in Table 1) are important aspects of prevention in patients taking ART, as in patients not taking ART.

Helping Patients Reduce the Risk of Sexual Transmission

Standard Condom Use

Make sure that the patient understands how HIV is transmitted and which types of sexual acts are more and less risky than others. For vaginal or anal sex, correct use of latex or polyurethane condoms reduces the risk of HIV transmission considerably. Patients should be encouraged to use condoms as much as possible. For HIV-infected individuals, condom use is effective in reducing the risk of contracting another illness (such as hepatitis C or another STD) and the (apparently low) risk of becoming reinfected with another strain of HIV. It should be noted that condoms are less effective in reducing the transmission of organisms such as human papillomavirus (HPV) and HSV, which may result from viral shedding from skin. In the event of allergy to latex or other difficulty with latex condoms, polyurethane male or female condoms may be substituted. "Natural skin" or "lambskin" condoms are not recommended for HIV prevention.

Of course, condoms must be used correctly to be highly effective in preventing HIV transmission. Be sure that the patient knows exactly how to use a condom. Table 2, in the Appendix, provides instructions for condom use.

Advise patients to avoid using nonoxynol-9 (N-9) spermicides. Data suggest that N-9 may increase risk of HIV transmission during vaginal intercourse and can damage the rectal lining. N-9 never should be used for anal intercourse.

For patients who complain about lack of sensitivity with condom use, the following techniques may help:

- Apply a drop of lubricant inside the condom (not more, because it increases the risk that the condom will come off).
- Use polyurethane condoms instead of latex because they conduct heat and may feel more natural.
- Use insertive (female) condoms, which are not as restrictive to the penis.
- Use specially designed condoms that do not restrict the top of the penis (e.g., Inspiral, Xtra Pleasure).

For patients who are unable or unwilling to use condoms, the following suggestions may help reduce HIV transmission risk:

- Use plenty of lubricant to reduce friction and microtrauma, which create portals of entry for the virus.
- Avoid spermicides that damage the vaginal or anorectal linings.
- Avoid douching products.
- Avoid recreational drugs, especially methamphetamine, that impair the ability to maintain “safer” sexual behaviors.
- Avoid the use of drugs such as nitrates (poppers) that enhance blood flow to the genitals.

Insertive (Female) Condom Use

The insertive “female” condom may be used for vaginal or anal intercourse. It is a thin polyurethane pouch with a flexible ring at the opening, and another unattached flexible ring that sits inside the pouch to keep it in position in the vagina (for use in the anus, the inner ring must be removed and discarded). The female condom may be an option for women whose male partners will not use male condoms or for couples who do not like standard condoms. Female condoms are more expensive than male condoms, but may be procured at a lower cost at some health departments or Planned Parenthood clinics. They generally are less well known to patients and may be unacceptable to some women whose culture or religion prohibits or discourages touching one’s own genitals. Note that the female condom cannot be used at the same time as a male condom.

Be sure the patient knows how to use the insertive condom before she or he needs it; after teaching, encourage practice when alone at home and unhurried. Women who have used the diaphragm, cervical cap, or contraceptive sponge may find it easy to use the female condom. Illustrated directions are included in each box of insertive condoms. Instructions on the use of insertive condoms are provided in Table 3, in the Appendix.

Oral Sex

Although there is evidence that some people have become infected through receptive oral sex, the risk of HIV transmission via oral sex, in general, is much lower than the risk of transmission by vaginal or anal sex. Thus, most public health and prevention specialists focus their attention on riskier sexual and drug-use behaviors. However, because HIV transmission can occur with oral sex, clinicians should address this issue with patients and help them make informed decisions about risk reduction. Sores or lesions

in or around the mouth or on the genitals may increase the risk of HIV transmission, as may a concurrent STD. Patients (and their partners) should avoid oral-genital contact if they have these conditions. Similarly, patients and partners can further reduce risk by not brushing or flossing teeth before oral sex. Individuals who wish to further reduce the risk of HIV transmission during oral sex may use barriers such as condoms, dental dams, and flexible plastic nonporous kitchen wrap.

Individuals who smoke crack cocaine often develop open burns, cracked lips, or damaged mucous membranes inside the mouth and thus may be at elevated risk of HIV transmission via oral sex. HIV-infected crack users should be counseled about the risk of transmitting HIV to uninfected partners through those portals of entry during oral sex and should receive risk-reduction counseling. In addition, they (or their partners) may benefit from techniques such as insulating the end of the crack pipe to reduce burns while smoking (e.g., with a rubber band or spark plug cap) and avoiding the brittle or sharp-edged copper scrubbing pads used as screens in the crack pipe.

Influence of Substance Use on Sexual Behavior

Alcohol and drug use can contribute significantly to the risk of sexual transmission of HIV, because of behavioral disinhibition. While intoxicated, substance users may, for example, forgo condom use, practice riskier sexual behaviors, have multiple partners, or use erectile dysfunction agents to sustain sexual activity. Addressing substance use issues is an important aspect of PWP. Patients should be assessed for HIV transmission risks associated with alcohol and injection or noninjection drug use, including crystal methamphetamine, in the context of their sexual behaviors (for injection drug use, see below). As always, it is important to approach the patient in a nonjudgmental manner. If

alcohol or other drugs are posing barriers to practicing safer behaviors, the provider should counsel the patient to reduce or avoid substance use before engaging in sex, or refer the patient to prevention case management for more specialized risk reduction. Often, the provider can help the patient identify methods for reducing HIV transmission risk, including means that do not require abstaining from alcohol and drug use.

Injection Drug Use and Prevention of HIV

Clinicians should discuss substance use, including steroid use, and reinforce the patient's understanding of the adverse effects that these drugs can have on the body and the immune system. Assess whether referral for treatment is appropriate, and be knowledgeable about referral resources and mechanisms. If the patient is using injection drugs (including steroids and other hormones), emphasize the fact that HIV is readily transmitted by sharing needles and other injection equipment and that reusing or sharing needles and syringes can cause additional infections (e.g., endocarditis, hepatitis C). Assess the patient's readiness to change his or her drug injection practices, and refer to drug treatment programs as appropriate. Refer to an addiction counselor for motivational interviewing or other interventions, if available. After completion of substance abuse treatment, relapse prevention programs and ongoing support will be needed. If the patient continues to use needles, discuss safer needle-use practices (Table 1) and consider referral to a syringe service (needle exchange) program, if one is available, so that syringes and needles are not reused. A partial listing of needle exchange sites may be found on the North American Syringe Exchange Network website at www.nasen.org, although many states either do not have facilities or are prohibited from listing them. Local harm-reduction activists may be

aware of specific programs for obtaining clean needles and syringes. Patient-education flyers on safer injection practices, safer stimulant use, overdose prevention, and other topics are available on the Midwest AIDS Education and Training Center website (www.uic.edu/depts/matec/resource.html).

Noninjection Drug Use and Prevention of HIV Transmission

Exposure to HIV through contaminated blood may occur with the use of noninjection drugs; for example, by sharing cocaine straws or sniffers through which cocaine is inhaled. These straws easily can penetrate fragile nasal mucosa and become contaminated with blood from one user before being used by another individual, who may then experience mucous membrane exposure or even a cut or break in the mucous membrane from the bloody object. Straws or sniffers should not be shared.

Tattoo, Piercing, and Acupuncture Equipment

Patients should be aware of the risk of contamination of tattoo equipment, inks, and piercing equipment, and they should avoid situations wherein they might either transmit HIV or pick up other bloodborne pathogens. Acupuncturists generally use sterile needles, but clients should verify that before using their services.

Perinatal HIV Transmission

HIV-infected women can have healthy pregnancies, with good health outcomes for both mother and baby. For this to occur, women must know their HIV status as early as possible, preferably before becoming pregnant, and must receive effective ART. Although intervention to reduce the risk of perinatal infection is most effective if begun early in pregnancy, or preferably before pregnancy, it may be beneficial at any point

in the pregnancy, even as late as during labor. For further information, see chapter *Reducing Perinatal HIV Transmission*.

Preexposure Prophylaxis (PrEP)

Preexposure prophylaxis (PrEP) refers to the use of oral or topical ARVs before HIV exposure with the goal of preventing HIV infection. Studies have evaluated PrEP strategies using either oral tenofovir + emtricitabine (Truvada), oral tenofovir, or vaginal tenofovir to prevent sexual acquisition of HIV in MSM and high-risk heterosexually active women and men. Most have shown efficacy (ranging from about 40% to 75%) in reducing infection risk, but two others have not demonstrated protective benefit. A study of PrEP using tenofovir in injection-drug users also showed a reduction in HIV infections in the tenofovir group (a 49% reduction in incidence). In all studies, the effectiveness of PrEP has been strongly related to the study participants' adherence to the PrEP medication. It should be noted that, in these PrEP studies, the ARV prophylaxis was given in conjunction with other risk-reduction interventions, including counseling, condom provision, and STD testing and treatment.

The CDC has issued interim guidelines on the use of oral tenofovir-emtricitabine as PrEP in MSM, heterosexually active adults, and injection-drug users (see "References," below); these guidelines offer recommendations for PrEP screening and use, as well as ongoing monitoring for adherence, safety, and HIV infection. They emphasize that PrEP should be delivered in the context of a comprehensive package of health and prevention services. In 2012, the FDA approved the fixed-dose combination tenofovir/emtricitabine (Truvada) to reduce the risk of sexually acquired HIV-1 in adults at high risk; it has not yet approved an indication for PrEP in injection-drug users.

U.S. Public Health Service (PHS) guidelines for PrEP use are currently in development.

Postexposure Prophylaxis for Nonoccupational HIV Exposure

Postexposure prophylaxis (PEP) may be considered for certain sexual exposures, sexual assaults, and other nonoccupational exposures to HIV. As with occupational PEP, a risk assessment must be completed and PEP medications, if indicated, must be started as soon after exposure as possible. The risks and toxicities of ARV drugs must be weighed against potential benefits, and the client's informed consent must be obtained. For further information, see chapter *Nonoccupational Postexposure Prophylaxis*.

Appendix

Table 2. Instructions for Use of Standard Condoms
<ul style="list-style-type: none"> • Use a new latex or polyurethane condom with each act of sex (oral, anal, or vaginal). Make sure that the condom is undamaged, and that its expiration date has not passed. • Carefully handle the condom to avoid damage (e.g., from fingernails, teeth). • Being sure that the condom roll faces out, unroll the condom onto the erect penis before any genital contact with partner. • Ensure that the tip of the condom is pinched when applying it to the top of the penis, to eliminate air in the tip that could cause breakage during ejaculation. • Use only water-based lubricants with latex condoms. Oil-based lubricants (such as mineral oil, cooking oil, massage oil, body lotion, and petroleum jelly) can weaken latex or cause it to break, although they are fine with the use of polyurethane condoms. Adequate lubrication during intercourse helps reduce the risk of condom breakage.

Table 3. Instructions for Use of Insertive (Female) Condoms

Vaginal Intercourse
<ul style="list-style-type: none"> • Open the pouch by tearing at notched edge of packet, and take out the female condom. Be sure that the lubricant is evenly distributed on the inside by rubbing the outsides together. • Find a comfortable position, such as standing with one foot on a chair, sitting with knees apart, or squatting. Be sure the inner ring is inside, at the closed end of the pouch. • Hold the pouch with the open end hanging down. While holding the outside of the pouch, squeeze the inner ring with your thumb and middle finger. Still squeezing, spread the labia with your other hand and insert the closed end of the pouch into the vagina. • Now, put your fingers into the pouch itself, which should be inside the vagina, and push the inner ring and the pouch the rest of the way up into the vagina with your index finger. Check to see that the front side of the inner ring is just past the pubic bone. The back part of the inner ring should be up behind the cervix. The outer ring and about an inch of the pouch will be hanging outside the vagina. • Until you and your partner become comfortable using the female condom, use your hand to guide the penis into the vagina, keeping it inside the pouch. If, during intercourse, the outer ring is pushed inside the vagina, stop, remove the female condom, and start over with a new one. Extra lubricant on the penis or the inside of the female condom may help keep this from happening. • After intercourse, take out the condom by squeezing and twisting the outer ring to keep the semen inside the pouch. Throw away in a trash can; do not flush. Do not reuse. • More information is available on the Planned Parenthood website (www.plannedparenthood.org).
Anal Intercourse
<ul style="list-style-type: none"> • Remove the inner ring and discard it. Put the female condom on the penis of the insertive partner and insert the condom with the penis, being careful not to push the outer ring into the rectum. The outer ring remains outside the anus, for ease of removal after ejaculation.

Immunizations for HIV-Infected Adults and Adolescents

Background

Immunocompromised individuals are at higher risk of acquiring many types of infections compared with immunocompetent people. Although HIV-infected persons could benefit greatly from immunization against preventable infections, little specific research on the effectiveness of immunizations in this population has been completed. In general, vaccines have better efficacy in HIV-infected patients when immune function is relatively well preserved, notably when the CD4 count is >200 cells/ μL . Persons with advanced immunodeficiency may have an impaired humoral response, and may not respond to vaccines, or they may require supplemental doses to develop serologic evidence of protection. If possible, vaccines should be administered before the CD4 count decreases to <200 cells/ μL ; if given when the CD4 count is <200 cells/ μL , consideration should be given to repeating the vaccination when the CD4 count increases to >200 - 300 cells/ μL (unless there is evidence of immunity).

Live vaccines generally should not be administered to individuals with HIV infection, particularly those with advanced immunodeficiency, unless the anticipated benefits of vaccination clearly outweigh the risks.

Administration of vaccines can be associated with a transient rise in plasma HIV RNA.

Recommendations about vaccination for patients with HIV infection are presented in Table 1.

HRSA HAB Performance Measures

Percentage of patients, aged 6 months and older seen for a visit between October 1 and March 31, who received an **influenza immunization** OR who reported previous receipt of an influenza immunization

(All-Age measure)

Percentage of patients with a diagnosis of HIV who completed the **vaccination series for hepatitis B**

(Adult and Adolescent measure)

Percentage of patients with a diagnosis of HIV who ever received **pneumococcal vaccine**

(Adult and Adolescent measure)

Table 1. Vaccine Recommendations

Vaccine Type	Recommendation
Pneumococcal Pneumococcal (polysaccharide) (PPV23) Pneumococcal 13-valent conjugate (PPV13)	<ul style="list-style-type: none"> Recommended for all. If CD4 count is <200 cells/μL, may be less effective; consider revaccination when CD4 count increases in response to ART. Two types of pneumococcal vaccine; both should be given, as follows. 1 dose as soon as possible after HIV diagnosis (or PCV13 may be given first, see below); revaccinate 5 years after initial vaccination. For those who received 1-2 doses of PPV23 before age 65, repeat at age ≥ 65 if ≥ 5 years since their previous dose. PPV23 should not be given <8 weeks after PPV13 (see below). 1 dose recommended for all HIV-infected adults; timing varies according to whether PPV23 has been given: <ul style="list-style-type: none"> No previous pneumococcal vaccination: <ul style="list-style-type: none"> 1 dose PCV13 followed by PPV23 ≥ 8 weeks after PCV13. (If CD4 <200 cells/μL, PPV23 can be offered ≥ 8 weeks after PCV13 or can await increase of CD4 to >200 cells/μL.) Previous PPV23 vaccination: <ul style="list-style-type: none"> 1 dose of PCV13, given ≥ 1 year after last receipt of PPV23.
Hepatitis A Virus (HAV)	<ul style="list-style-type: none"> Recommended, for persons with chronic liver disease, injection drug users, men who have sex with men, international travelers, and hemophiliacs. Consider for all, unless there is serologic evidence of previous disease. Serologic response (HAV IgG Ab) should be checked 1 month after completion of series, and nonresponders should be revaccinated. 2 doses (Havrix: 0, 6-12 months; Vaqta: 0, 6-18 months).
Hepatitis B Virus (HBV)	<ul style="list-style-type: none"> Recommended for all, unless there is evidence of immunity (HBV surface Ab+) or active HBV infection (HBV surface Ag+, or HBV core Ab+ and evidence of HBV activity). Many experts recommend giving a high dose of HBV vaccine (40 mcg), as is standard for hemodialysis patients; this may improve immunologic response in HIV-infected patients. Most HIV-infected patients with isolated HBV core Ab+ (without HBV viremia) are not immune and should receive a complete series of HBV vaccine. Anti-HBV surface Ab titers should be checked 1 month after completion of vaccine series. Patients whose titer level is ≤ 10 IU/mL should be revaccinated. Standard dosing schedule is 3 doses (0, 1, and 6 months). If 40 mcg is given, the recommended schedule is 3 doses of Recombivax HB at 0, 1, and 6 months or 4 doses of Engerix-B at 0, 1, 2, and 6 months.
Influenza (inactivated vaccine)	<ul style="list-style-type: none"> Recommended (yearly). Vaccination is most effective among persons with CD4 counts of >100 cells/μL and HIV RNA of <30,000 copies/mL. In patients with advanced disease and low CD4 cell counts, inactivated vaccine may not produce protective antibodies. A second dose of vaccine does not improve response in these patients. Live, attenuated cold-adapted vaccine (LAIV, FluMist) is not recommended for use in patients with HIV infection as the efficacy of the vaccine in this population has not been evaluated. Close contacts of severely immunocompromised persons (including household members and health care personnel) should not receive live, attenuated influenza vaccine.

Vaccine Type	Recommendation
Tetanus, Diphtheria (Td); Tetanus, Diphtheria, Pertussis (Tdap)	<ul style="list-style-type: none"> Recommended (booster is recommended every 10 years in adults; or, if potential exposure [wound], after 5 years). To protect against pertussis, substitute single dose of Tdap for Td booster in all patients aged 19-65 who have not received Tdap previously.
Measles, Mumps, Rubella (MMR)	<ul style="list-style-type: none"> Live vaccine is contraindicated for use in patients with severe immunosuppression (CD4 count of <200 cells/μL). Recommended for all nonimmune persons with CD4 counts of \geq200 cells/μL.
Varicella-Zoster (VZV) Varicella vaccine (primary immunization) Zoster vaccine	<ul style="list-style-type: none"> Two doses (0, 3 months). Live vaccine; contraindicated for use in patients with severe immunosuppression (CD4 count of <200 cells/μL). Consider for HIV-infected, VZV-seronegative persons with CD4 counts of \geq200 cells/μL. If vaccination results in infection with attenuated virus, treat with acyclovir. Transmission of vaccine virus from vaccine recipients to susceptible individuals is possible; vaccine recipients should avoid close contact with high-risk susceptible individuals for 6 weeks after vaccination. One dose. Live vaccine; contraindicated in persons with AIDS or other clinical manifestations of HIV infection. Consider for select patients aged >50 with CD4 counts of >200 cells/μL and with evidence of varicella immunity (if no evidence of varicella immunity, give primary varicella vaccination). Limited data show safety and immunogenicity in this group. Transmission of vaccine virus to susceptible contacts is possible.
Human Papillomavirus (HPV)	<ul style="list-style-type: none"> Two vaccines: <ul style="list-style-type: none"> Gardasil includes HPV strains 16 and 18 (oncogenic) and 6 and 11 (wart causing); approved for use in women and men. Cervarix: includes HPV strains 16 and 18; approved for use in women. Gardasil or Cervarix recommended for females aged 9-26. Gardasil vaccine recommended for males aged 9-26. Not contraindicated for use in HIV-infected individuals; limited data on efficacy; may be less effective if CD4 count is <200 cells/μL.
Meningococcal	<ul style="list-style-type: none"> Two doses (0, \geq8 weeks). Recommended if risk factor is present (e.g., college freshmen living in dormitory, military recruits, asplenia, complement component deficiency, travel to or residence in area with outbreaks,* occupational exposure).

Abbreviations: Ab = antibody; Ag = antigen; ART = antiretroviral therapy

* In 2012, the New York City Department of Health and Mental Hygiene reported ongoing outbreak of meningococcal meningitis in men who have sex with men (MSM) and recommended vaccination for those with recent or future exposure risk. Many health departments in other areas have recommended vaccination of MSM, including HIV-infected MSM, who recently had or expect to have close contact with a man who is known to be, or could potentially be, from New York City.

Immunizations for HIV-Infected Patients Traveling to Developing Countries

Routine vaccinations should be reviewed and updated before travel. All patients traveling to other countries should be evaluated for both routine and destination-specific immunizations and prophylaxes. Inactivated (killed) and recombinant vaccines (e.g., diphtheria-tetanus, rabies, hepatitis A, hepatitis B, Japanese encephalitis) should be used for HIV-infected persons just as they would be used for HIV-uninfected persons anticipating travel. For further information, see the U.S. Centers for Disease Control and Prevention (CDC) webpage (wwwnc.cdc.gov/travel). Recommendations specific to HIV-infected travelers are located in "The Immunocompromised Traveler" under the section called "Advising Travelers with Special Needs." Select the "Traveler's Health" option for regional travel documents and information on outbreaks.

Decision making about immunization for the HIV-infected traveler should take into consideration the traveler's current CD4 cell count, history of AIDS-defining illness, and clinical manifestations of symptomatic HIV. In the CDC recommendations, asymptomatic HIV-infected persons with CD4 counts of 200-500 cells/ μ L are considered to have limited immune deficits, whereas patients with CD4 counts of >500 cells/ μ L are considered to have no immunologic compromise. For patients taking antiretroviral therapy, current CD4 counts rather than nadir counts should be used in deciding about immunizations. The CDC recommends that newly diagnosed, treatment-naive patients with CD4 counts of <200 cells/ μ L delay travel until after immunologic reconstitution with antiretrovirals to minimize risk of infection and immune reconstitution illness during travel.

The following should be noted about specific vaccinations:

- Inactivated (killed), enhanced-potency polio and typhoid vaccines should be given instead of the live, attenuated forms. In adults aged >18 , vaccinate 8 weeks before travel to allow time for the initial 2 doses of polio vaccine.
- Measles or measles, mumps, and rubella (MMR; omit if patient has evidence of immunity) should not be given to severely immunocompromised patients. Instead, immune globulin should be given to measles-susceptible, severely immunocompromised persons traveling to measles-endemic countries.
- Yellow fever vaccine is a live-virus vaccine with uncertain safety and efficacy for HIV-infected persons, and it should be avoided if possible. Travelers with asymptomatic HIV infection and relatively high CD4 counts who cannot avoid potential exposure to yellow fever should be offered the choice of vaccination. If travel to a zone with yellow fever is necessary and vaccination is not administered, patients should be advised about the risk of yellow fever, instructed about avoiding the bites of vector mosquitoes, and provided with a vaccination waiver letter (though travelers should be warned that not all countries accept waiver letters).
- The influenza season in the Southern Hemisphere is April through September, but in the tropics, influenza is a year-round infection. Immunocompromised patients should be protected on the basis of influenza risk at the destination. HIV-infected patients should not be given live intranasal influenza vaccine.

Preventing Exposure to Opportunistic and Other Infections

Background

Persons with HIV infection are more susceptible than others to certain infections. HIV-infected persons may come into contact with opportunistic pathogens in the course of various aspects of their daily activities. Pets, children, personal and sexual contacts, and food and water, as well as involvement in occupational tasks, recreation, hobbies, and other activities all potentially can expose an HIV-infected person to opportunistic pathogens, some of which are ubiquitous and cannot be avoided. Among the ubiquitous pathogens are *Candida*, *Mycobacterium avium*, *Pneumocystis jiroveci*, and human herpesvirus 6 and 7. Exposure to other opportunistic pathogens may be minimized if patients are aware of the risks.

The following tables group opportunistic pathogens by type of exposure. Mechanisms of transmission and recommendations for avoidance are outlined. Note that a number of infections can be transmitted by several of these modes.

For information about vaccinations, see chapter *Immunizations for HIV-Infected Adults and Adolescents*; for opportunistic infection (OI) prophylaxis, see chapter *Opportunistic Infection Prophylaxis*.

Topics:

- Water related
- Food associated
- Environmental
- Respiratory and bodily contact
- Associated with sexual contact
- Injection drug use associated
- Other bloodborne related
- Pet and animal related
- Contact with children
- Travel related

Water Related	
Pathogens	<ul style="list-style-type: none"> • Hepatitis A virus (HAV) • <i>Cryptosporidium</i> • <i>Shigella</i> • <i>Campylobacter</i> • <i>Amoeba</i> • <i>Giardia</i> • <i>Isospora</i> • Microsporidia
Transmission	<ul style="list-style-type: none"> • Infection occurs through drinking contaminated water or eating produce or other food that has been washed in contaminated water. • Water ingested accidentally during recreation also can make people sick.
Recommended avoidance measures	<ul style="list-style-type: none"> • To decrease exposure from water in developing countries, take the following precautions: <ul style="list-style-type: none"> • Do not drink tap water or use it to brush teeth. • Avoid ice that is not made from bottled water. • Avoid raw fruits or vegetables, as they may have been washed in tap water. • Bring tap water to a rolling boil for at least 1 minute before consuming. If this is not possible, treatment with iodine or chlorine, especially in conjunction with filtering, reduces risk of infection. • Additional recommendations, include the following: <ul style="list-style-type: none"> • Avoid drinking untreated water. • When choosing a home water filter, especially for filtering untreated water, be aware that not all filters remove the pathogens listed above. • Do not drink water from lakes or rivers. • Avoid swimming in water that may be contaminated with stool. • Avoid swallowing water during recreational activities (lakes, rivers, saltwater beaches, pools, hot tubs, and ornamental fountains may be contaminated with <i>Cryptosporidium</i>). • In the event of a cryptosporidiosis outbreak in the municipal water supply, boil tap water for at least 1 minute to eliminate risk of infection. • <i>Cryptosporidium</i> may be present in municipal water outside outbreak settings, though the magnitude of this risk is unknown. Some HIV-infected patients may choose to take precautions to decrease risk. • Be aware that bottled water may be contaminated with <i>Cryptosporidium</i>. • See the discussion of travel-related topics, below.

Food Associated	
Pathogens	<ul style="list-style-type: none"> • <i>Toxoplasma</i> • <i>Salmonella, Shigella, Campylobacter</i> (enteric infections) • <i>Listeria</i> • <i>Cryptosporidium</i> • Other enteric pathogens
Transmission	<ul style="list-style-type: none"> • Exposure may occur through eating or handling contaminated food.
Recommended avoidance measures	<ul style="list-style-type: none"> • Always wash hands before preparing and consuming food. • Wash hands, cutting boards, counters, and utensils thoroughly after contact with uncooked foods. • Do not allow raw meat or eggs to come into contact with other foods. • Wash produce thoroughly. • Cook meat and poultry to an internal temperature of 165-170°F. It is safest to confirm temperature with a thermometer. Meat that is no longer pink inside likely has reached a temperature of 165°F. • Avoid raw or unpasteurized milk, including goat milk, and foods that contain unpasteurized milk or milk products. • Avoid foods that might contain raw egg (e.g., Hollandaise sauce, Caesar salad dressing, some mayonnaises, uncooked cake and cookie batter, eggnog, homemade ice cream). Pasteurized eggs can be used safely in recipes that call for raw egg. • Avoid eating raw or lightly steamed shellfish. • Avoid eating raw seed sprouts, as these may be contaminated with enteric pathogens. • Avoid foods from street vendors, especially in developing countries. • Be aware that unpasteurized juices may be contaminated with <i>Cryptosporidium</i>. • Rates of infection with <i>Listeria</i> are low, but HIV-infected people who are severely immunocompromised are at increased risk. • HIV-infected persons who wish to decrease their risk of listeriosis should take the following precautions: <ul style="list-style-type: none"> • Avoid soft cheeses including feta, brie, camembert, blue-veined, and Mexican-style cheeses such as queso fresco unless they are clearly labeled as pasteurized. Hard cheeses, processed cheeses, cream cheese, cottage cheese, and yogurt generally are safe. • Before eating leftover foods or ready-to-eat foods, such as hot dogs, cook them until they are steaming hot. • Avoid foods from deli counters, such as prepared meats, salads, and cheeses, or heat these foods until steaming hot before eating them. • Avoid refrigerated pâté, or heat until steaming hot. Canned or shelf-stable pâté generally is safe. • Avoid refrigerated smoked seafood, unless it is part of a cooked dish. Canned or shelf-stable smoked seafood generally is safe. • Also see information on travel-related infections, below.

Environmental	
Pathogens	<ul style="list-style-type: none"> • <i>Toxoplasma gondii</i> • <i>Cryptosporidium</i> • <i>Coccidioides</i> • <i>Histoplasma capsulatum</i> • <i>Cryptococcus neoformans</i> • <i>Aspergillus</i>
Transmission	<ul style="list-style-type: none"> • <i>Cryptosporidium</i> and <i>Toxoplasma</i> may be present in soil and sands, and infection can occur through handling soil during gardening or playing in or cleaning sandboxes. • Infection with <i>Coccidioides</i> and <i>Histoplasma</i> occurs with inhalation of fungal spores that become airborne owing to disturbance of contaminated soil.

Environmental	
Recommended avoidance measures	<ul style="list-style-type: none"> • Wash hands thoroughly after contact with soil or sand. • Endemic fungi cannot be completely avoided in certain geographic areas; however, avoiding high-risk activities can decrease risk of infection. • In endemic coccidioidomycosis areas, avoid exposure to soil disturbance such as that which occurs during dust storms and at excavation and construction sites. • Risk of <i>Aspergillus</i> infection also may be decreased by avoidance of dusty environments. • Patients with CD4 counts of <150 cells/μL should avoid activities that put them at increased risk of exposure to <i>Histoplasma</i> in endemic areas, such as: <ul style="list-style-type: none"> • Cleaning, remodeling, or demolishing old buildings • Disturbing soil beneath bird roosting sites • Cave exploration • Other contact with bird or bat droppings • Limiting exposure to bird droppings may decrease risk of infection with <i>C. neoformans</i>.

Respiratory and Bodily Contact	
Pathogens	<ul style="list-style-type: none"> • <i>Mycobacterium tuberculosis</i> • Enteric pathogens • Influenza • Varicella-zoster virus (VZV)
Transmission	<ul style="list-style-type: none"> • Tuberculosis (TB) is transmitted when a person with pulmonary or laryngeal TB coughs, sneezes, shouts, or sings, generating infected droplets that are inhaled by a susceptible person. • HIV-infected persons working or residing in certain environments, such as hospitals, nursing homes, homeless shelters, and correctional institutions, may become exposed to TB. • Influenza virus is spread by exposure to infected respiratory droplets or contaminated surfaces. • VZV is transmitted through contact with aerosolized respiratory droplets or by contact with skin lesions. • Many respiratory and enteric pathogens may be spread by contact with contaminated fomites.
Recommended avoidance measures	<ul style="list-style-type: none"> • HIV-infected persons should be aware of the increased risk of TB infection associated with certain environments. The following measures decrease risk of infection: <ul style="list-style-type: none"> • In settings with a high risk of TB transmission, patients with known or suspected TB should be physically separated from others. • All HIV-infected persons should be tested for latent TB infection. • All HIV-infected patients with latent TB infection (LTBI) should receive a complete course of LTBI treatment. • HIV-infected persons with a history of significant TB exposure should be treated presumptively for LTBI regardless of the results of LTBI testing, once active infection has been ruled out. • Bacillus Calmette-Guérin (BCG) vaccination is not recommended in the United States, and it is contraindicated for HIV-infected persons. • People susceptible to VZV should avoid persons with active chickenpox or herpes zoster (shingles). • VZV-susceptible, HIV-negative household contacts should be vaccinated against VZV, so that they will not transmit VZV to their HIV-infected contact. • Frequent handwashing can reduce risk of diarrhea in HIV-infected persons.

Associated with Sexual Contact		
Pathogens	<ul style="list-style-type: none"> • HIV • Hepatitis B virus (HBV) • Hepatitis C virus (HCV) • Hepatitis A virus (HAV) • Human papillomavirus (HPV) • Cytomegalovirus (CMV) • Herpes simplex virus (HSV) • Syphilis • <i>Chlamydia</i> • <i>Gonorrhea</i> • <i>Trichomonas</i> • Lymphogranuloma venereum (LGV) serovars of <i>Chlamydia trachomatis</i> • <i>Cryptosporidium</i> • <i>Shigella</i> • <i>Campylobacter</i> • <i>Amoeba</i> • <i>Giardia</i> • <i>Isospora</i> • Microsporidia 	
Transmission	<ul style="list-style-type: none"> • Depending on the pathogen, infection may be transmitted by exchange of body fluids, by skin-skin contact, or by oral-fecal contact. • Sexually transmitted diseases (STDs) can occur at genitals, rectum, or mouth, depending on sexual practices. • A number of enteric pathogens can be transmitted during sex (by oral-fecal contact). 	
Recommended avoidance measures	<ul style="list-style-type: none"> • Male latex condoms, when used consistently and correctly: <ul style="list-style-type: none"> • Are highly effective in preventing sexual transmission of HIV and many other STDs, including syphilis, chlamydia, gonorrhea, and trichomoniasis. • Decrease risk of acquiring HSV-2, HPV, CMV, HBV, and HCV. • Do not prevent enteric pathogen exposure (which is via fecal-oral contact). • HIV-infected persons should be screened for STDs at least annually. Those with multiple partners or high-risk partners or sexual practices should be screened more frequently. • To avoid infection with HSV, HIV-infected persons should avoid sexual contact when a partner has an overt herpetic lesion (genital or oral-labial), though HSV transmission also can occur during asymptomatic shedding. Consistent use of male condoms also has been shown to reduce HSV transmission risk in heterosexual couples. • The use of suppressive antiviral therapy by persons with genital herpes reduces HSV-2 transmission to susceptible partners, though the effectiveness of this approach in HIV-infected patients has not been evaluated. • Patients who are CMV seronegative should be advised that CMV can be sexually transmitted. • To decrease risk of exposure to enteric pathogens during sex, patients can: <ul style="list-style-type: none"> • Use barriers such as dental dams during oral-anal contact. • Change condoms after anal sex. • Wear latex gloves during digital-anal contact. • Wash hands after sex. 	

Injection Drug Use Associated	
Pathogens	<ul style="list-style-type: none"> • HIV • HCV • HBV • CMV • <i>Staphylococcus aureus</i>, including MRSA • <i>Pseudomonas aeruginosa</i> • <i>Streptococcus</i> • <i>Clostridium</i> • Enteric bacteria and oral anaerobes • <i>Leishmania</i> • Fungi
Transmission	<ul style="list-style-type: none"> • Injection drug users are at risk of a host of infections, including viral hepatitis, skin and soft-tissue infections, infective endocarditis, and pulmonary infections. • Injection drug use also may put users at risk of acquiring TB and STDs. • Infection may occur from contaminated drug-injection equipment (needles, syringes, water, and other preparation equipment). • Infection also may occur from the user's own skin or mouth bacteria, which can enter the bloodstream. • The drug itself, or an adulterating substance, may be contaminated.
Recommended avoidance measures	<ul style="list-style-type: none"> • Injection drug users should be advised not to share needles or drug preparation equipment, and should be educated about needle exchange programs. • If receptive, injection drug users should be referred to substance abuse treatment programs. • Injection drug users should be educated about methods of reducing risk, including the following: <ul style="list-style-type: none"> • If equipment is being reused, clean with bleach and water. • Avoid dangerous injection sites such as groin and neck. • Do not crush capsules or tablets in the mouth prior to injecting, as this may introduce harmful oral bacteria into the bloodstream. • Do not lick injection needles or syringes. • Use boiled water for preparing drugs for injection; if not available, use tap water. • Boil the drug before injecting. • Use a new or disinfected "cooker," and a new filter to prepare drugs for injection. • Always clean injection sites with alcohol before injecting. • Be aware that black tar heroin may be contaminated with <i>Clostridium</i> spores, which are not killed by heating the drug prior to use.

Other Bloodborne Related	
Pathogens	<ul style="list-style-type: none"> • HIV • HCV • HBV • CMV
Transmission	<ul style="list-style-type: none"> • Tattooing and body piercing. • Reuse of medical equipment and transfusion of infected blood (primarily outside the United States). • Occupational exposures (e.g., needlesticks) of health care workers.
Recommended avoidance measures	<ul style="list-style-type: none"> • Persons considering tattooing or piercing should be educated about the potential risk of bloodborne pathogen transmission if proper infection control procedures are not followed. • When receiving a transfusion, HIV-infected patients who are seronegative for CMV should be administered only CMV antibody-negative or leukocyte-reduced cellular blood products in nonemergency situations. • Universal precautions always should be followed by health care workers.

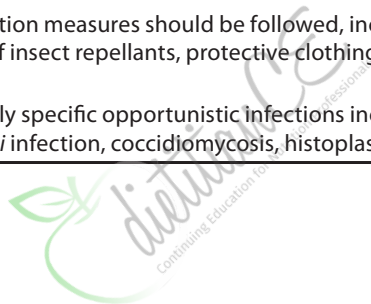
Pet and Animal Related	
Pathogens	<ul style="list-style-type: none"> • <i>Toxoplasma</i> • <i>Cryptosporidium</i> • <i>Salmonella</i> • <i>Campylobacter</i> • Shiga toxin-producing <i>Escherichia coli</i> • <i>Bartonella</i> • <i>Leptospira</i> • <i>Brucella</i> • <i>Capnocytophaga</i> • <i>Cryptococcus</i> • <i>Mycobacterium avium</i> and <i>marinum</i> • <i>H. capsulatum</i>
Transmission	<ul style="list-style-type: none"> • For the most part, people with HIV infection can and should keep their pets. • HIV-infected persons should be made aware of the potential risks posed by animals and of the avoidance measures for decreasing risks of infection. • Exposure may occur though a lick, a bite, or a scratch, or through contact with a pet's stool. Some infections may be spread though contact with an animal's coat or skin. • Fleas may spread some infections to pet owners. • Patients also may be exposed while performing occupational tasks that bring them into contact with animals (e.g., in pet stores, veterinary clinics, farms, and slaughterhouses).
Recommended avoidance measures	<ul style="list-style-type: none"> • Always wash hands after handling animals, and after cleaning cages or aquariums. • When acquiring a new pet, avoid animals <6 months of age (cats younger than 1 year) and those with diarrhea. • Stray animals may carry many infections and should be avoided. • Avoid contact with animal stool. • Avoid animals with diarrhea. • Pets with diarrhea should be examined by a veterinarian and should have stool checked for <i>Cryptosporidium</i>, <i>Salmonella</i>, <i>Campylobacter</i>, and Shiga toxin-producing <i>E. coli</i>. • Wash any bites or scratches with soap and water, and seek medical attention. • Animals should not be allowed to lick people in the mouth, or on any open cuts or wounds. • Cats may increase risk of <i>Toxoplasma</i> and <i>Bartonella</i> infection. • To minimize risk of <i>Toxoplasma</i> exposure: <ul style="list-style-type: none"> • Litter boxes should be cleaned daily, preferably by someone who is not HIV infected or pregnant. • If an HIV-infected person is cleaning a litter box, gloves should be used, and hands should be washed afterward. • Keep cats indoors and do not allow them to hunt. • Do not feed cats raw or undercooked meat. • In areas where histoplasmosis is endemic, avoid contact with bird droppings, including soil under bird roosting sites. • Always use gloves when cleaning aquariums to avoid contact with <i>Mycobacterium marinum</i>. • Avoid contact with reptiles (such as lizards, snakes, and turtles), as well as chicks and ducklings, as these may carry <i>Salmonella</i>. • Avoid exotic pets such as monkeys, ferrets, and other wild animals.

Contact with Children	
Pathogens	<ul style="list-style-type: none"> • CMV • <i>Cryptosporidium</i> • <i>Giardia</i> • HAV • Influenza • VZV • Enteric pathogens
Transmission	<ul style="list-style-type: none"> • HIV-infected persons who work as childcare providers, or who have children in daycare, may be exposed to opportunistic pathogens. • The poor personal hygiene habits of children facilitate spread of infection. • Risks specific to the individual, given his/her immune status and medical history, should be discussed with a health care provider. • CMV infection may occur through contact with many body fluids, including stool, urine, and saliva. • Diapering may bring a person into contact with <i>Cryptosporidium</i> and other enteric pathogens. • In addition to opportunistic pathogens, childcare providers are exposed to other illnesses, carried by children, to which they may be more susceptible.
Recommended avoidance measures	<ul style="list-style-type: none"> • Wash hands thoroughly after contact with stool or urine. • Wash hands after diapering and disinfect changing station often. • Wash hands after contact with saliva or objects covered with saliva, such as cups or pacifiers. • Ensure that the immunization status of HIV-infected persons is up to date, as appropriate for their immune status. • HIV-infected persons who are susceptible to VZV should avoid exposure to people with chickenpox or shingles. • VZV-susceptible household contacts of HIV-infected persons should be vaccinated against VZV if they are HIV negative, so that they will not transmit VZV to their HIV-infected contact.

Travel Related	
Pathogens	<ul style="list-style-type: none"> • Enteric pathogens • <i>Plasmodium</i> species (malaria) • Yellow fever virus • Dengue virus • Other geographically specific infections
Transmission	<ul style="list-style-type: none"> • Travelers to developing countries are at risk of foodborne and waterborne infections. • Malaria is transmitted by the bite of an infected female <i>Anopheles</i> mosquito. • HIV-infected patients are at higher risk of severe malaria. • Yellow fever and dengue fever are spread by mosquito bites.

Travel Related	
Recommended avoidance measures	<ul style="list-style-type: none"> Plan the travel itinerary, vaccinations, and prophylaxis in consultation with a health care provider experienced in travel medicine. Discuss area-specific risks and avoidance measures with the health care provider. The U.S. Centers for Disease Control and Prevention (CDC) Traveler's Health website has detailed information on most issues pertaining to infections in travelers (wwwnc.cdc.gov/travel). Review and update routine vaccination history prior to travel. Generally, live vaccines for HIV-infected persons should be avoided, with some exceptions: <ul style="list-style-type: none"> Measles vaccination is recommended for all nonimmune persons with CD4 counts of ≥ 200 cells/μL. Measles immune globulin should be considered for those with CD4 counts of < 200 cells/μL who are traveling in measles-endemic areas. Varicella vaccination can be considered for VZV-seronegative persons with CD4 counts of ≥ 200 cells/μL. Yellow fever vaccination may be considered, see below. Inactivated (killed) enhanced-potency polio and typhoid vaccines should be given instead of the live, attenuated forms. Killed and recombinant vaccines including influenza, diphtheria-tetanus, rabies, HAV, HBV, Japanese encephalitis, and meningococcal vaccines should be administered as they would be for HIV-uninfected persons preparing for travel. The oral cholera vaccine (not available in the United States) is not recommended for most travelers by the CDC. <p>Traveler's diarrhea:</p> <ul style="list-style-type: none"> See sections on foodborne and waterborne infections (above) for risk-reduction strategies. Antimicrobial prophylaxis is not routinely recommended for HIV-infected persons traveling in developing countries. Prophylaxis may be appropriate in select situations (for example, high risk of infection and short length of travel). For those to whom prophylaxis is given, fluoroquinolones (such as ciprofloxacin 500 mg PO QD) may be considered for nonpregnant patients. HIV-infected patients traveling in developing countries should bring antibiotics to be used empirically in the event of developing diarrhea. Appropriate regimens include: <ul style="list-style-type: none"> Ciprofloxacin 500 mg PO BID for 3-7 days Azithromycin 500 mg PO QD as an alternative, and for pregnant women Antiperistaltic agents such as loperamide or diphenoxylate can be useful in the treatment of traveler's diarrhea. Do not use antiperistaltic agents if high fever or blood in the stool is present. Stop use if symptoms persist > 48 hours. Seek medical care if diarrhea is severe, bloody, accompanied by fever and chills, leads to dehydration, or does not respond to empiric therapy.

Travel Related	
Recommended avoidance measures	<p>Malaria:</p> <ul style="list-style-type: none"> • HIV-infected patients should be advised to avoid travel in malarious areas. • If travel to a malarious area cannot be avoided, effective chemoprophylaxis should be given. Consult the CDC Traveler's Health website (wwwnc.cdc.gov/travel) for specific information. • Be aware that some malaria prophylaxis medications may have drug-drug interactions with antiretrovirals. • Personal protection measures should be followed, including avoidance of peak biting times and use of insect repellants, protective clothing, and permethrin-soaked bed netting. <p>Yellow fever:</p> <ul style="list-style-type: none"> • HIV-infected patients should be discouraged from visiting areas where yellow fever infection is a risk. • Vaccination may be considered in some HIV-infected persons with high CD4 counts who cannot avoid potential exposure, after discussion of risks and benefits. • Vaccine response may be poor, and serologic testing can be considered. • If vaccination is not administered, patients should be advised about the risk of yellow fever, instructed about avoiding the bites of vector mosquitoes, and provided with a vaccination waiver letter. • Personal protection measures should be followed, including avoidance of peak biting times and use of insect repellants, protective clothing, and permethrin-soaked bed netting. <p>Other geographically specific opportunistic infections include visceral leishmaniasis, <i>Penicillium marneffei</i> infection, coccidiomycosis, histoplasmosis, and TB.</p>



Opportunistic Infection Prophylaxis

Background

Prophylaxis against an opportunistic infection (OI) is treatment given to HIV-infected individuals to prevent either a first episode of an OI (primary prophylaxis) or the recurrence of an OI (secondary prophylaxis). Prophylaxis is recommended to prevent three important OIs: *Pneumocystis jiroveci* pneumonia (PCP), *Mycobacterium avium* complex (MAC), and toxoplasmosis. Prophylaxis also is recommended to prevent tuberculosis (TB) in patients with latent *Mycobacterium tuberculosis* infection (see chapter *Latent Tuberculosis Infection*). In endemic regions, prophylaxis against *Histoplasma capsulatum* and *Coccidioides* species is advised. And in some situations, prophylaxis against other OIs may be reasonable; see the OI prevention recommendations of the U.S. Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association (reference below) for additional information.

HRSA HAB Performance Measures

Percentage of patients, aged 6 weeks or older with a diagnosis of HIV/AIDS, who were prescribed ***Pneumocystis jiroveci* pneumonia** prophylaxis

(Core measure)

Pneumocystis jiroveci Pneumonia

Background

PCP remains the most common life-threatening infection among U.S. residents with advanced HIV disease.

Primary Prophylaxis: Indications

- Prophylaxis should be administered to all HIV-infected patients with a CD4 count of <200 cells/ μ L, a history of an AIDS-defining illness, or a history of oral thrush. PCP prophylaxis also is indicated for patients with CD4 counts of >200 cells/ μ L in the presence of a CD4 percentage <14%.
- For patients whose CD4 counts are declining toward 200 cells/ μ L, the CD4 count should be monitored closely. PCP prophylaxis should be considered for patients with a CD4 count of 200-250 cells/ μ L if laboratory monitoring will not be possible within 3 months.

Prophylaxis Options: Recommended Regimens

- Trimethoprim-sulfamethoxazole (TMP-SMX) (also known as cotrimoxazole, Bactrim, and Septra) 1 double-strength (DS) tablet PO QD (Note: This regimen also is effective in preventing toxoplasmosis.)
- TMP-SMX 1 single-strength tablet PO QD (this lower-dose regimen may be better tolerated) (Note: This also is likely to be effective in preventing toxoplasmosis.)
- **Warning:** Many patients have adverse reactions to sulfa medications. Severe reactions may include persistent neutropenia, rash (including severe erythroderma), and Stevens-Johnson syndrome (bullae and desquamation of the skin). For patients with milder reactions, chemoprophylaxis with TMP-SMX should be continued if clinically possible. Some patients with a history of serious adverse reaction may undergo desensitization, but this must be done cautiously and it requires diligence from the patient and careful management by the provider (see chapter *Sulfa Desensitization*).

Prophylaxis Options: Alternative Regimens

Other options for prophylaxis include the following:

- TMP-SMX DS, 1 tablet TIW (e.g., Monday, Wednesday, and Friday) (Note: This regimen also is likely to be effective in preventing toxoplasmosis.)
- Dapsone 100 mg PO QD or 50 mg PO BID (Note: These regimens do not prevent toxoplasmosis.)
- Dapsone 50 mg PO QD + pyrimethamine 50 mg PO once weekly + leucovorin 25 mg PO once weekly (Note: This regimen also is effective in reducing the risk of toxoplasmosis.)
 - **Warning:** Glucose-6-phosphate dehydrogenase (G6PD) deficiency can increase the risk of hemolytic anemia or methemoglobinemia in patients receiving dapsone. Screen for G6PD deficiency before starting dapsone. (G6PD deficiency is found in approximately 10% of African-American males, and in 1-2% of males of Mediterranean, Indian, and Asian descent.)
- Dapsone 200 mg PO once weekly + pyrimethamine 75 mg PO once weekly + leucovorin 25 mg PO once weekly
- Aerosolized pentamidine 300 mg once per month, via Respigard II nebulizer (Note: This regimen does not prevent toxoplasmosis.)
 - **Warning:** Aerosolized pentamidine may increase the risk of extrapulmonary pneumocystosis, pneumothorax, and bronchospasm. It increases the risk of TB transmission to others if the patient has active pulmonary tubercular disease, unless ventilation (negative-pressure facility with outside venting) is adequate. Do not use for patients in whom TB is suspected. The availability of treatment facilities offering aerosolized pentamidine may be limited.

- Atovaquone 1,500 mg QD (Note: This also is effective in reducing the risk of toxoplasmosis.) Atovaquone is more expensive than dapsone. It should be taken with high-fat meals for optimal absorption.
- Atovaquone 1,500 mg + pyrimethamine 25 mg + folinic acid 10 mg, all taken PO QD (Note: This regimen also is effective in reducing the risk of toxoplasmosis.)

Secondary Prophylaxis Indications

Prophylaxis should be given to all patients with a history of PCP.

Discontinuing Prophylaxis

Primary or secondary prophylaxis can be discontinued if the CD4 count has increased to ≥ 200 cells/ μ L for at least 3 months in response to effective antiretroviral therapy (ART), with the following cautions:

- If the patient had PCP in the past and the episode of PCP occurred at a CD4 count of >200 cells/ μ L, it may be prudent to continue PCP prophylaxis for life, regardless of how high the CD4 count rises as a consequence of ART.
- PCP prophylaxis should be reinitiated if the CD4 count decreases to <200 cells/ μ L or the patient meets other criteria as indicated above.

Prophylaxis During Pregnancy

TMP-SMX is the recommended agent for use during pregnancy; dapsone may be used as an alternative. Some experts recommend high-dose folate supplementation (e.g., 4 mg daily) for pregnant women receiving TMP-SMX, because TMP-SMX may worsen folate deficiency; however, this may increase risk of TMP-SMX failure; if high-dose folate supplementation is given, it should be limited to the first trimester. Prophylaxis that includes pyrimethamine generally should be deferred until after pregnancy. During the first trimester, aerosolized

pentamidine (which is not systemically absorbed) can be used if the potential teratogenicity of oral agents is a concern.

***Mycobacterium avium* Complex**

Background

MAC is common among patients with advanced HIV disease and it generally occurs in people with CD4 counts of <50 cells/ μ L.

Primary Prophylaxis: Indications

Prophylaxis should be administered to all HIV-infected patients with CD4 counts of <50 cells/ μ L. Before starting prophylaxis, rule out active MAC infection by clinical assessment and, if warranted, by acid-fast bacilli (AFB) blood cultures (see chapter *Mycobacterium avium Complex Disease*). Also rule out active TB prior to starting any rifabutin-containing regimen for MAC prophylaxis. Review the current drug regimen for medications that may interact with MAC prophylaxis.

Prophylaxis Options: Recommended Regimens

- Azithromycin 1,200 mg PO weekly
- Clarithromycin 500 mg PO BID (Note: Clarithromycin is not recommended for use during pregnancy, and it can have significant interactions with efavirenz, atazanavir, and other drugs; see chapter *Drug-Drug Interactions with HIV-Related Medications*.)
- Azithromycin 600 mg PO BIW

Prophylaxis Options: Alternative Regimens

Rifabutin 300 mg QD (Note: Rifabutin has significant interactions with many drugs; certain nonnucleoside reverse transcriptase inhibitors and protease inhibitors should be avoided or dosage adjustment of rifabutin

may be required. See chapter *Drug-Drug Interactions with HIV-Related Medications*.)

Secondary Prophylaxis

Patients should receive lifelong chronic maintenance therapy, unless immune reconstitution occurs in response to ART. See chapter *Mycobacterium avium Complex Disease*.

Discontinuing Prophylaxis

Primary prophylaxis for MAC can be discontinued in persons who have responded to effective ART with sustained increases in CD4 counts to >100 cells/ μ L for at least 3 months. Careful observation and monitoring are required, and prophylaxis should be restarted if the patient's CD4 count decreases to <50 cells/ μ L.

Secondary prophylaxis can be discontinued in patients who received at least 12 months of treatment for MAC, are asymptomatic, and have sustained (for at least 6 months) CD4 counts of >100 cells/ μ L on ART. Secondary prophylaxis should be reintroduced if the CD4 count decreases to <100 cells/ μ L.

Prophylaxis During Pregnancy

Azithromycin is the prophylactic drug of choice during pregnancy, although evidence for its safety in the first trimester is limited. Clarithromycin is teratogenic in animals.

Toxoplasmosis

Background

Toxoplasmic encephalitis (TE) usually is caused by reactivation of latent *Toxoplasma gondii* infection in patients with advanced immunosuppression (especially those with CD4 counts of <100 cells/ μ L). The CDC/NIH recommendations state that all HIV-infected patients should be tested for *Toxoplasma* immunoglobulin G (IgG) antibody soon after the diagnosis of HIV infection. *Toxoplasma* IgG-negative patients should be counseled

to avoid sources of infection (see chapter *Preventing Exposure to Opportunistic and Other Infections*), and should be retested for *Toxoplasma* IgG if CD4 counts fall to <100 cells/ μ L to determine whether they have seroconverted and are therefore at risk of TE. (See chapter *Toxoplasmosis* for more information on active disease and secondary prophylaxis.)

Primary Prophylaxis: Indications

Prophylaxis should be administered to all HIV-infected patients with CD4 counts of <100 cells/ μ L who are seropositive for *Toxoplasma*. IgG-negative patients should avoid exposure to *Toxoplasma*; see “Patient Education,” below, and chapter *Preventing Exposure to Opportunistic and Other Infections*.

Prophylaxis Options: Recommended Regimens

- TMP-SMX DS, 1 tablet QD (Note: This option also is effective in preventing PCP.)

Prophylaxis Options: Alternative Regimens

(Note: The following options also are effective in preventing PCP.)

- TMP-SMX DS, 1 tablet PO TIW
- TMP-SMX single strength, 1 tablet PO QD
- Dapsone 50 mg PO QD + pyrimethamine 50 mg PO weekly + folinic acid 25 mg PO weekly
- Dapsone 200 mg PO weekly + pyrimethamine 75 mg PO weekly + folinic acid 25 mg PO weekly
- **Warning:** G6PD deficiency can increase the risk of hemolytic anemia or methemoglobinemia in patients receiving dapsone. Screen for G6PD deficiency before starting dapsone. (G6PD deficiency is found in approximately 10% of African-

American males, and in 1-2% of males of Mediterranean, Indian, and Asian descent.)

- Atovaquone 1,500 mg PO QD, with or without pyrimethamine 25 mg PO QD + folinic acid 10 mg PO QD (This alternative is quite expensive.)
- Neither aerosolized pentamidine nor dapsone alone provides protection against TE.

Secondary Prophylaxis

Patients should receive lifelong chronic maintenance therapy, unless immune reconstitution occurs in response to ART (see chapter *Toxoplasmosis*).

Discontinuing Prophylaxis

Primary prophylaxis for TE can be discontinued in patients who have responded to effective ART with sustained CD4 counts of >200 cells/ μ L for at least 3 months. CD4 counts should be monitored carefully, and prophylaxis should be restarted in patients whose CD4 counts decrease to <100-200 cells/ μ L.

Secondary prophylaxis may be discontinued if TE signs and symptoms have resolved with treatment and if patients have sustained (for at least 6 months) CD4 counts of >200 cells/ μ L on ART. Secondary prophylaxis should be reintroduced if CD4 counts drop to <200 cells/ μ L.

Prophylaxis During Pregnancy

TMP-SMX may be used as primary prophylaxis during pregnancy. Risks of TMP-SMX in the first trimester must be balanced against the risks of reactivated toxoplasmosis. Some experts recommend high-dose folate supplementation (e.g., 4 mg QD) for pregnant women receiving TMP-SMX, because TMP-SMX may worsen folate deficiency; however, this may increase risk of TMP-SMX failure; if high-dose folate supplementation is given,

it should be limited to the first trimester. Pyrimethamine has been associated with birth defects in animal studies, but limited data in human studies have not shown an increased risk; guidelines support its use after the first trimester. Secondary prophylaxis generally should be provided using the same guidelines as for nonpregnant women.

Histoplasmosis

Background

Infection with *Histoplasma capsulatum* is common in several geographic areas, including the Ohio and Mississippi River Valleys as well as parts of Central and South America, Asia, and Africa. Symptomatic disease can occur via primary infection or reactivation of previously silent infection in the setting of waning cellular immunity. CD4 counts of ≤ 150 cells/ μL , along with positive *Histoplasma* serology and environmental exposure, are associated with increased risk of symptomatic disease. Histoplasmosis can cause a range of clinical manifestations including respiratory, gastrointestinal, central nervous system (CNS), and cutaneous disease.

Primary Prophylaxis: Indications

Prophylaxis can be considered for HIV-infected patients with CD4 counts of ≤ 150 cells/ μL who are at high risk because of occupational exposure and for those who live in an area where histoplasmosis is highly endemic. HIV-infected patients with CD4 counts of ≤ 150 cells/ μL should be educated to avoid exposure.

Prophylaxis Options: Recommended Regimens

- Itraconazole 200 mg PO QD (Note: Itraconazole has significant interactions with many drugs, including nonnucleoside reverse transcriptase inhibitors, protease inhibitors, and maraviroc. Dosage adjustments may be required, and some combinations may be contraindicated; consult with a pharmacist or other specialist.)

Secondary Prophylaxis

Patients with a history of severe disseminated disease or CNS infection and those who have relapsed despite receiving appropriate therapy should receive long-term suppressive therapy.

Discontinuing Prophylaxis

Primary prophylaxis can be discontinued once CD4 counts are ≥ 150 cells/ μL for at least 6 months. CD4 counts should be monitored carefully, and prophylaxis should be restarted for patients whose CD4 counts decrease to < 150 cells/ μL .

Secondary prophylaxis may be discontinued if patients have received at least 1 year of itraconazole, have negative blood cultures, have had CD4 counts of ≥ 150 cells/ μL for at least 6 months on ART, and have serum *Histoplasma* antigen < 2 units. Suppressive therapy should be restarted for patients whose CD4 counts decrease to < 150 cells/ μL .

Prophylaxis During Pregnancy

Azoles should be avoided during pregnancy, especially during the first trimester, because of teratogenicity concerns.

Coccidiomycosis

Background

The *Coccidioides* species fungus is endemic to many arid regions. In the United States, it is found primarily in the Sonoran Desert in Arizona and the San Joaquin "Central" Valley in California, but also in areas of New Mexico, western Texas, Nevada, and Utah. It also is endemic to many arid regions in Central and South America. Immune response to *Coccidioides* species declines as CD4 counts decrease, and risk of developing symptomatic disease in endemic areas is increased when the CD4 count is <250 cells/ μ L. In HIV-infected patients, six syndromes have been described: focal pneumonia, diffuse pneumonia, cutaneous involvement, meningitis, liver or lymph node involvement, and positive serology without localized infection.

Primary Prophylaxis: Indications

- Primary prophylaxis is not beneficial and is not recommended. Patients in endemic areas cannot avoid *Coccidioides* but should be educated to avoid extensive exposure (e.g., through disturbed soil and dust storms). Annual monitoring for seroconversion of HIV-infected patients in endemic areas is reasonable; in patients with CD4 counts of <250 cells/ μ L who develop a new positive IgM or IgG, antifungal therapy is recommended to preempt active disease (fluconazole 400 mg PO QD).

Secondary Prophylaxis

Patients who have completed initial treatment for coccidiomycosis should receive lifelong suppressive therapy.

Discontinuing Prophylaxis

Patients with a history of meningeal disease should be treated with suppressive therapy for life, as they are at high risk of relapse. Patients with a history of diffuse pulmonary disease or nonmeningeal disseminated infection also are at high risk of relapse; consult with experts. Patients with focal coccidioidal pneumonia who have had good clinical response to antifungals can discontinue secondary prophylaxis once they have received 12 months of therapy, and have CD4 counts of >250 cells/ μ L on ART. These patients should undergo close radiologic and serologic monitoring for recurrence.

Prophylaxis During Pregnancy

Women who acquire coccidiomycosis in the second or third trimester of pregnancy are at increased risk of dissemination. Azoles should be avoided during the first trimester of pregnancy because of teratogenicity concerns.

Patient Education

- Discuss adverse effects of the selected medication(s) and how the patient should respond in the event of rashes, diarrhea, and other complications.
- Explain the purpose of each medication, and be sure that patients understand the dosage and frequency of administration.
- Reinforce the need to continue taking the medication indefinitely (potentially for life) to reduce the risk of the OI.
- OIs can occur despite prophylaxis. Instruct patients to contact their health care provider if they become ill.
- Counsel patients who are *Toxoplasma* IgG negative to avoid exposure to *Toxoplasma*. Specifically, they should avoid eating raw or undercooked meat, especially pork, lamb, game, and venison. Patients should wash hands after handling raw meat and after gardening or contact with soil. Encourage patients not to adopt or handle stray cats, and, if they own cats, to wash hands thoroughly after cleaning litter boxes. (See chapter *Preventing Exposure to Opportunistic and Other Infections*.)
- For women of childbearing potential who are taking clarithromycin, emphasize the need for effective contraception to avoid potential teratogenic effects of clarithromycin.
- Educate patients in *Histoplasma*- and *Coccidioides*-endemic areas regarding measures to decrease exposure. (See chapter *Preventing Exposure to Opportunistic and Other Infections*.)

Latent Tuberculosis Infection

Background

Latent (or inactive) tuberculosis (TB) infection occurs when an individual has dormant *Mycobacterium tuberculosis* organisms and no active disease. It can be diagnosed by a tuberculin skin test (TST) or by a blood test called an interferon-gamma release assay (IGRA); both are described below. HIV-infected persons with latent TB infection (LTBI) have a much higher risk of developing active TB (estimated at 3-16% per year) than the general population (estimated at <10% in a lifetime). Whereas treatment of HIV infection with antiretroviral therapy (ART) reduces the risk of active TB, this risk remains higher than that for HIV-uninfected persons. The risk of an HIV-infected individual with LTBI developing active TB can be reduced 60% with treatment of LTBI. Hence, identifying and treating HIV-infected persons with LTBI is a high priority. Treatment of LTBI not only reduces the risk of disease to the individual but also reduces the risk of further TB transmission within the community. Standard treatment with isoniazid (INH) is effective and safe.

Issues of concern regarding treatment of LTBI among HIV-infected persons include the following:

- Excluding active pulmonary or extrapulmonary TB disease before treatment with INH alone
- Assessing the risk of latent infection with drug-resistant TB
- Avoiding or managing drug interactions if rifamycin-containing regimens are used (rifampin, rifabutin, rifapentine)

HRSA HAB Performance Measures

Percentage of patients aged 3 months and older with a diagnosis of HIV/AIDS, for whom there was **documentation that a tuberculosis screening test was performed** and results interpreted (for tuberculin skin tests) at least once since the diagnosis of HIV infection

(All-Age measure)

S: Subjective

Ask about symptoms of active TB, including fever, cough, and weight loss; see chapter *Mycobacterium tuberculosis*. Patients with symptoms that could represent active TB must be evaluated for active TB and ruled out by appropriate diagnostic methods before initiating treatment (see "Assessment," below). HIV-infected persons are eligible for LTBI treatment if they have positive LTBI screening results, no symptoms of active TB, and have not been treated previously for active or latent TB (re-treatment of LTBI should be considered if a patient is a close contact to an active TB case).

Persons who have had bacillus Calmette-Guérin (BCG) vaccine can be evaluated by an IGRA (preferably) or by a TST with correct interpretation. Immigrants from many countries

will have had childhood BCG vaccination.

Health care providers should ask about a history of potential exposure to TB. Close contact with an active TB case is an indication for LTBI treatment, after active TB has been excluded, regardless of the screening results on TST or IGRA.

O: Objective Diagnostic Evaluation

Current U.S. Centers for Disease Control and Prevention (CDC) and U.S. Department of Health and Human Services (HHS) guidelines strongly recommend LTBI testing for all newly diagnosed HIV-infected persons. Repeat testing is recommended for patients whose CD4 lymphocyte count increases

from low numbers to counts of >200 cells/ μ L, and annual testing is suggested for patients whose initial test result is negative and who are considered at high risk of repeated or ongoing exposure to TB (risk factors include incarceration, residence in a congregate setting, active drug use, and residence in or travel to a TB-endemic setting).

CDC and HHS guidelines recommend use of either the TST or one of the three currently available IGRAs (QuantiFERON-TB Gold, QuantiFERON-TB Gold In-Tube [QFT-GIT], or TSPOT-TB). The TST evaluates delayed hypersensitivity to antigens from a number of *Mycobacterium* species (including non-tuberculosis species). The IGRAs are in vitro tests of lymphocyte recognition and response to antigens more specific to *M. tuberculosis*, but they still may cross-react with *M. kansasii*, *M. marinum*, or *M. szulgai*. Because the IGRAs use antigens more specific to *M. tuberculosis*, they generally are thought to have greater specificity and a lower false-positive rate. A positive TST or IGRA result suggests previous contact with *M. tuberculosis*, and it implies latent or active TB infection. Neither TST nor IGRA screening can distinguish between LTBI and active TB infection.

Use of an IGRA is preferred for persons with previous BCG exposure and for patient groups at risk of not returning for TST readings. The TST is preferred for children under 5 years of age. The cost of an IGRA is higher than the cost of a TST, and individual clinics should compare the total costs of both testing approaches, including the costs involved in TST protocols of recalling patients who miss visits, repeating TSTs, and treating persons with previous BCG exposure who may have false-positive TST results. Both IGRAs and TST testing have increased rates of anergic test results in HIV-infected patients with advanced immunosuppression (particularly those with CD4 counts of <100 cells/ μ L).

Tuberculin skin test

The TST is administered as an intradermal injection of 0.1 mL (5 tuberculin units) of purified protein derivative (PPD), which raises a wheal in the skin. This is sometimes referred to as the Mantoux test. Multiple-puncture tests such as tine tests and the use of other strengths of PPD are considered unreliable. Anergy testing with *Candida* and mumps antigens is not routinely recommended because a randomized controlled study of HIV-infected patients in the United States did not show an advantage to treating anergic, tuberculin-negative persons.

PPD tests are not designed for reading by the patient; a trained health care worker must measure the area of induration (not erythema) 48-72 hours after the test is administered. Induration of 5 mm or more is considered a positive result for HIV-infected persons, other immunosuppressed persons, anyone with recent TB exposure, and anyone with fibrosis on chest X-ray that is consistent with previous TB. For HIV-uninfected health care workers, 10 mm of induration is a positive result; in various other populations, either 10 mm or 15 mm of induration may be considered positive. Care providers at many large HIV clinics find it challenging to ensure that their patients return for the PPD reading. One randomized study found that offering incentives (e.g., a fast-food coupon) plus counseling was more effective than counseling alone in obtaining return visits for PPD readings.

Interferon-gamma release assay

IGRA tests performed on peripheral blood samples are available in the United States from two manufacturers. Although the tests are expensive, results are obtained without the patient having to make a return visit to the clinic, and false-positive readings following BCG vaccination do not occur. In addition, IGRAs do not appear to be boosted by prior TST testing and two-step testing is not required. Three test results

are possible with IGRA testing: positive, negative, and indeterminate. Unlike the TST, interpretation of IGRA test results does not vary by the risk category of the person tested. An indeterminate test indicates either a high background IFN-gamma level or failure of the mitogen to respond, and should be interpreted as “no test result” (not as “partially positive”). Repeating the IGRA once may yield interpretable test results. However, if the subsequent IGRA result is indeterminate, no further testing is recommended until there is a change in the patient’s immune status, such as reconstitution with ART.

Limited data suggest that the QFT-GIT is the most specific test (lowest rate of false-positive results) and the T-SPOT is the most sensitive test (with the lowest rate of false-negative results). However, few studies have compared the IGRA assays, and there is no reliable “gold standard” for sensitivity or specificity for latent TB infection. Although these tests do not detect previous BCG exposure, they will yield positive results in all three TB-causing species of the *M. tuberculosis* complex – *M. tuberculosis*, *M. bovis*, and *M. africanum* – and may yield positive results in persons with exposure to certain mycobacteria other than *M. tuberculosis* (*M. kansasii*, *M. marinum*, and *M. szulgai*).

There are accumulating data to support the use of IGRA testing in HIV infection. Data suggest that IGRAs are more specific than the TST and correlate more closely with risk factors for TB infection. As with TST, false-negative and indeterminate test results are more likely with advanced immunosuppression. One case series suggests that a significant number of QFT tests may be falsely positive on initial testing but negative on retesting, particularly in patients who were not born in TB-endemic settings. Accordingly, for patients with a positive IGRA result but no risk factors for TB other than HIV infection, it may be reasonable to repeat the IGRA and confirm positivity before treatment.

A: Assessment

After screening for symptoms (see “Subjective”), a chest X-ray should be obtained for all HIV-infected persons with positive TST or IGRA test results. Asymptomatic patients with negative chest X-ray results should be offered treatment for LTBI. (As above, it may be reasonable to repeat the IGRA for HIV-infected patients in non-TB-endemic settings who have no other risk factors for TB prior to LTBI treatment.) Persons with symptoms consistent with pulmonary or extrapulmonary TB, and those with abnormal chest radiography, require further assessment before LTBI treatment. This assessment may include sending two to three separate sputum specimens for acid-fast bacilli (AFB) stain, nucleic acid amplification testing if available, and culture, or obtaining other specimens depending on the suspected site of extrapulmonary TB. If suspicion of TB is low, patients with negative sputum smears (or other biopsy or tissue samples) can begin LTBI treatment. If suspicion of active disease is high, treatment for active disease should be started while the culture results are pending (see chapter *Mycobacterium tuberculosis*). HIV-infected persons with significant exposure (close contact) to someone with infectious TB should receive a full course of TB prophylaxis regardless of TST or IGRA results. Health departments can assist clinicians in assessing the degree of exposure for an HIV-infected patient and in determining whether there is a need for a full course of treatment.

An HIV-infected person with fibrosis on a chest X-ray that is consistent with previous TB and with no history of TB treatment (or a history of inadequate treatment) should be evaluated for active TB regardless of TST or IGRA results. If found not to have active TB, the patient should be treated for LTBI. If the patient is strongly suspected to have active TB, standard treatment for active TB should be given while culture analysis is under way. If

cultures are negative, patients may be switched to LTBI treatment. Highly suspect but culture-negative patients may be given a 4-month total course of treatment for active TB. (See chapter *Mycobacterium tuberculosis*.)

P: Plan

As with any treatment of TB, adherence to the regimen is required for success. Treatment regimens for LTBI in the United States and other low-prevalence TB countries are presented in Table 1. Treatment should be offered to all HIV-infected persons with evidence of LTBI or close contact with an active TB case, regardless of age.

In some highly TB-endemic settings outside the United States, LTBI treatment given to TST-negative patients or patients of unknown TB status has led to reduction of active TB, although TST- or IGRA-positive patients appear to benefit most from LTBI treatment.

INH is preferred for treatment of LTBI because of extensive data supporting its efficacy and

because it has no significant interactions with ARV medications. Treatment with INH for 9 months is recommended. Rifampin-based LTBI treatment is an alternative and is given for 4 months. However, rifampin has substantial drug interactions with a number of ARVs (see “Potential ARV Interactions,” below). Rifabutin is an alternative for patients on PI-based regimens, although there are limited data for use in LTBI. Rifapentine, in combination with INH, has been approved as part of a 12-week treatment course for LTBI; however, it is not recommended for ART-treated patients outside clinical trials because of possible interactions with ARV medications. Rifampin + pyrazinamide is not recommended for LTBI treatment owing to unacceptable rates of hepatotoxicity.

For treatment of LTBI in persons exposed to drug-resistant TB, there are limited data on efficacy of various regimens in preventing progression to disease; consult with experts.

ART is indicated for all persons with LTBI.

Table 1. Treatment Regimens for Latent Tuberculosis

Drug	Dosage (taken orally)	Frequency	Duration (minimum number of doses for completion)
Preferred therapies			
INH*	Adults: 300 mg Children: 5 mg/kg	Daily	9 months or 270 doses within 12 months
INH*	Adults: 900 mg Children: 10-20 mg/kg	Twice weekly (DOT)**	9 months or 76 supervised doses within 12 months
Alternative therapies			
Rifampin [#]	Adults: 600 mg Children: 10-20 mg/kg	Daily	4 months or 120 doses in 6 months; if used in children, 6 months is recommended
Rifabutin [#]	Dose according to ARV medications	Daily	4 months or 120 doses in 6 months
Exposure to Multidrug-Resistant TB			
Treatment options depend on sensitivity of the organism.	Seek expert advice from public health authorities and those experienced in treatment of multidrug-resistant TB. Treatment may be postponed until sensitivity test results are available or may be based on resistance pattern of index case, if known.		

* 25 mg of pyridoxine (vitamin B6) should be given with each INH dose to reduce the risk of INH-induced peripheral neuropathy.

** DOT = directly observed treatment

[#] Rifampin and rifabutin have significant interactions with a number of ARV and other medications. See text and “Potential ARV Interactions,” below, about contraindicated combinations and dosage adjustments.

Length of LTBI Treatment

LTBI treatment is recommended for 9 months with INH (4 months with rifampin/rifabutin) in low-prevalence TB settings such as the United States. Accumulating data suggest that 36 months or indefinite LTBI treatment may be of benefit in some highly TB-endemic settings where TB reinfection may be common.

Monitoring on therapy

INH may cause liver toxicity and it should be used cautiously in patients with active alcohol consumption, liver disease, or chronic hepatitis B or C infection. INH is contraindicated for use in patients with acute hepatitis or decompensated liver disease. Baseline liver function tests are recommended for all HIV-infected persons prior to starting LTBI treatment. Monthly assessment to screen for signs and symptoms of hepatotoxicity (e.g., abdominal pain, jaundice, nausea, vomiting, and fatigue) and neuropathy is recommended. Patients with abnormal hepatic enzymes at baseline or liver disease such as viral hepatitis should receive regular checks of transaminases. If patients develop abnormalities in liver transaminases while taking INH (ALT or AST >3 times the upper limit of normal [ULN] with symptoms, or >5 times above the ULN in the absence of symptoms), the INH should be withheld. Obtain expert consultation before treating patients with abnormal liver function or advanced liver disease. All patients should receive pyridoxine (vitamin B6) 25 mg QD during INH treatment to reduce the risk of peripheral neuropathy.

Rifampin and rifabutin may cause liver and bone marrow toxicity. Before use, obtain baseline liver and renal function tests and a complete blood count. Given the potential for interaction with ARV and other drugs, a careful review of current medications should be done to assess for possible drug interactions. Follow-up is the same as for INH use.

Potential ARV Interactions

Rifampin and rifabutin have important interactions with certain antiretroviral drugs, and dosage adjustments or treatment modifications may be required. Rifampin reduces the blood levels of nonnucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), integrase inhibitors, and the CCR5 antagonist maraviroc; it also may decrease elvitegravir/cobicistat levels. Rifampin can be used by persons taking efavirenz or the integrase inhibitors raltegravir or dolutegravir, though dosage adjustments may be required. Coadministration of rifampin and maraviroc is not recommended, but may be possible with appropriate dosage adjustment of maraviroc; consult with an expert. Rifampin should not be used with nevirapine, etravirine, or rilpivirine, or with PIs or elvitegravir/cobicistat. (In some cases, the adverse pharmacokinetic effect of rifampin on PIs may be overcome with large doses of ritonavir, but consultation with a specialist should be obtained before this approach is undertaken; rifampin should not be used in combination with ritonavir-boosted saquinavir because of high rates of hepatic toxicity.)

No data are available on the use of rifabutin for treatment of LTBI. Nevertheless, rifabutin may be considered in place of rifampin for patients taking antiretroviral combinations that include certain NNRTIs (other than efavirenz) or PIs (other than ritonavir alone), and the integrase inhibitor raltegravir. In these cases, the dosages of both rifabutin and the antiretroviral agent usually require adjustment.

See Table 3 in chapter *Mycobacterium tuberculosis* for details on dosage adjustments.

Other Drug Interactions

Rifampin decreases the blood concentrations of estrogens, anticonvulsants, hypoglycemic agents, and many other drugs. Review all medications a patient is taking before initiating rifampin and make adjustments as necessary. (See Table 12, “Clinically Significant Drug-Drug Interactions Involving the Rifamycins,” at www.cdc.gov/mmwr/preview/mmwrhtml/rr5211a1.htm#tab12.)

Pregnancy

HIV-infected pregnant women with positive LTBI test results and no evidence of active TB should be evaluated for prophylaxis. The potential risks of INH should be evaluated in light of the potential risks of active TB. Consult with an expert. All pregnant women should receive ART for prevention of perinatal HIV transmission; ART also serves to reduce risk of LTBI progression.

Patient Education

- Patients should know that TB bacteria in their bodies cannot be passed to others while the TB is latent. However, because they have HIV infection, the TB bacteria is more likely to make them sick at some point in the future.
- Treatment for LTBI will help kill the TB bacteria and reduce patients' chances of becoming sick with active TB.
- Patients must take all of their medicine, every day, to prevent the TB from spreading and making them sick.
- Advise patients to contact their health care provider immediately if they have adverse effects to the medication, such as rash or itching. Occasionally, INH can cause tingling or numbness in the hands or feet. The pyridoxine (vitamin B6) they are taking should help prevent that, but they should let their provider know if it occurs.
- Advise patients to avoid the consumption of alcohol while taking INH. The medicines for TB are processed by the liver and, when combined with alcohol, they easily can overload the liver. Acetaminophen (Tylenol) also is processed by the liver, so patients should keep their intake to a minimum. (Patients with hepatitis C, liver disease, or chronic alcohol consumption should be cautioned to strictly limit their use of acetaminophen.)
- Tell patients that blood tests may be done regularly to make sure the liver is working well, so it is important to keep follow-up appointments. They should take all their medications, vitamins, and supplements with them to the clinic so that their health care provider can review them and make sure there are no drug interactions.
- If patients experience nausea, vomiting, poor appetite, or abdominal pain; if they notice their urine darkening or becoming “cola” colored; or if they notice their eyes or skin yellowing, they should contact the clinic immediately. These problems may indicate that the liver is being overwhelmed, and it is important to find out before permanent damage is done.
- Rifampin and rifabutin will cause sweat, tears, urine, and plastic contact lenses to turn orange; this is not harmful.
- Rifampin and rifabutin can make birth control pills ineffective. Patients should use a backup method of contraception until treatment is complete. Condoms can help prevent HIV transmission and reduce the likelihood of pregnancy.

Smoking Cessation

Background

According to the U.S. Centers for Disease Control and Prevention, smoking prevalence among the general adult population in the United States is approximately 20%. Among HIV-infected persons, the prevalence of cigarette smoking appears to be two to three times greater than in the general population, with estimates ranging from 50% to 70%.

The health effects of cigarette smoking are extensive and have been well documented. There are approximately 400,000 smoking-related deaths annually in the United States. HIV-infected smokers appear to be at higher risk of a variety of tobacco-related conditions than HIV-uninfected smokers. These include lung cancer, head and neck cancers, cervical and anal cancers, oral candidiasis, and oral hairy leukoplakia. HIV-infected smokers who smoke are more likely to develop the conditions listed above, as well as bacterial pneumonia, *Pneumocystis jiroveci* pneumonia, other pulmonary conditions, and cardiovascular disease. Additionally, HIV-infected smokers have been shown to have a decreased immunologic and virologic response to antiretroviral therapy.

Thus, for HIV-infected persons, even more so than for HIV-uninfected persons, clinicians should consider smoking cessation a health care priority. Although many care providers may feel that they can do little to affect the smoking behaviors of patients, evidence suggests that brief interventions by physicians are quite effective. Studies indicate that smoking cessation interventions as brief as 3 minutes in duration, when delivered by a provider, have a positive impact on abstinence rates of current smokers. Furthermore, studies have found that more than half of current HIV-infected smokers have expressed interest in, or have thought about, smoking cessation.

Cigarettes are highly addictive; the U.S. Surgeon General has equated the addictive potential of cigarettes to that of heroin and cocaine. This is in part because nicotine stimulates the release of several neurotransmitters in the brain, including dopamine. Over time, chronic exposure to nicotine causes physiologic changes in the brain that contribute to the addictive potential of cigarettes.

Cigarette smoking involves dependence on more than a single chemical compound, however. It is a multidimensional behavior that has both physiologic and psychological components. Therefore, smoking cessation efforts often require a combined approach to be successful.

HRSA HAB Performance Measures

Percentage of patients aged 18 years and older who were **screened for tobacco use** one or more times within 24 months AND who **received cessation counseling intervention** if identified as a tobacco user

(Adult and Adolescent measure)

Behavioral Model for Smoking Cessation

Several behavioral models present a psychological framework for understanding individuals who are attempting to change behaviors. The transtheoretical model of health

behavior change is one of the more frequently cited frameworks for understanding the stages of behavior change of smokers. According to this model, there are five phases of behavior change: precontemplation, contemplation, preparation, action, and maintenance. Using this framework, clinicians can devise

interventions that are most appropriate for the patient's current stage on the continuum.

- **Precontemplation:** The individual does not expect to make any change in behavior within the next 6 months. At this stage, the individual is resistant to hearing or learning about health behavior change.
- **Contemplation:** The individual plans to make a behavior change within the next 6 months. This stage is characterized by ambivalence about smoking.
- **Preparation:** The individual anticipates making a behavior change within the next month. Individuals in this phase have made plans for taking action and intend to make a change.
- **Action:** The individual has made a significant change; in the case of smoking cessation, this means that the individual

has quit completely.

- **Maintenance:** The individual attempts to prevent relapse.

Patients may move back and forth among these stages at various points during the process of smoking cessation.

Cessation interventions in the clinic

As suggested above, brief smoking cessation interventions delivered by clinicians can significantly increase abstinence rates of current smokers. The U.S. Surgeon General has developed guidelines for clinicians to use during clinic visits to help patients who are interested in smoking cessation. These include use of the Five A's model, which provides a brief and structured framework for addressing smoking cessation in clinical settings (see Table 1).

Table 1. The Five A's Model for Treating Tobacco Use and Dependence

Component	Action	Example
ASK every patient about tobacco use	Identify and document tobacco use at every visit .	Incorporate questions about tobacco use when obtaining vital signs or when reviewing a patient's history. <ul style="list-style-type: none"> • "Do you currently use tobacco?" • "Do you currently smoke cigarettes?"
ADVISE to quit	Using a clear, strong, and personalized message , urge every tobacco user to quit.	<ul style="list-style-type: none"> • "It is important for you to quit smoking now." • "Quitting is the most important thing you can do to protect your health." • "I can help you quit." Also link smoking with something specific to the patient, such as secondhand exposure to children or partners, his/her own lung, cardiovascular, or cancer risk, or the expense of cigarettes.
ASSESS readiness to make a quit attempt	Determine whether the tobacco user is willing and ready to make a quit attempt within 30 days.	<ul style="list-style-type: none"> • "Are you willing to give quitting cigarettes a try?"
ASSIST in the quit attempt	For the patient willing to quit, assist in developing a quit plan . Provide practical counseling, support, and supplementary materials.	<ul style="list-style-type: none"> • Have patient set a quit date and enlist the support of his/her family and friends. • Offer pharmacotherapy, as appropriate, including nicotine replacement. • Provide counseling that includes problem solving and skills building.

Component	Action	Example
ARRANGE for follow-up	Arrange for follow-up contacts beginning within the first week after the quit date.	<ul style="list-style-type: none"> • Contact patient via telephone or in person soon after the quit date. This can be done by the primary clinician or other trained staff members. • During the follow-up encounter, assess and identify any problems, review medication use and side effects, provide reminders about additional resources. • Congratulate patients on their successes. • Help those with relapses assess problems with and barriers to quitting, and offer additional or different assistance. • For patients who report a relapse, help them identify the circumstances that led the relapse and assist them with recommitting to smoking abstinence.

Adapted from Fiore MC, Jaén CR, Baker TB, et al. *Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline*. Rockville, MD: U.S. Department of Health and Human Services, Public Health Service; May 2008. Available at www.ncbi.nlm.nih.gov/books/NBK63952. Accessed December 1, 2013.

For patients who are not ready to quit, techniques such as motivational interviewing (MI) can be used in conjunction with the stages-of-change model to explore the smokers' beliefs, feelings, and barriers to successful cessation efforts. Components of MI include: a) expressing empathy; b) developing discrepancy; c) rolling with resistance; and d) supporting self-efficacy. Effective use of MI involves specialized training. Partnering with clinic staff or outside agencies that are familiar with MI techniques can help improve behavior change outcomes, such as smoking cessation. (For further information, see "References," below.)

Pharmacologic interventions

In addition to counseling, the use of pharmacologic interventions such as nicotine replacement therapy and other adjuvant therapies should be considered. These therapies were developed for the general population, but current clinical guidelines suggest that they should be efficacious for HIV-infected smokers.

Clinicians should be aware of potential medication adverse effects (see Table 2).

S: Subjective

- Ask all patients about their smoking status at every visit. This can be easily incorporated as part of the initial intake when vital signs are obtained.
- Document smoking history, including the number of cigarettes smoked per day.
- If the patient is not ready to quit, use MI techniques to identify beliefs and barriers and to create ambivalence about smoking.
- For the smoker interested in quitting:
 - Help identify triggers to smoking, and develop a quit plan.
 - Assess for potential complications or considerations related to pharmacologic smoking cessation treatments such as history of seizure disorders, sleep disturbances, mood disorders, and pregnancy.
- For patients who recently quit, congratulate them on their accomplishments and reinforce the benefits of continued cessation.
- For patients who recently relapsed, help them identify what led to the relapse and how to avoid relapses in the future. Assist them in getting back on track with a cessation program.

O: Objective

During the physical examination, assess for evidence of smoking-related illnesses and the comorbid conditions that may be affected by smoking. At a minimum, measure blood pressure and oxygen saturation and examine for oral lesions, abnormal breath sounds, and decreased peripheral perfusion.

A/P: Assessment and Plan

Determine the smoker's readiness to change (see behavioral model for smoking cessation, above). For those smokers in the preparation or action stage, assist with implementing a quit plan. For those who are in the relapse stage, reinforce self-efficacy and encourage them to recommit to cessation. For those in the maintenance stage, congratulate them and reinforce the benefits of smoking cessation.

For patients willing to quit, offer resources and information that will help them to be successful in their quit attempt. Evidence suggests that the combination of counseling and medication is more effective than either intervention alone. Therefore, every effort should be made to combine counseling sessions with pharmacotherapy for patients who are motivated and ready to quit smoking.

Components of effective counseling include problem solving, skills training, and social support. Problem solving and skills training should focus on how to deal with triggers or urges that may lead to relapse. Examples

include recognition of situations or events that may prompt a person to smoke (e.g., drinking alcohol, being around other cigarette smokers, situational stress) and means of reducing or coping with these situations. Social support interventions include providing reassurance that the patient has the ability to succeed with smoking cessation, communicating caring and concern, and encouraging the patient to talk about the quit process.

Offer medications, if there are no contraindications to pharmacologic interventions (see Table 2). All currently available over-the-counter and prescription medications have been shown to be effective. However, studies have shown that combination therapy may be more efficacious than monotherapy. The current tobacco cessation guidelines recommend the following combinations, all of which include nicotine preparations: long-term nicotine patch (>14 weeks) with ad lib use of nicotine gum or spray, nicotine patch with nicotine inhaler, and nicotine patch with sustained-release (SR) bupropion.

Both bupropion SR and varenicline may cause sleep disturbance, and varenicline may cause exacerbation of neuropsychiatric symptoms. For HIV-infected patients who take efavirenz as part of their antiretroviral therapy, concomitant use of either bupropion SR or varenicline may increase the possibility of these side effects. Additional research in this area is needed.

Table 2. Pharmacologic Options for Smoking Cessation

Drug Recommended	Dosing	Common Side Effects	Comments
Nicotine Formulations*			
Nicotine Patch (available OTC) <i>Dosage varies by brand:</i> Nicoderm or Habitrol: <ul style="list-style-type: none"> • 21 mg/24 hours • 14 mg/24 hours • 7 mg/24 hours Nicotrol: <ul style="list-style-type: none"> • 15 mg/24 hours • 10 mg/24 hours • 5 mg/24 hours 	<p>Dosing recommendations vary based on the number of cigarettes smoked. Individualize treatment.</p> <p>Sample treatment recommendation for smokers who smoke ≥ 10 cigarettes per day:</p> <ul style="list-style-type: none"> • High-dose patch for 4-6 weeks, then • Medium-dose patch for 2 weeks, then • Low-dose patch for 2 weeks <p>For smokers who smoke < 10 cigarettes per day:</p> <ul style="list-style-type: none"> • Medium-dose patch for 6-8 weeks, then • Low-dose patch for 2 weeks 	<p>Local skin reaction, insomnia or vivid dreams</p>	<ul style="list-style-type: none"> • Apply upon awakening. • Place patch on a relatively hairless location, rotating sites to avoid irritation. • If experiencing sleep disturbance, remove patch prior to bedtime or use the 16-hour patch.
Nicotine Lozenge (available OTC) <ul style="list-style-type: none"> • 2 mg and 4 mg 	<ul style="list-style-type: none"> • For patients who smoke their first cigarette > 30 minutes after waking, start with 2 mg dose. For patients who smoke their first cigarette within the first 30 minutes after waking, start with 4 mg. • Most patients should use 1 lozenge Q1-2H during the first 6 weeks. • Allow lozenges to dissolve, do not chew or swallow. Most individuals use 9 lozenges per day; maximum is 20 per day. • Lozenges should be used for up to 12 weeks, decreasing dosing from 1 lozenge Q1-2H for the first 6 weeks, to 1 lozenge Q2-4H during weeks 7-9, and 1 lozenge Q4-8H during weeks 9-12. 	<p>Nausea, hiccups, heartburn, headache, cough</p>	<ul style="list-style-type: none"> • Do not eat or drink anything except water for 15 minutes before using a lozenge.

Drug	Recommended Dosing	Common Side Effects	Comments
Nicotine Formulations*			
Nicotine Inhaler (prescription only) <ul style="list-style-type: none"> • 4 mg per inhalation • 10 mg cartridge 	Recommended dosage: 6-16 cartridges per day. Duration of therapy: up to 6 months, taper dosage in last 3 months.	Local irritation in the mouth and throat, cough, rhinitis; may cause bronchospasm (<1%)	<ul style="list-style-type: none"> • Use caution in persons with severe reactive airway disease.
Nicotine Nasal Spray (prescription only) <ul style="list-style-type: none"> • 0.5 mg per spray 	<ul style="list-style-type: none"> • Patient should use 1-2 sprays each nostril per hour (total 1-2 mg per hour), increasing as needed for symptom relief. • Minimum recommended treatment is 16 sprays (8 mg) per day, with a maximum limit of 80 sprays per day (10 sprays per hour). • Recommended duration of therapy: 3-6 months. • Do not sniff, swallow, or inhale through the nose while administering doses. Tilt head slightly back when dosing. 	Nasal irritation, transient changes in sense of smell and taste; may cause bronchospasm (<1%)	<ul style="list-style-type: none"> • Use caution in persons with severe reactive airway disease. • Nicotine nasal spray has highest dependence potential of the nicotine replacement therapies.
Non-Nicotine Medications, First Line			
Bupropion SR <ul style="list-style-type: none"> • 150 mg 	Begin 1-2 weeks before quit date. <ul style="list-style-type: none"> • Start at 150 mg daily for 3 days, then increase to 150 mg BID for 7-12 weeks. • May consider longer-term therapy. 	Insomnia, dry mouth	<ul style="list-style-type: none"> • May lower seizure threshold in certain patients. • Levels increased in patients on P450 3A4 inhibitors. • Use with caution in patients with history of seizures or eating disorders, and those who have used a monoamine oxidase (MAO) inhibitor in the past 14 days.

Drug	Recommended Dosing	Common Side Effects	Comments
Varenicline <ul style="list-style-type: none"> 0.5 mg and 1 mg 	Begin 1 week before quit date. <ul style="list-style-type: none"> Start with 0.5 mg daily for 3 days, increase to 0.5 mg BID for 4 days, then 1 mg BID for duration of therapy. Typical duration: 12 weeks. Varenicline is approved for maintenance therapy for up to 6 months. 	Nausea; flatulence; headache; sleep disturbance; abnormal, vivid, or strange dreams; depression; agitation; suicidal ideation; and suicide FDA Black Box warning regarding neuropsychiatric adverse effects	<ul style="list-style-type: none"> Use with caution in patients with history of psychiatric illness. Monitor closely for mood and behavior changes. Dosage reduction recommended for patients who have creatinine clearance (CrCl) of <30 mL/min or are on dialysis. To reduce nausea, should be taken with food. To reduce insomnia, second pill can be taken at dinner rather than at bedtime. Dosage may be reduced for patients with adverse effects.
Non-Nicotine Medications, Second Line			
Clonidine <ul style="list-style-type: none"> 0.1 mg tablet 0.1 mg transdermal patch 	<ul style="list-style-type: none"> 0.1 mg tablet PO BID OR <ul style="list-style-type: none"> 0.1 mg transdermal patch per day. Can increase by 0.1 mg/day per week if needed. Duration of treatment: 3-10 weeks. Do not discontinue therapy abruptly. 	Dry mouth, drowsiness, dizziness, sedation, and constipation Rebound hypertension if discontinued abruptly	<ul style="list-style-type: none"> Monitor blood pressure when using this medication. If discontinuing, taper medication to avoid rebound hypertension. If using patch, place on relatively hairless location between the neck and waist. Avoid in elderly patients
Nortriptyline	<ul style="list-style-type: none"> Begin 10-28 days before quit date. Start at 25 mg QD and increase to target dosage of 75-100 mg QD if tolerated. Treatment duration: approximately 12 weeks; some may consider extending treatment up to 6 months. 	Sedation, dry mouth, blurred vision, urinary retention, lightheadedness, tremor, cardiac conduction abnormalities	<ul style="list-style-type: none"> Use with caution in patients with cardiac conduction abnormalities disease. Do not coadminister with MAO inhibitors. Overdose may produce life-threatening cardiovascular toxicity, as well as seizures and coma. Avoid in elderly patients

* Use with caution for patients with cardiovascular disease (particularly those within 2 weeks of myocardial infarction), those with serious arrhythmias, and those with unstable angina pectoris (however, note that, for many patients, continued smoking may be more dangerous than nicotine replacement).
 The adverse effects of cigarette smoking during pregnancy are well established, and smoking generally is more harmful than the use of nicotine replacements. Smoking cessation aids may help motivated patients quit during pregnancy.

All patients who are actively quitting should have close follow-up, and they should be offered support. Research has shown that ongoing support during the quit phase results in higher abstinence rates.

Follow-up can include telephone calls or in-person evaluation.

For patients who recently quit or relapsed, continue to provide support and encouragement. Assist individuals who relapsed with the opportunity to continue with cessation plans.

Refer patients to smoking cessation groups, classes, and other resources.

Patient Education

- For patients who have decided on pharmacologic interventions and for whom there are no contraindications, provide education regarding medication side effects, anticipated withdrawal symptoms, and strategies for managing withdrawal.
- Review and reinforce strategies in the event of relapse.
- For those who are not ready to quit, inform them of the consequences of continued smoking and remind them about the available resources.

Suggested Resources:

- National Telephone Counseling and Quit Line (800-QUIT-NOW) (800-784-8669)
- American Cancer Society (www.cancer.org)
- American Lung Association (maintains profiles of state tobacco control activities) (www.lungusa.org)
- National Cancer Institute (www.cancer.gov)
- Office on Smoking and Health at the Centers for Disease Control and Prevention (www.cdc.gov/tobacco)

Nutrition

Background

Maintaining good nutritional status is important to support overall health and immune system function for people with HIV/AIDS. Many HIV-related conditions affect and are affected by the body's nutritional status. These include conditions related to HIV itself (e.g., opportunistic infections and other illnesses), comorbid conditions, and adverse effects of therapies.

Inadequate nutrition in people with HIV infection may result from many factors, including conditions such as nausea, vomiting, and anorexia (see chapter *Nausea and Vomiting*) that may prevent adequate intake of nutrients and medications; diarrheal infections (see chapter *Diarrhea*) that prevent absorption of nutrients and medications; poor oral health conditions that interfere with chewing or tasting food (see chapter *Oral Health*); systemic illnesses (including HIV itself) that create a catabolic state; and psychological conditions (such as depression) that impair patients' ability to nourish themselves. In addition, financial constraints may limit patients' access to nutritious food.

Evaluation and enhancement of patients' nutritional status may help correct or compensate for deficiencies (e.g., in the case of weight loss or nutrient deficits), may be a key treatment modality for certain conditions (e.g., dyslipidemia, hyperglycemia), and may help to maintain good health and immune function. This chapter focuses on the evaluation of patients with nutritional deficiencies, particularly weight loss, and on simple strategies for maintaining good nutrition in individuals with barriers to maintaining adequate weight.

It should be noted that obesity and overweight conditions are increasingly common in HIV-infected individuals; many of the principles described here also may be applied to the evaluation of overweight patients. Recommendations for weight reduction for HIV-infected patients are the same as for the general population and will not be discussed in detail; for overweight patients with lipohypertrophy, diabetes, dyslipidemia, or coronary artery disease, see the respective chapters on these conditions.

Ideally, HIV-infected individuals will receive the services of HIV-experienced nutrition specialists, who may contribute to the patient care team in the following ways:

- Conducting routine screening to identify and treat nutritional problems
- Preparing a tailored nutritional plan to optimize patients' nutritional status, immune status, and overall well-being
- Screening and developing interventions for growth problems in children
- Developing strategies to prevent loss of weight and lean body mass
- Adapting dietary recommendations to help reduce the risk of comorbid conditions such as diabetes and heart disease, or treating these complications
- Educating patients about how to modify their dietary habits to maximize the effectiveness of medical and pharmacologic treatments
- Tailoring nutritional recommendations to fit patients' lifestyles and financial resources
- Counseling patients to promote nutrition self-care using available resources

- Providing nutritional support to patients may help to do the following:
 - Address common problems associated with HIV disease and its treatment (e.g., weight loss, wasting, fatigue, loss of appetite, adverse changes in taste, dental problems, gastrointestinal complaints)
 - Treat chronic comorbid conditions (e.g., cardiovascular disease, hypertension, diabetes, cirrhosis)
 - Improve quality of life
 - Enhance immune responses, slow disease progression, and prolong life

S: Subjective

History

Identify nutrition risk factors at the start of care through interview, questionnaire, or both. Update the history at least annually.

The history should elicit signs and symptoms related to nutrition issues, indications regarding dietary habits, and symptoms that suggest nutritional deficiencies.

Nutrition-Related Questions		
Factor	Areas to Explore	
Signs, Symptoms, and Comorbid Conditions	<ul style="list-style-type: none"> • Poor or sporadic appetite • Early satiety • Weight gain or loss • Trouble chewing or swallowing • Dental problems including poor dental hygiene • Gastrointestinal complaints, including nausea, diarrhea, constipation, heartburn, gas 	<ul style="list-style-type: none"> • Changes in body contours with fat gain in abdomen, back of neck, and breasts (lipodystrophy) or fat loss in extremities and face (lipoatrophy) • Depression, stress • Fatigue • Chronic pain • Other diseases affecting diet and nutrition • Medications, including over-the-counter and herbal products
Medication-Related Factors	<ul style="list-style-type: none"> • Medication side effects • Difficulty coordinating meals with medicines 	<ul style="list-style-type: none"> • Use of nutritional supplements
Social and Behavioral Factors	<ul style="list-style-type: none"> • Frequent eating out • Smoking • Alcohol or substance abuse • Erratic meal patterns • Unbalanced diet (e.g., high intake of low-nutrient foods; deficiency in key nutrients) 	<ul style="list-style-type: none"> • Resources to ensure secure, continued food access • Availability of food storage and preparation facilities • Housing (stable, homeless, marginally housed, or in transition) • Nutrition literacy

To develop a specific dietary history, ask about the following:

Dietary History	
Usual Dietary Intake	Factors That May Affect or Limit Intake
<ul style="list-style-type: none"> Frequency of intake of foods providing key nutrients (e.g., dairy products, fortified or whole grains, fruits and vegetables, eggs, beans, fluids, meat) as well as those that perhaps should be limited (fast-food items, highly processed or salted products) Usual meal patterns (number of times per day, snacks) and whether meals are prepared and eaten at home or eaten at restaurants or fast-food establishments Specific information about nutritional supplements (e.g., vitamins, minerals, herbs, protein), including contents, amounts, formulation (pills, powders, drinks), cost, and overlap among products 	<ul style="list-style-type: none"> Amount of money available for food, or participation in food assistance programs (e.g., food stamps, food pantries) Appetite, general well-being (e.g., fatigue, pain, depression) Food allergies, intolerances Problems with dentition, swallowing, heartburn, diarrhea, constipation Coordination of foods and supplements with medications (HIV or other)

Elicit symptoms that may be related to nutritional deficiencies.

Symptoms with Possible Relationship to Nutritional Deficiencies	
<ul style="list-style-type: none"> General symptoms (e.g., fatigue, decreased cognitive function, headache) Behavioral changes (e.g., irritability, apathy, decreased responsiveness, anxiety, attention deficit) Body habitus changes (e.g., loss or gain of fat) 	<ul style="list-style-type: none"> Gastrointestinal symptoms (e.g., diarrhea, constipation, bloating) Changes in skin, nails, hair (e.g., dryness, breaking, thinning) Muscle loss Neurologic symptoms (e.g., weakness, sensory changes, gait abnormalities)

O: Objective

Physical Examination

Perform a careful physical examination, if possible with anthropometric and body composition testing as described below (Table 1). Compare current findings with past assessments and review at least every 6 months.

The physical examination should include the following:

- Vital signs, with orthostatic vital signs if dehydration is suspected
- Weight (compare with previous values) and body mass index (BMI)
- General appearance and gross nutritional status (e.g., obesity, cachexia, wasting)
- Body habitus: loss of subcutaneous fat in face, buttocks, arms and legs and/or

increased fat in abdomen, breasts, neck, and upper back (“buffalo hump”)

- Muscle mass
- Mouth: breakdown in oral mucosa, cheilosis, angular stomatitis, glossitis, papillar atrophy
- Abdomen: hepatomegaly (may be caused by fatty infiltration)
- Skin: dryness, peeling, breakdown, pallor, hypopigmentation or hyperpigmentation
- Nails: pale nail beds, fissures or ridges
- Neurologic system, including strength, sensation, coordination, gait, deep tendon reflexes

Anthropometric and body composition tests are usually performed by registered dietitians. They can provide important information about patients’ nutritional status.

Table 1. Anthropometric Measurements for Adults and Children

	Height	Weight	Assessment for Changes over Time
Adults	Measure at baseline (self-report is not accurate).	<ul style="list-style-type: none"> Measure at least quarterly and consider intervention when small changes are observed. Do not wait until major amounts of weight have been lost or gained. Record sequentially at the front of the patient's chart and monitor for trends. 	Use healthy, premorbid weight to assess change, not the first clinic weight or the ideal weight. (Use the patient's weight at a time when the patient is healthy, feels well, and can easily maintain that weight.)*
Children	Measure at least quarterly using length board (0-2 years) or wall-mounted stadiometer (≥ 2 years).	<ul style="list-style-type: none"> Measure at least quarterly and consider intervention when small changes are observed. Do not wait until the patient has dropped significantly on the growth chart. Calculate age and plot the measurements on growth charts specific for age, sex, and country.# 	Assessment of optimal growth is based on the observed pattern over time. General goals include a weight relatively "matched" for length or height (about the same percentile) and relative stability of percentile tracking over time.* #

* BMI (body mass index) is useful as an evaluative index. See chapter *Initial Physical Examination*, and the U.S. Centers for Disease Control and Prevention (CDC) online calculator at www.cdc.gov/healthyweight/assessing/bmi. Accessed December 1, 2013.

Growth charts for children in the United States are available online from the CDC at www.cdc.gov/growthcharts. A variety of growth charts are available for children from specific ethnic groups (e.g., Chinese, Vietnamese, Thai), children with selected conditions affecting growth (e.g., Down syndrome), or those who are born prematurely. Percentiles for both height and weight should be recorded sequentially.

Body Composition Testing

Body composition commonly is tested by bioelectrical impedance analysis (BIA) (Table 2) or skinfold thickness and circumference (Table 3).

Table 2. Bioelectrical Impedance Analysis

BIA testing is the standard of care for adults but has not been well validated for children:

- BIA is useful for assessing disease progression or health maintenance, documenting response to treatment, and justifying the cost of nutritional supplements and AIDS-wasting medications.
- The test is simple, noninvasive, and quick (<5 minutes). However, staff training and specialized software are required to interpret the results.
- Perform BIA at baseline, if possible. Update every 6-12 months or more frequently if the patient is ill, has a decline in immune status, or has a weight change of 5-10%.
- The BIA test reports the following:
 - Body cell mass (BCM):** the target component, reflecting cells in muscles, organs, and the circulation; losses may indicate AIDS wasting. BCM is recorded in pounds. Monitor for trends.
 - Fat:** an index of energy stores; recorded in pounds and percentage.
 - Phase angle:** a measure of cellular integrity, an independent indicator of morbidity and mortality in HIV-infected patients.

Table 3. Skinfold Thickness and Circumference Measures

Skinfold thickness and circumference measures can be used for adults and children in resource-limited settings, and for situations in which bioelectrical impedance analysis is not available. Circumference measures also can be used to monitor changes over time associated with lipodystrophy in adults.

- Skinfold thickness is measured with calipers.
- Circumference measures are taken at specific anatomical landmarks with nonstretchable tape.
- Techniques and protocols for taking anthropometric measurements can be found at the CDC website (www.cdc.gov/nchs/data/nhanes/nhanes_03_04/BM.pdf).

Laboratory Testing

Perform basic laboratory (blood) tests, including the following:

- Hemoglobin and/or hematocrit
- Total protein, albumin
- Fasting blood glucose
- Fasting lipids (triglycerides, total cholesterol, low-density lipoprotein cholesterol [LDL], high-density lipoprotein cholesterol [HDL])
- CD4 cell count and HIV viral load, if no recent values are available
- Specific vitamin and nutrient tests as indicated by symptoms (e.g., iron studies in case of anemia, vitamin B12 in case of peripheral neuropathy)
- Others tests, such as testosterone and thyroid hormone levels as appropriate, to rule out other causes of symptoms

A: Assessment

Assess subjective information and objective findings to evaluate nutritional status.

Identify Nutrition Concerns

Several factors may influence nutrition, including the following:

- Barriers to good nutrition (e.g., lack of knowledge or motivation for self-care, poor appetite, lack of money for food, lack of facilities for food storage and preparation)
- Lifestyle factors (e.g., smoking, substance abuse, frequent eating out, erratic eating patterns, hectic schedule, high stress)

- Physical problems affecting food and nutrient intake (e.g., poor appetite, nausea, fatigue, pain, weakness, mouth or throat pain, acid reflux, missing or decayed teeth, poorly fitting dentures, poor eyesight, constipation)
- Nutrient losses (e.g., owing to diarrhea, vomiting)
- Potential confounding factors (e.g., use of multiple overlapping or questionable supplements, eating disorders)

Evaluate Dietary Intake

Assess the following diet-related issues:

- Expected excesses or deficiencies from dietary history or interview
- Rating of food security, including access to cooking and refrigeration
- Food intolerances, aversions, or allergies likely to affect adequacy of intake
- Special needs related to other conditions (e.g., documented cardiovascular disease, diabetes, hypertension)

Evaluate Weight, Body Composition, and Weight Distribution

Assess physical findings of malnutrition and confirm with nutrition history, laboratory tests, and anthropometric evidence. Normal and abnormal findings of anthropometric tests and recommendations for monitoring changes over time are presented in Table 4.

Table 4. Evaluating the Findings of Anthropometric Tests	
Monitoring Trends and Recommendations	
Adults <ul style="list-style-type: none"> Chart trends over time relative to previous measurements and the following population norms: <ul style="list-style-type: none"> BMI (healthy range: 19-25) BIA: <ul style="list-style-type: none"> BCM (percentage of weight): women 30-35%; men 40-45% Fat (percentage of weight): women 20-30%; men 15-25% Phase angle: women >5; men >6 Skinfold thicknesses and circumferences: Chart changes in absolute measures and percentiles Changes in body contours: Evaluate lipodystrophy (excess accumulation of fat in abdomen, breasts, dorsocervical area) and lipoatrophy (loss of subcutaneous fat in face, extremities, buttocks) 	Children <ul style="list-style-type: none"> Plot measurements on growth charts and track percentiles over time (the consistency of percentiles rather than the absolute percentile is important) Skinfold thicknesses and circumferences: Chart changes in absolute measures and percentiles

Abbreviations: BCM = body cell mass; BIA = bioelectrical impedance analysis; BMI = body mass index

Evaluate Laboratory Findings

- Evidence of malnutrition (e.g., low iron or protein stores)
- Evidence of disease or risk of disease for which dietary treatment is indicated (e.g., high fasting glucose, hypertension, hyperlipidemia)

Develop a Problem List

The following suggests a useful format for a nutrition-related problem list.

Nutrition-Related Problem List

Problem Number	Description of Problem (circle/describe)
	Nutrition barriers: insufficient knowledge, poor appetite, food insecurity, no food preparation or storage facilities, homelessness
	Lifestyle: substance abuse, smoking, erratic eating, frequent fast-food intake, high stress
	Weight or body composition: undesirable weight gain or loss (adult), changes in growth trajectory (children), loss of lean body mass (wasting), gain of excess fat (obesity), lipoatrophy or lipodystrophy
	Physical problems: fatigue, pain, early satiety, poor dentition, clinical signs of malnutrition
	Laboratory findings: low hematocrit or hemoglobin, low protein or albumin, low or high fasting glucose, high total cholesterol, high LDL, high triglycerides, low HDL, low testosterone
	Gastrointestinal: diarrhea, vomiting, reflux, constipation
	Poor diet: poor food choices, bingeing, skipping meals, high sugar intake, high alcohol consumption, high intake of refined foods, low fruit and vegetable intake, insufficient protein, insufficient calcium, food allergies or intolerances that limit intake
	Comorbid conditions: diabetes, hypertension, cardiovascular disease, cancer, gastroesophageal reflux disease (GERD)
	Medications: drug-drug or drug-nutrient interactions or difficulty coordinating medicines with meals
	Supplements: insufficient or excessive intakes, cost of supplements unaffordable, supplements with potential or unknown risks

P: Plan

Develop a nutritional plan and provide practical nutrition education for common problems (see “Resources,” below).

Evaluate and treat concurrent medical problems (e.g., diarrhea, nausea, infections, malignancies, depression, pain). For severe or persistent nutritional problems, or for

specific needs, refer to a nutrition specialist for evaluation and treatment.

Common nutrition-related problems are presented in Table 5, along with simple management suggestions that may help resolve them and help patients maintain adequate nutrition.

Table 5. Practical Interventions for Common Nutrition-Related Problems

Problem	Suggestions
Weight Loss (decrease in both body cell mass and fat)	<ul style="list-style-type: none">• Early identification and ongoing monitoring are key.• Identify and treat underlying risk factors.• Try to add calories without adding “bulk”:<ul style="list-style-type: none">• Fat (9 calories/gram): butter, margarine, avocado, cream, mayonnaise, salad dressing• Carbohydrate (4 calories/gram): jam, jelly, sugar, icing, gum drops• Protein (4 calories/gram): protein powders, cheese, nut butters, trail mix, powdered breakfast drinks, nonfat dry milk• Eat more frequently.• Maximize good days.• Use canned supplements (e.g., Ensure, Boost).• For wasting or substantial weight loss, consider referral for therapies such as appetite stimulants or human growth hormone.
Diarrhea	<ul style="list-style-type: none">• Increase soluble fiber; decrease insoluble fiber.• Replenish beneficial bacteria (e.g., with lactobacilli or other probiotic preparations).• Avoid intestinal irritants and stimulants.• Decrease dietary fat.• Decrease or eliminate lactose.• Increase fluids and provide electrolytes (sodium, potassium).• Treat with pancreatic enzymes.
Early Fullness	<ul style="list-style-type: none">• Take small, frequent meals.• Concentrate on solid foods, with liquids between meals.• Eat lower-fat, lower-fiber foods.• Wear loose-fitting clothing.• Sit up while eating.• Eat, walk, and eat again.
Nausea	<ul style="list-style-type: none">• Take small, frequent meals.• Try dry snack foods.• Avoid fried foods, very sweet foods, spicy foods, and foods with strong odors.• Try cool, clear beverages, popsicles.• Try ginger-containing foods and drinks.• Keep liquids to a minimum at meals.

Problem	Suggestions
Changes in Taste	<ul style="list-style-type: none"> • Eat a variety of foods, not only favorite foods. • Try protein sources other than red meat. • Marinate foods, use sauces. • Use more and stronger seasonings. • Try tart foods. • Use sugar or salt to tone down the flavor of foods. • Try a mouth rinse of 1 teaspoon of baking soda in 1 cup of warm water before eating.
Loss of Appetite	<ul style="list-style-type: none"> • Rely on favorite foods. • Ask family members and friends to prepare meals. • Eat small, frequent meals. • Keep snacks handy for nibbling. • Eat before bedtime. • Eat in a pleasant place, with other people. • Make the most of good days. • Try light exercise to stimulate appetite. • Add extra calories without adding bulk. • Consider appetite stimulants (e.g., megestrol, dronabinol).
Difficulty Chewing or Swallowing or Sore Mouth and Throat	<ul style="list-style-type: none"> • Choose soft, nutritious foods. • Blend or puree foods (e.g., soup or stew, smoothies). • Add cream sauces, butter, or gravy for lubrication. • Sip liquids with foods. • Use a straw or drink foods from a cup. • Choose bland, low-acid foods. • If hot foods cause pain, serve foods cold or at room temperature. • Avoid alcohol and tobacco. • Soothing lozenges or sprays may help.
Food Insecurity	<ul style="list-style-type: none"> • Refer to social services for assistance with accessing resources such as food stamps, community meals, or a food pantry program. • Refer to a dietitian for assistance with low-cost food ideas. • Use materials provided by CheapCooking.com (www.cheapcooking.com/index.htm).
Unbalanced Diet and Other Conditions Requiring Dietary Modification	<ul style="list-style-type: none"> • Refer to a dietitian for counseling and education.

Nutrition Specialists

Whenever possible, nutritional services should be provided by a registered dietitian (RD) who is a qualified HIV care provider. In the United States, holding this status requires a nutrition degree from an accredited college, graduation from an approved internship or master's degree program, and maintenance with 75 continuing-education units every 5 years, including specific and ongoing HIV training. An RD with HIV/AIDS expertise in the United States can be located by going to www.eatright.org, clicking on "Find a Registered Dietitian," entering the patient's zip code or city, and selecting "HIV/AIDS" under areas of specialty. Membership in the Infectious Diseases Nutrition Dietetic Practice Group (idndpg.org) also may indicate HIV experience.





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