Guidelines for the Prevention of Opportunistic Infections Among HIV-Infected Persons – 2002

Recommendations of the U.S. Public Health Service and the Infectious Diseases Society of America

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Summary

In 1995, the U.S. Public Health Service (USPHS) and the Infectious Diseases Society of America (IDSA) developed guidelines for preventing opportunistic infections (OIs) among persons infected with human immunodeficiency virus (HIV); these guidelines were updated in 1997 and 1999. This fourth edition of the guidelines, made available on the Internet in 2001, is intended for clinicians and other health-care providers who care for HIV-infected persons. The goal of these guidelines is to provide evidencebased guidelines for preventing OIs among HIV-infected adults and adolescents, including pregnant women, and HIV-exposed or infected children. Nineteen OIs, or groups of OIs, are addressed, and recommendations are included for preventing exposure to opportunistic pathogens, preventing first episodes of disease by chemoprophylaxis or vaccination (primary prophylaxis), and preventing disease recurrence (secondary prophylaxis). Major changes since the last edition of the guidelines include 1) updated recommendations for discontinuing primary and secondary OI prophylaxis among persons whose CD4+ T lymphocyte counts have increased in response to antiretroviral therapy; 2) emphasis on screening all HIV-infected persons for infection with hepatitis C virus; 3) new information regarding transmission of human herpesvirus 8 infection; 4) new information regarding drug interactions, chiefly related to rifamycins and antiretroviral drugs; and 5) revised recommendations for immunizing HIV-infected adults and adolescents and HIV-exposed or infected children.

Introduction

In 1995, the U.S. Public Health Service (USPHS) and the Infectious Diseases Society of America (IDSA) developed guidelines for preventing opportunistic infections (OIs) among persons infected with human immunodeficiency virus (HIV) (*1-3*). These guidelines, which are intended for clinicians and health-care providers and their HIV-infected patients, were revised in 1997 (*4*) and again in 1999 (*5*), and have been published in *MMWR* (*1,4,5*), *Clinical Infectious Diseases* (*2,6,7*), *Annals of Internal Medicine* (*3,8*), *American Family Physician* (*9,10*), and *Pediatrics* (*11*); accompanying editorials have appeared in *JAMA* (*12,13*). Response to these guidelines (e.g., a substantial number of requests for reprints, website contacts, and observations from health-care providers) demonstrates that they have served as a valuable reference for HIV health-care providers. Because the 1995, 1997, and 1999 guidelines included ratings indicating the strength of each recommendation and the quality of supporting evidence, readers have been able to assess the relative importance of each recommendation.

Since acquired immunodeficiency syndrome (AIDS) was first recognized 20 years ago, remarkable progress has been made in improving the quality and duration of life for HIV-infected persons in the industrialized world. During the first decade of the epidemic, this improvement occurred because of improved recognition of opportunistic disease processes, improved therapy for acute and chronic complications, and introduction of chemoprophylaxis against key opportunistic

* See inside front cover for list of working group members.

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pathogens. The second decade of the epidemic has witnessed extraordinary progress in developing highly active antiretroviral therapies (HAART) as well as continuing progress in preventing and treating OIs. HAART has reduced the incidence of OIs and extended life substantially (*14–16*). HAART is the most effective approach to preventing OIs and should be considered for all HIV-infected persons who qualify for such therapy (*14–16*). However, certain patients are not ready or able to take HAART, and others have tried HAART regimens but therapy failed. Such patients will benefit from prophylaxis against OIs (*15*). In addition, prophylaxis against specific OIs continues to provide survival benefits even among persons who are receiving HAART (*15*).

Clearly, since HAART was introduced in the United States in 1995, chemoprophylaxis for OIs need not be lifelong. Antiretroviral therapy can restore immune function. The period of susceptibility to opportunistic processes continues to be accurately indicated by $CD4^+$ T lymphocyte counts for patients who are receiving HAART. Thus, a strategy of stopping primary or secondary prophylaxis for certain patients whose immunity has improved as a consequence of HAART is logical. Stopping prophylactic regimens can simplify treatment, reduce toxicity and drug interactions, lower cost of care, and potentially facilitate adherence to antiretroviral regimens.

In 1999, the USPHS/IDSA guidelines reported that stopping primary or secondary prophylaxis for certain pathogens was safe if HAART has led to an increase in $CD4^+$ T lymphocyte counts above specified threshold levels. Recommendations were made for only those pathogens for which adequate clinical data were available. Data generated since 1999 continue to support these recommendations and allow additional recommendations to be made concerning the safety of stopping primary or secondary prophylaxis for other pathogens.

For recommendations regarding discontinuing chemoprophylaxis, readers will note that criteria vary by such factors as duration of $CD4^+$ T lymphocyte count increase, and, in the case of secondary prophylaxis, duration of treatment of the initial episode of disease. These differences reflect the criteria used in specific studies. Therefore, certain inconsistencies in the format of these criteria are unavoidable.

Although considerable data are now available concerning discontinuing primary and secondary OI prophylaxis, essentially no data are available regarding restarting prophylaxis when the $CD4^+$ T lymphocyte count decreases again to levels at which the patient is likely to again be at risk for OIs. For primary prophylaxis, whether to use the same threshold at which prophylaxis can be stopped (derived from data in studies addressing prophylaxis discontinuation) or to use the threshold below which initial prophylaxis is recommended, is unknown. Therefore, in this revision of the guidelines, in certain cases, ranges are provided for restarting primary or secondary prophylaxis. For prophylaxis against *Pneumocystis carinii* pneumonia (PCP), the indicated threshold for restarting both primary and secondary prophylaxis is 200 cells/µL. For all these recommendations, the Roman numeral ratings reflect the lack of data available to assist in making these decisions (Box).

During the development of these revised guidelines, working group members reviewed published manuscripts as well as abstracts and material presented at professional meetings. Periodic teleconferences were held to develop the revisions.

BOX. System used to rate the strength of recommendations and quality of supporting evidence

Rating	Strength of recommendation
A	Both strong evidence for efficacy and substantial clinical benefit support recommendation for use; should always be offered.
B	Moderate evidence for efficacy or strong evidence for efficacy, but only limited clinical benefit, supports recommendation for use; should usually be offered.
C	Evidence for efficacy is insufficient to support a recommendation for or against use, or evidence for efficacy might not outweigh adverse consequences (e.g., drug toxicity, drug interactions) or cost of the chemoprophylaxis or alternative approaches; use is optional.
D	Moderate evidence for lack of efficacy or for adverse outcome supports a recommendation against use; should usually not be offered.
E	Good evidence for lack of efficacy or for adverse outcome supports a recommendation against use; should never be offered.

Rating	Quality of evidence supporting the recommendation
I	Evidence from ≥1 correctly randomized, controlled trials.
II	Evidence from ≥1 well-designed clinical trials without randomization, from cohort or case-controlled analytic studies (preferably from more than one center), or from multiple time-series studies, or dramatic results from uncontrolled experiments.
III	Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of consulting committees.

Major Changes in These Recommendations

Major changes in the guidelines since 1999 include the following:

- Higher level ratings have been provided for discontinuing primary prophylaxis for PCP and *Mycobacterium avium* complex (MAC) when $CD4^+$ T lymphocytes have increased to >200 cells/µL and >100 cells/µL, respectively, for ≥3 months in response to HAART (AI), and a new recommendation to discontinue primary toxoplasmosis prophylaxis has been provided when the $CD4^+$ T lymphocyte count has increased to >200 cells/µL for ≥3 months (AI).
- Secondary PCP prophylaxis should be discontinued among patients whose $CD4^+$ T lymphocyte counts have increased to >200 cells/µL for ≥3 months as a consequence of HAART (BII).
- Secondary prophylaxis for disseminated MAC can be discontinued among patients with a sustained (e.g., ≥6-month) increase in $CD4^+$ count to >100 cells/µL in response to HAART, if they have completed 12 months of MAC therapy and have no symptoms or signs attributable to MAC (CIII).
- Secondary prophylaxis for toxoplasmosis and cryptococcosis can be discontinued among patients with a sustained increase in $CD4^+$ counts (e.g. ≥6 months) to >200 cells/µL and >100–200cells/µL respectively, in response to HAART, if they have completed their initial therapy and have no symptoms or signs attributable to these pathogens (CIII).
- The importance of screening all HIV-infected persons for hepatitis C virus (HCV) is emphasized (BIII).
- Additional information concerning transmission of human herpesvirus 8 infection (HHV-8) is provided.
- New information regarding drug interactions is provided, chiefly related to rifamycins and antiretroviral drugs.
- Revised recommendations for vaccinating HIV-infected adults and HIV-exposed or infected children are provided.

Using the Information in This Report

For each of the 19 diseases covered in this report, specific recommendations are provided that address 1) preventing exposure to opportunistic pathogens, 2) preventing first episodes of disease, and 3) preventing disease recurrences. Recommendations are rated by a revised version of the IDSA rating system (*17*). In this system, the letters A–E signify the strength of the recommendation for or against a preventive measure, and Roman numerals I–III indicate the quality of evidence supporting the recommendation (Box).

Because of their length and complexity, tables in this report are grouped together and follow the references. Tables appear in the following order:

Table 1 Dosages for prophylaxis to prevent first episode of opportunistic disease among infected adults and adolescents;
Table 2 Dosages for prophylaxis to prevent recurrence of opportunistic disease among HIV-infected adults and adolescents;
Table 3 Effects of food on drugs used to treat OIs;
Table 4 Effects of medications on drugs used to treat OIs;
Table 5 Effects of OI medications on drugs commonly administered to HIV-infected persons;
Table 6 Adverse effects of drugs used to manage HIV infection;
Table 7 Dosages of drugs for preventing OIs for persons with renal insufficiency;
Table 8 Costs of agents recommended for preventing OIs among adults with HIV infection;
Table 9 Immunologic categories for HIV-infected children;
Table 10 Immunization schedule for HIV-infected children;
Table 11 Dosages for prophylaxis to prevent first episode of opportunistic disease among HIV-infected infants and children;
Table 12 Dosages for prophylaxis to prevent recurrence of opportunistic disease among HIV-infected infants and children; and
Table 13 Criteria for discontinuing and restarting OI prophylaxis for adult patients with HIV infection.

Recommendations advising patients how to prevent exposure to opportunistic pathogens are also included in this report (Appendix).

This report is oriented toward preventing specific OIs among HIV-infected persons in the United States and other industrialized countries. Recommendations for using HAART, which is designed to prevent immunologic deterioration, to restore immune function, and delay the need for certain chemoprophylactic strategies described in this report, were originally published elsewhere (*14*) and are updated regularly (available at http://www.hivatis.org) (*16*).

Pamphlets related to preventing OIs can be obtained from the HIV/AIDS Treatment Information Service (ATIS) by calling 800-448-0440, 301-519-0459 (international), or 888-480-3739 (TTY). They also can be accessed on the CDC and ATIS websites at http://www.cdc.gov/hiv/pubs/brochure.htm and http://www.hivatis.org, respectively.

New data regarding preventing OIs among HIV-infected persons are emerging, and randomized controlled trials addressing unresolved concerns related to OI prophylaxis are ongoing. The OI Working Group reviews emerging data routinely and updates the guidelines regularly.

Disease-Specific Recommendations

PCP

Preventing Exposure

Although certain authorities might recommend that HIV-infected persons who are at risk for PCP not share a hospital room with a patient who has PCP, data are insufficient to support this recommendation as standard practice (CIII).

Preventing Disease

Initiating Primary Prophylaxis. HIV-infected adults and adolescents, including pregnant women and those on HAART, should receive chemoprophylaxis against PCP if they have a $CD4^+$ T lymphocyte count of <200/µL (AI) or a history of oropharyngeal candidiasis (AII) (*18–20*). Persons who have a $CD4^+$ T lymphocyte percentage of <14% or a history of an AIDS-defining illness, but do not otherwise qualify, should be considered for prophylaxis (BII) (*18–20*). When monitoring $CD4^+$ T lymphocyte counts for ≥3 months is not possible, initiating chemoprophylaxis at a $CD4^+$ T lymphocyte count of >200, but <250 cells/µL, also should be considered (BII) (*19*).

Trimethoprim-sulfamethoxazole (TMP-SMZ) is the recommended prophylactic agent (AI) (*20–23*). One double-strength tablet daily is the preferred regimen (AI) (*23*). However, one single-strength tablet daily (*23*) is also effective and might be better tolerated than one double-strength tablet daily (AI). One double-strength tablet three times weekly is also effective (BI) (*24*). TMP-SMZ at a dose of one double-strength tablet daily confers cross-protection against toxoplasmosis (*25*) and selected common respiratory bacterial infections (*21,26*). Lower doses of TMP-SMZ also might confer such protection. For patients who have an adverse reaction that is not life-threatening, treatment with TMP-SMZ should be continued if clinically feasible; for those who have discontinued such therapy because of an adverse reaction, reinstituting TMP-SMZ should be strongly considered after the adverse event has resolved (AII). Patients who have experienced adverse events, including fever and rash, might better tolerate reintroduction of the drug with a gradual increase in dose (i.e., desensitization), according to published regimens (BI) (*27,28*) or reintroduction of TMP-SMZ at a reduced dose or frequency (CIII); ≤70% of patients can tolerate such reinstitution of therapy (*26*).

If TMP-SMZ cannot be tolerated, prophylactic regimens that can be recommended as alternatives include dapsone (BI), (*21*) dapsone plus pyrimethamine plus leucovorin (BI) (*29,30*), aerosolized pentamidine administered by the Respirgard II™ nebulizer (manufactured by Marquest, Englewood, Colorado) (BI), (*22*) and atovaquone (BI) (*31,32*). Apparently, atovaquone is as effective as aerosolized pentamidine (*31*) or dapsone (BI) (*32*) but is substantially more expensive than the other regimens. For patients seropositive for *Toxoplasma gondii* who cannot tolerate TMP-SMZ, recommended alternatives to TMP-SMZ for prophylaxis against both PCP and toxoplasmosis include dapsone plus pyrimethamine (BI) (*29,30*) or atovaquone with or without pyrimethamine (CIII). The following regimens cannot be recommended as alternatives because data regarding their efficacy for PCP prophylaxis are insufficient to do so:

- aerosolized pentamidine administered by other nebulization devices,
- intermittently administered parenteral pentamidine,
- oral pyrimethamine plus sulfadoxine,
- oral clindamycin plus primaquine, and
- intravenous trimetrexate.

However, clinicians might consider using these agents in unusual situations in which the recommended agents cannot be administered (CIII).

Discontinuating Primary Prophylaxis. Primary pneumocystis prophylaxis should be discontinued for adult and adolescent patients who have responded to HAART with an increase in $CD4^+$ T lymphocyte counts to >200 cells/µL for ≥3 months (AI). In observational and randomized studies supporting this recommendation, the majority of patients were taking antiretroviral regimens that included a protease inhibitor (PI), and the majority had a $CD4^+$ T lymphocyte cell count of >200 cells/µL for ≥3 months before discontinuing PCP prophylaxis (*33–41*). The median $CD4^+$ T lymphocyte count at the time prophylaxis was discontinued was >300 cells/µL, and certain patients had a sustained suppression of HIV plasma ribonucleic acid (RNA) levels below detection limits of the assay employed. Median follow-up ranged from 6 to 16 months.

Discontinuing primary prophylaxis among these patients is recommended because, apparently, prophylaxis adds limited disease prevention (i.e., for PCP, toxoplasmosis, or bacterial infections) and because discontinuing drugs reduces pill burden, potential for drug toxicity, drug interactions, selection of drug-resistant pathogens, and cost.

Restarting Primary Prophylaxis. Prophylaxis should be reintroduced if the CD4+ T lymphocyte count decreases to <200 cells/µL (AIII).

Preventing Recurrence

Patients who have a history of PCP should be administered chemoprophylaxis for life (i.e., secondary prophylaxis or chronic maintenance therapy) with the regimens listed (Table 2) (AI), unless immune reconstitution occurs as a consequence of HAART (see the following recommendation).

Discontinuing Secondary Prophylaxis (Chronic Maintenance Therapy). Secondary prophylaxis should be discontinued for adult and adolescent patients whose CD4+ T lymphocyte cell count has increased from <200 cells/µL to >200 cells/µL for ≥3 months as a result of HAART (BII). Reports from observational studies (*37,41,42*) and from a randomized trial (*39*), as well as a combined analysis of eight European cohorts being followed prospectively (*43*), support this recommendation. In these studies, patients had responded to HAART with an increase in CD4+ T lymphocyte counts to >200 cells/µL for ≥3 months. The majority of patients were taking PI-containing regimens. The median CD4+ T lymphocyte count at the time prophylaxis was discontinued was >300 cells/µL. The majority of patients had sustained suppression of plasma HIV RNA levels below the detection limits of the assay employed; the longest follow-up was 13 months. If the episode of PCP occurred at a CD4+ T lymphocyte count of >200 cells/µL, continuing PCP prophylaxis for life, regardless of how high the CD4+ T lymphocyte count rises as a consequence of HAART, is probably prudent (CIII).

Discontinuing secondary prophylaxis for patients is recommended because, apparently, prophylaxis adds limited disease prevention (i.e., for PCP, toxoplasmosis, or bacterial infections) and because discontinuing drugs reduces pill burden, potential for drug toxicity, drug interactions, selection of drug-resistant pathogens, and cost.

Restarting Secondary Prophylaxis. Prophylaxis should be reintroduced if the CD4+ T lymphocyte count decreases to <200 cells/µL (AIII) or if PCP recurred at a CD4+ T lymphocyte count of >200 cells/µL (CIII).

Special Considerations

Children. Children born to HIV-infected mothers should be administered prophylaxis with TMP-SMZ beginning at age 4–6 weeks (*44*) (AII). Prophylaxis should be discontinued for children who are subsequently determined not to be infected with HIV. HIV-infected children and children whose infection status remains unknown should continue to receive prophylaxis for the first year of life. Need for subsequent prophylaxis should be determined on the basis of age-specific CD4+ T lymphocyte count thresholds (Table 11) (AII). The safety of discontinuing prophylaxis among HIV-infected children receiving HAART has not been studied extensively.

Children who have a history of PCP should be administered lifelong chemoprophylaxis to prevent recurrence (*44*) (AI). The safety of discontinuing secondary prophylaxis among HIV-infected children has not been studied extensively.

Pregnant Women. Chemoprophylaxis for PCP should be administered to pregnant women as is done for other adults and adolescents (AIII). TMP-SMZ is the recommended prophylactic agent; dapsone is an alternative. Because of theoretical concerns regarding possible teratogenicity associated with drug exposures during the first trimester, health-care providers might choose to withhold prophylaxis during the first trimester. In such cases, aerosolized pentamidine can be considered because of its lack of systemic absorption and the resultant lack of exposure of the developing embryo to the drug (CIII).

Toxoplasmic Encephalitis

Preventing Exposure

HIV-infected persons should be tested for immunoglobulin G (IgG) antibody to *Toxoplasma* soon after the diagnosis of HIV infection to detect latent infection with *T. gondii* (BIII).

All HIV-infected persons, including those who lack IgG antibody to *Toxoplasma*, should be counseled regarding sources of toxoplasmic infection. They should be advised not to eat raw or undercooked meat, including undercooked lamb, beef, pork, or venison (BIII). Specifically, lamb, beef, and pork should be cooked to an internal temperature of 165°F–170°F (*44,45*); meat cooked until it is no longer pink inside usually has an internal temperature of 165°F–170°F and therefore, from a more practical perspective, satisfies this requirement. HIV-infected persons should wash their hands after contact with raw meat and after gardening or other contact with soil; in addition, they should wash fruits and vegetables well before eating them raw (BIII). If the patient owns a cat, the litter box should be changed daily, preferably by an HIV-negative, nonpregnant person; alternatively, patients should wash their hands thoroughly after changing the litter box (BIII). Patients should be encouraged to keep their cats inside and not to adopt or handle stray cats (BIII). Cats should be fed only canned or dried commercial food or well-cooked table food, not raw or undercooked meats (BIII). Patients need not be advised to part with their cats or to have their cats tested for toxoplasmosis (EII).

Preventing Disease

Initiating Primary Prophylaxis. *Toxoplasma*-seropositive patients who have a CD4+ T lymphocyte count of <100/µL should be administered prophylaxis against toxoplasmic encephalitis (TE) (AII) (*25*). Apparently, the double-strength tablet daily dose of TMP-SMZ recommended as the preferred regimen for PCP prophylaxis is effective against TE as well and is therefore recommended (AII) (*25*). If patients cannot tolerate TMP-SMZ, the recommended alternative is dapsone-pyrimethamine, which is also effective against PCP (BI) (*29,30*). Atovaquone with or without pyrimethamine also can be considered (CIII). Prophylactic monotherapy with dapsone, pyrimethamine, azithromycin, or clarithromycin cannot be recommended on the basis of available data (DII). Aerosolized pentamidine does not protect against TE and is not recommended (EI) (*21,25*).

Toxoplasma-seronegative persons who are not taking a PCP prophylactic regimen known to be active against TE should be retested for IgG antibody to *Toxoplasma* when their CD4+ T lymphocyte counts decline to <100/µL to determine whether they have seroconverted and are therefore at risk for TE (CIII). Patients who have seroconverted should be administered prophylaxis for TE as described previously (AII).

Discontinuing Primary Prophylaxis. Prophylaxis against TE should be discontinued among adult and adolescent patients who have responded to HAART with an increase in CD4+ T lymphocyte counts to >200 cells/µL for ≥3 months (AI). Multiple observational studies (*37,41,46*) and two randomized trials (*38,47*) have reported that primary prophylaxis can be discontinued with minimal risk for experiencing TE among patients who have responded to HAART with an increase in CD4+ T lymphocyte count from <200 cells/µL to >200 cells/µL for ≥3 months. In these studies, the majority of patients were taking PI-containing regimens and the median CD4+ T lymphocyte count at the time prophylaxis was discontinued was >300 cells/µL. At the time prophylaxis was discontinued, certain patients had sustained suppression of plasma HIV RNA levels below the detection limits of available assays; the median follow-up ranged from 7 to 22 months. Although patients with CD4+ T lymphocyte counts of <100 cells/µL are at greatest risk for experiencing TE, the risk for TE occurring when the CD4+ T lymphocyte count has increased to 100–200 cells/µL has not been studied as rigorously as an increase to >200 cells/µL. Thus, the recommendation specifies discontinuing prophylaxis after an increase to >200 cells/µL. Discontinuing primary TE prophylaxis is recommended because prophylaxis apparently adds limited disease prevention for toxoplasmosis and because discontinuing drugs reduces pill burden, potential for drug toxicity, drug interaction, selection of drug-resistant pathogens, and cost.

Restarting Primary Prophylaxis. Prophylaxis should be reintroduced if the CD4+ T lymphocyte count decreases to <100–200 cells/µL (AIII).

Preventing Recurrence

Patients who have completed initial therapy for TE should be administered lifelong suppressive therapy (i.e., secondary prophylaxis or chronic maintenance therapy) (AI) (*48,49*) unless immune reconstitution occurs as a consequence of HAART (see the following recommendation). The combination of pyrimethamine plus sulfadiazine plus leucovorin is highly effective for this purpose (AI). A commonly used regimen for patients who cannot tolerate sulfa drugs is pyrimethamine plus clindamycin (BI); however, apparently, only the combination of pyrimethamine plus sulfadiazine provides protection against PCP as well (AII).

Discontinuing Secondary Prophylaxis (Chronic Maintenance Therapy). Adult and adolescent patients receiving secondary prophylaxis (i.e., chronic maintenance therapy) for TE are, apparently, at low risk for recurrence of TE when they have successfully completed initial therapy for TE, remain asymptomatic with regard to signs and symptoms of TE, and have a sustained increase in their CD4+ T lymphocyte counts of >200 cells/µL after HAART (e.g., ≥6 months) (*41,42,47*). Although the numbers of patients who have been evaluated remain limited and occasional recurrences have been reported, on the basis of these observations and inference from more extensive cumulative data indicating the safety of discontinuing secondary prophylaxis for other OIs during advanced HIV disease, discontinuing chronic maintenance therapy among such patients is a reasonable consideration (CIII). Certain specialists would obtain a magnetic resonance image of the brain as part of their evaluation to determine whether discontinuing therapy is appropriate.

Restarting Secondary Prophylaxis. Secondary prophylaxis (chronic maintenance therapy) should be reintroduced if the CD4+ T lymphocyte count decreases to <200 cells/µL (AIII).

Special Considerations

Children. TMP-SMZ, when administered for PCP prophylaxis, also provides prophylaxis against toxoplasmosis. Atovaquone might also provide protection (CIII). Children aged >12 months who qualify for PCP prophylaxis and who are receiving an agent other than TMP-SMZ or atovaquone should have serologic testing for *Toxoplasma* antibody (BIII) because alternative drugs for PCP prophylaxis might not be effective against *Toxoplasma*. Severely immunosuppressed children who are not receiving TMP-SMZ or atovaquone who are determined to be seropositive for *Toxoplasma* should be administered prophylaxis for both PCP and toxoplasmosis (i.e.,

dapsone plus pyrimethamine) (BIII). Children with a history of toxoplasmosis should be administered lifelong prophylaxis to prevent recurrence (AI). The safety of discontinuing primary or secondary prophylaxis among HIV-infected children receiving HAART has not been studied extensively.

Pregnant Women. TMP-SMZ can be administered for prophylaxis against TE as described for PCP (AIII). However, because of the low incidence of TE during pregnancy and the possible risk associated with pyrimethamine treatment, chemoprophylaxis with pyrimethamine-containing regimens can reasonably be deferred until after pregnancy (CIII). For prophylaxis against recurrent TE, health-care providers and clinicians should be well-informed regarding benefits of lifelong therapy and concerns related to teratogenicity of pyrimethamine. Guidelines provided previously should be used when making decisions regarding secondary prophylaxis for TE during pregnancy.

In rare cases, HIV-infected pregnant women who have serologic evidence of remote toxoplasmic infection have transmitted *Toxoplasma* to the fetus in utero. Pregnant HIV-infected women who have evidence of primary toxoplasmic infection or active toxoplasmosis, including TE, should be evaluated and managed during pregnancy in consultation with appropriate specialists (BIII). Infants born to women who have serologic evidence of infections with HIV and *Toxoplasma* should be evaluated for congenital toxoplasmosis (BIII).

Cryptosporidiosis

Preventing Exposure

HIV-infected persons should be educated and counseled concerning the different ways that *Cryptosporidium* can be transmitted (BIII). Modes of transmission include having direct contact with infected adults, diaper-aged children, and infected animals; drinking contaminated water; coming into contact with contaminated water during recreational activities; and eating contaminated food.

HIV-infected persons should avoid contact with human and animal feces. They should be advised to wash their hands after contact with human feces (e.g., diaper changing), after handling pets, and after gardening or other contact with soil. HIV-infected persons should avoid sexual practices that might result in oral exposure to feces (e.g., oral-anal contact) (BIII).

HIV-infected persons should be advised that newborn and young pets might pose a limited risk for transmitting cryptosporidial infection, but they should not be advised to destroy or give away healthy pets. Persons contemplating acquiring a new pet should avoid bringing any animal that has diarrhea into their households, should avoid purchasing a dog or cat aged <6 months, and should not adopt stray pets. HIV-infected persons who wish to assume the limited risk for acquiring a puppy or kitten aged <6 months should request that their veterinarian examine the animal's stool for *Cryptosporidium* before they have contact with the animal (BIII). HIV-infected persons should avoid exposure to calves and lambs and to premises where these animals are raised (BII).

HIV-infected persons should not drink water directly from lakes or rivers (AIII). Waterborne infection also might result from swallowing water during recreational activities. HIV-infected persons should be aware that lakes, rivers, and saltwater beaches and certain swimming pools, recreational water parks, and ornamental water fountains might be contaminated with human or animal waste that contains *Cryptosporidium*. They should avoid swimming in water that is likely to be contaminated and should avoid swallowing water while swimming or playing in recreational waters (BIII).

Outbreaks of cryptosporidiosis have been linked to municipal water supplies. During outbreaks or in other situations in which a community advisory to boil water is issued, boiling water for 1 minute will eliminate the risk for cryptosporidiosis (AI). Using submicron personal-use water filters[†] (home/office types) or bottled water[§] also might reduce the risk (CIII). The magnitude of the risk for acquiring cryptosporidiosis from drinking water in a nonoutbreak setting is uncertain, and available data are inadequate to recommend that all HIV-infected persons boil water or avoid drinking tap water in nonoutbreak settings. However, HIV-infected persons who wish to take independent action to reduce the risk for waterborne cryptosporidiosis might choose to take precautions similar to those recommended during outbreaks. Such decisions should be made in conjunction with health-care providers. Persons who opt for a personal-use filter or bottled water should be aware of the complexities involved in selecting appropriate

[†] Only filters capable of removing particles 1 µm in diameter should be considered. Filters that provide the greatest assurance of oocyst removal include those that operate by reverse osmosis, those labeled as absolute 1-µm filters, and those labeled as meeting NSF (National Sanitation Foundation) Standard No. 53 for cyst removal. The nominal 1-µm filter rating is not standardized, and filters in this category might not be capable of removing 99% of oocysts. For a list of filters certified as meeting NSF standards, consult the International Consumer Line at 800-673-8010 or http://www.nsf.org/notice/crypto.html.

[§] Sources of bottled water (e.g., wells, springs, municipal tap-water supplies, rivers, and lakes) and methods for its disinfection differ; therefore, all brands should not be presumed to be cryptosporidial oocyst-free. Water from wells and springs is much less likely to be contaminated by oocysts than water from rivers or lakes. Treatment of bottled water by distillation or reverse osmosis ensures oocyst removal. Water passed through an absolute 1-µm filter or a filter labeled as meeting NSF Standard No. 53 for cyst removal before bottling will provide approximately the same level of protection. Using nominal 1-µm filters by bottlers as the only barrier to *Cryptosporidia* might not result in the removal of 99% of oocysts. For more information, the International Bottled Water Association can be contacted at 703-683-5213 or at http://www.bottledwater.org.

products, the lack of enforceable standards for the destruction or removal of oocysts, costs of the products, and the logistic difficulty of using these products consistently.

Patients who take precautions to avoid acquiring cryptosporidiosis from drinking water should be advised that ice made from contaminated tap water also can be a source of infection (BII). Such persons also should be aware that fountain beverages served in restaurants, bars, theaters, and other places also might pose a risk because these beverages, as well as the ice they contain, are made from tap water. Nationally distributed brands of bottled or canned carbonated soft drinks are safe to drink. Commercially packaged noncarbonated soft drinks and fruit juices that do not require refrigeration until after they are opened (i.e., those that can be stored unrefrigerated on grocery shelves) also are safe. Nationally distributed brands of frozen fruit juice concentrate are safe if they are reconstituted by the user with water from a safe source. Fruit juices that must be kept refrigerated from the time they are processed to the time of consumption might be either fresh (i.e., unpasteurized) or heat-treated (i.e., pasteurized); only those juices labeled as pasteurized should be considered free of risk from *Cryptosporidium*. Other pasteurized beverages and beers also are considered safe to drink (BII). No data are available concerning survival of *Cryptosporidium* oocysts in wine.

HIV-infected persons should avoid eating raw oysters because cryptosporidial oocysts can survive in oysters for >2 months and have been found in oysters taken from certain commercial oyster beds (BIII). *Cryptosporidium*-infected patients should not work as food handlers, including if the food to be handled is intended to be eaten without cooking (BII). Because the majority of foodborne outbreaks of cryptosporidiosis are believed to have been caused by infected food handlers, more specific recommendations to avoid exposure to contaminated food cannot be made.

In a hospital, standard precautions (i.e., use of gloves and hand-washing after removal of gloves) should be sufficient to prevent transmission of cryptosporidiosis from an infected patient to a susceptible HIV-infected person (BII). However, because of the potential for fomite transmission, certain specialists recommend that HIV-infected persons, specifically those who are severely immunocompromised, should not share a room with a patient with cryptosporidiosis (CIII).

Preventing Disease

Rifabutin or clarithromycin, when taken for MAC prophylaxis, have been found to protect against cryptosporidiosis (*50,51*). However, data are insufficient to warrant a recommendation for using these drugs as chemoprophylaxis for cryptosporidiosis.

Preventing Recurrence

No drug regimens are known to be effective in preventing the recurrence of cryptosporidiosis.

Special Considerations

Children. No data indicate that formula-preparation practices for infants should be altered to prevent cryptosporidiosis (CIII). However, in the event of a boil-water advisory, similar precautions for preparing infant formula should be taken as for drinking water for adults (AII).

Microsporidiosis

Preventing Exposure

Other than general attention to hand-washing and other personal hygiene measures, no precautions to reduce exposure can be recommended.

Preventing Disease

No chemoprophylactic regimens are known to be effective in preventing microsporidiosis.

Preventing Recurrence

No chemotherapeutic regimens are known to be effective in preventing recurrence of microsporidiosis.

Tuberculosis

Preventing Exposure

HIV-infected persons should be advised that certain activities and occupations might increase the likelihood of exposure to tuberculosis (TB) (BIII). These include volunteer work or employment in health-care facilities, correctional institutions, and shelters for the homeless, as well as in other settings identified as high-risk by local health authorities. Decisions concerning whether to continue with activities in these settings should be made in conjunction with the health-care provider and should be based on such factors as the patient's specific duties in the workplace, prevalence of TB in the community, and the degree to which precautions are taken to prevent TB transmission in the workplace (BIII). Whether the patient continues with such activities might affect the frequency with which screening for TB needs to be conducted.

Preventing Disease

When HIV infection is first recognized, the patient should receive a tuberculin skin test (TST) by administration of intermediate-strength (5-TU) purified protein derivative (PPD) by the Mantoux method (AI). Routine evaluation for anergy is not recommended. However, situations exist in which

anergy evaluation might assist in guiding decisions concerning preventive therapy (*52,53*).

All HIV-infected persons who have a positive TST result (≥5 mm of induration) should undergo chest radiography and clinical evaluation to rule out active TB. HIV-infected persons who have symptoms indicating TB should promptly undergo chest radiography and clinical evaluation regardless of their TST status (AII).

All HIV-infected persons, regardless of age, who have a positive TST result but have no evidence of active TB and no history of treatment for active or latent TB should be treated for latent TB infection. Options include isoniazid daily (AII) or twice weekly (BII) for 9 months; 4 months of therapy daily with either rifampin (BIII) or rifabutin (CIII); or 2 months of therapy with either rifampin and pyrazinamide (BI) or rifabutin and pyrazinamide (CIII) (*52–54*). Reports exist of fatal and severe liver injury associated with treatment of latent TB infection among HIV-uninfected persons treated with the 2-month regimen of daily rifampin and pyrazinamide; therefore, using regimens that do not contain pyrazinamide among HIV-infected persons whose completion of treatment can be ensured is prudent (*55*). Because HIV-infected persons are at risk for peripheral neuropathy, those receiving isoniazid should also receive pyridoxine (BIII). Decisions to use a regimen containing either rifampin or rifabutin should be made after carefully considering potential drug interactions, including those related to PIs and nonnucleoside reverse transcriptase inhibitors (NNRTIs) (see the following section on Drug Interactions). Directly observed therapy should be used with intermittent dosing regimens (AI) and when otherwise operationally feasible (BIII) (*53*).

HIV-infected persons who are close contacts of persons who have infectious TB should be treated for latent TB infection, regardless of their TST results, age, or prior courses of treatment, after a diagnosis of active TB has been excluded (AII) (*52–54*). In addition to household contacts, such persons might also include contacts in the same drug-treatment or health-care facility, coworkers, and other contacts if transmission of TB is demonstrated.

For persons exposed to isoniazid- or rifampin-resistant TB, decisions to use chemoprophylactic antimycobacterial agents other than isoniazid alone, rifampin or rifabutin alone, rifampin plus pyrazinamide, or rifabutin plus pyrazinamide should be based on the relative risk for exposure to resistant organisms and should be made in consultation with public health authorities (AII). TST-negative, HIV-infected persons from groups at risk or geographic areas with a high prevalence of *M. tuberculosis* infection might be at increased risk for primary or reactivation TB. However, efficacy of treatment among this group has not been demonstrated. Decisions concerning using chemoprophylaxis in these situations must be considered individually.

Although the reliability of TST might diminish as the $CD4^+$ T lymphocyte count declines, annual repeat testing should be considered for HIV-infected persons who are TST-negative on initial evaluation and who belong to populations in which a substantial risk for exposure to *M. tuberculosis* exists (BIII). Clinicians should consider repeating TST for persons whose initial skin test was negative and whose immune function has improved in response to HAART (i.e., those whose $CD4^+$ T lymphocyte count has increased to >200 cells/µL) (BIII) (*52*). In addition to confirming TB infection, TST conversion in an HIV-infected person should alert health-care providers to the possibility of recent *M. tuberculosis* transmission and should prompt notification of public health officials for investigation to identify a possible source case. Administering bacille Calmette-Guérin (BCG) vaccine to HIV-infected persons is contraindicated because of its potential to cause disseminated disease (EII).

Preventing Recurrence

Chronic suppressive therapy for a patient who has successfully completed a recommended regimen of treatment for TB is unnecessary (DII).

Special Considerations

Drug Interactions. Rifampin can induce metabolism of all PIs and NNRTIs. This can result in more rapid drug clearance and possibly subtherapeutic drug concentrations of the majority of these antiretroviral agents. Rifampin should not be coadministered with the following PIs and NNRTIs: amprenavir, indinavir, lopinavir/ritonavir, nelfinavir, saquinavir, and delavirdine (*54*). However, it can be used with ritonavir, ritonavir plus saquinavir, efavirenz, and possibly with nevirapine. Rifabutin is an acceptable alternative to rifampin but should not be used with the PI hard-gel saquinavir or delavirdine; caution is advised if the drug is coadministered with soft-gel saquinavir because data are limited. Rifabutin can be administered at one half the usual daily dose (i.e., reduce from 300 mg to 150 mg/day) with indinavir, nelfinavir, or amprenavir or with one fourth the usual dose (i.e., 150 mg every other day or three times a week), with ritonavir, ritonavir plus saquinavir, or lopinavir/ritonavir. When rifabutin is administered with indinavir as a single PI, the dose of indinavir should be increased from 800 mg/8 hours to 1,000 mg/8 hours. Pharmacokinetic data indicate that rifabutin at an increased dose can be administered with efavirenz; doses of 450–600 mg/day have been recommended (*54*). However, available information is limited concerning appropriate dosing if a PI

is used concurrently with efavirenz and rifabutin; with such a combination, the rifabutin dose might need to be reduced. Rifabutin can be used without dose adjustment with nevirapine.

Children. Infants born to HIV-infected mothers should have a TST (5-TU PPD) at or before age 9–12 months, and the infants should be retested ≥1 times/year (AIII). HIV-infected children living in households with TST-positive persons should be evaluated for TB (AIII); children exposed to a person who has active TB should be administered preventive therapy after active TB has been excluded, regardless of their TST results (AII).

Pregnant Women. Chemoprophylaxis for TB is recommended during pregnancy for HIV-infected patients who have either a positive TST or a history of exposure to active TB, after active TB has been excluded (AIII). A chest radiograph should be obtained before treatment and appropriate abdominal or pelvic lead apron shields should be used to minimize radiation exposure to the embryo or fetus. When an HIV-infected person has not been exposed to drug-resistant TB, isoniazid daily or twice weekly is the prophylactic regimen of choice. Because of concerns regarding possible teratogenicity associated with drug exposures during the first trimester, health-care providers might choose to initiate prophylaxis after the first trimester. Preventive therapy with isoniazid should be accompanied by pyridoxine to reduce the risk for neurotoxicity. Experience with rifampin or rifabutin during pregnancy is more limited, but anecdotal information with rifampin has not been associated with adverse pregnancy outcomes. Pyrazinamide should usually be avoided, chiefly in the first trimester, because of lack of information concerning fetal effects.

Disseminated MAC Infection

Preventing Exposure

Organisms of MAC are common in environmental sources (e.g., food and water). Available information does not support specific recommendations regarding exposure avoidance.

Preventing Disease

Initiating Primary Prophylaxis. Adults and adolescents who have HIV infection should receive chemoprophylaxis against disseminated MAC disease if they have a $CD4^+$ T lymphocyte count of <50 cells/µL (AI) (*56*). Clarithromycin (*57,58*) or azithromycin (*59*) are the preferred prophylactic agents (AI). The combination of clarithromycin and rifabutin is no more effective than clarithromycin alone for chemoprophylaxis and is associated with a higher rate of adverse effects than either drug alone; this combination should not be used (EI) (*59*). The combination of azithromycin with rifabutin is more effective than azithromycin alone; however, the additional cost, increased occurrence of adverse effects, potential for drug interactions, and absence of a difference in survival when compared with azithromycin alone do not warrant a routine recommendation for this regimen (CI) (*59*). In addition to their preventive activity for MAC disease, clarithromycin and azithromycin each confer protection against respiratory bacterial infections (BII). If clarithromycin or azithromycin cannot be tolerated, rifabutin is an alternative prophylactic agent for MAC disease, although rifabutin-associated drug interactions make this agent difficult to use (BI) (*54*). Tolerance, cost, and drug interactions are among the concerns that should be considered in decisions regarding the choice of prophylactic agents for MAC disease. Particular attention to interactions with antiretroviral PIs and NNRTIs is warranted (see the following section on Drug Interactions). Before prophylaxis is initiated, disseminated MAC disease should be ruled out by clinical assessment, which might include obtaining a blood culture for MAC if warranted. Because treatment with rifabutin could result in rifampin resistance among persons who have active TB, active TB should also be excluded before rifabutin is used for prophylaxis.

Although detecting MAC organisms in the respiratory or gastrointestinal tract might predict disseminated MAC infection, no data are available regarding efficacy of prophylaxis with clarithromycin, azithromycin, rifabutin, or other drugs among patients with MAC organisms at these sites and a negative blood culture. Therefore, routine screening of respiratory or gastrointestinal specimens for MAC cannot be recommended (DIII).

Discontinuing Primary Prophylaxis. Primary MAC prophylaxis should be discontinued among adult and adolescent patients who have responded to HAART with an increase in $CD4^+$ T lymphocyte counts to >100 cells/µL for ≥3 months (AI). Two substantial randomized, placebo controlled trials and observational data have demonstrated that such patients can discontinue primary prophylaxis with minimal risk for experiencing MAC (*37,60–62*). Discontinuing primary prophylaxis among patients meeting these criteria is recommended because, apparently, prophylaxis adds limited disease prevention for MAC or for bacterial infections and because discontinuing drugs reduces pill burden, potential for drug toxicity, drug interactions, selection of drug-resistant pathogens, and cost.

Restarting Primary Prophylaxis. Primary prophylaxis should be reintroduced if the $CD4^+$ T lymphocyte count decreases to <50–100 cells/µL (AIII).

Preventing Recurrence

Adult and adolescent patients with disseminated MAC should receive lifelong therapy (i.e., secondary prophylaxis or maintenance therapy) (AII), unless immune reconstitution occurs as a consequence of HAART (see the following recommendation). Unless substantial clinical or laboratory evidence of macrolide resistance exists, using a macrolide (i.e., clarithromycin or, alternatively, azithromycin) is recommended in combination with ethambutol (AII) with or without rifabutin (CI) (*63,64*). Treatment of MAC disease with clarithromycin in a dose of 1,000 mg twice/day is associated with a higher mortality rate than has been observed with clarithromycin administered at 500 mg twice/day; thus, the higher dose should not be used (EI) (*65,66*). Clofazimine has been associated with adverse clinical outcomes in the treatment of MAC disease and should not be used (DII) (*67*).

Discontinuing Secondary Prophylaxis (Chronic Maintenance Therapy). Apparently, patients are at low risk for recurrence of MAC when they have completed a course of ≥12 months of treatment for MAC, remain asymptomatic with respect to MAC signs and symptoms, and have a sustained increase (e.g., ≥6 months), in their $CD4^+$ T lymphocyte counts to >100cells/µL after HAART. Although the numbers of patients who have been evaluated remain limited and recurrences could occur (*41,42,68–70*), on the basis of these observations and on inference from more extensive data indicating the safety of discontinuing secondary prophylaxis for other OIs during advanced HIV disease, discontinuing chronic maintenance therapy among such patients is reasonable (CIII). Certain specialists recommend obtaining a blood culture for MAC, even for asymptomatic patients, before discontinuing therapy to substantiate that disease is no longer active.

Restarting Secondary Prophylaxis. Secondary prophylaxis should be reintroduced if the $CD4^+$ T lymphocyte count decreases to <100 cells/µL (AIII).

Special Considerations

Drug Interactions. Rifabutin should not be administered to patients receiving certain PIs and NNRTIs because the complex interactions have been incompletely studied, and the clinical implications of those interactions are unclear (*16,54*) (see Drug Interactions in the Tuberculosis section). PIs can increase clarithromycin levels, but no recommendation to adjust the dose of either clarithromycin or PIs can be made on the basis of existing data. Efavirenz can induce metabolism of clarithromycin. This can result in reduced serum concentration of clarithromycin but increased concentration of 14-OH clarithromycin, an active metabolite of clarithromycin. Although the clinical significance of this interaction is unknown, the efficacy of clarithromycin in MAC prophylaxis could be reduced because of this interaction. Azithromycin pharmacokinetics are not affected by the cytochrome P450 (CYP450) system; azithromycin can be used safely in the presence of PIs or NNRTIs without concerns of drug interactions.

Children. HIV-infected children aged <13 years who have advanced immunosuppression also can experience disseminated MAC infections, and prophylaxis should be offered to children at high risk according to the following $CD4^+$ T lymphocyte thresholds:

- children aged ≥6 years, <50 cells/µL;
- children aged 2–6 years, <75 cells/µL;
- children aged 1–2 years, <500 cells/µL; and
- children aged <12 months, <750 cells/µL (AII).

For the same reasons that clarithromycin and azithromycin are the preferred prophylactic agents for adults, they should also be considered for children (AII); oral suspensions of both agents are commercially available in the United States. No liquid formulation of rifabutin suitable for pediatric use is commercially available in the United States. Children with a history of disseminated MAC should be administered lifelong prophylaxis to prevent recurrence (AII). The safety of discontinuing MAC prophylaxis among children whose $CD4^+$ T lymphocyte counts have increased in response to HAART has not been studied.

Pregnant Women. Chemoprophylaxis for MAC disease should be administered to pregnant women as is done for other adults and adolescents (AIII). However, because of concerns related to administering drugs during the first trimester of pregnancy, certain health-care providers might choose to withhold prophylaxis during the first trimester. Animal studies and anecdotal evidence of safety among humans indicate that, of the available agents, azithromycin is the drug of choice (BIII) (*71*). Experience with rifabutin is limited. Clarithromycin has been demonstrated to be a teratogen among animals and should be used with caution during pregnancy (*72*). For secondary prophylaxis (chronic maintenance therapy), azithromycin plus ethambutol are the preferred drugs (BIII) (*71*).

Bacterial Respiratory Infections

Preventing Exposure

Because *Streptococcus pneumoniae* and *Haemophilus influenzae* are common in the community, no effective way exists to reduce exposure to these bacteria.

Preventing Disease

Adults and adolescents who have a $CD4^+$ T lymphocyte count of ≥200 cells/µL should be administered a single dose of 23-valent polysaccharide pneumococcal vaccine (PPV) if they have not received this vaccine during the previous five

years (BII) (*73–77*). One randomized placebo-controlled trial of pneumococcal vaccine in Africa paradoxically determined that an increase had occurred in pneumonia among vaccinated subjects (*78*). However, multiple observational studies in the United States have not identified increased risk associated with vaccination and have identified benefit among this group (*73–77*). The majority of HIV specialists believe that the potential benefit of pneumococcal vaccination in the United States outweighs the risk. Immunization should also be considered for patients with $CD4^+$ T lymphocyte counts of <200 cells/µL, although clinical evidence has not confirmed efficacy (CIII). Revaccination can be considered for patients who were initially immunized when their $CD4^+$ T lymphocyte counts were <200 cells/µL and whose $CD4^+$ counts have increased to >200 cells/µL in response to HAART (CIII). The recommendation to vaccinate is increasingly pertinent because of the increasing incidence of invasive infections with drug-resistant (including TMP-SMZ–, macrolide-, and ß-lactam–resistant) strains of *S. pneumoniae*.

The duration of the protective effect of primary pneumococcal vaccination is unknown. Periodic revaccination can be considered; an interval of 5 years has been recommended for persons not infected with HIV and also might be appropriate for persons infected with HIV (CIII) (*76*). However, no evidence confirms clinical benefit from revaccination.

Incidence of *H. influenzae* type B (Hib) infection among adults is low. Therefore, Hib vaccine is not usually recommended for adult use (DIII). TMP-SMZ, when administered daily for PCP prophylaxis, reduces the frequency of bacterial respiratory infections. This should be considered in selecting an agent for PCP prophylaxis (AII). However, indiscriminate use of this drug (when not indicated for PCP prophylaxis or other specific reasons) might promote development of TMP-SMZ-resistant organisms. Thus, TMP-SMZ should not be prescribed solely to prevent bacterial respiratory infection (DIII). Similarly, clarithromycin administered daily and azithromycin administered weekly for MAC prophylaxis might be effective in preventing bacterial respiratory infections; this should be considered in selecting an agent for prophylaxis against MAC disease (BII). However, these drugs should not be prescribed solely for preventing bacterial respiratory infection (DIII).

An absolute neutrophil count that is depressed because of HIV disease or drug therapy is associated with an increased risk for bacterial infections, including pneumonia. To reduce the risk for such bacterial infections, health-care providers might consider taking steps to reverse neutropenia, either by stopping myelosuppressive drugs (CII) or by administering granulocyte-colony-stimulating factor (G-CSF) (CII).

Preventing Recurrence

Clinicians can administer anti-biotic chemoprophylaxis to HIV-infected patients who have frequent recurrences of serious bacterial respiratory infections (CIII). TMP-SMZ, administered for PCP prophylaxis, and clarithromycin or azithromycin, administered for MAC prophylaxis, are appropriate for drug-sensitive organisms. However, health-care providers should be cautious when using antibiotics solely for preventing the recurrence of serious bacterial respiratory infections because of the potential development of drug-resistant microorganisms and drug toxicity.

Special Considerations

Children. HIV-infected children aged <5 years should be administered Hib vaccine (AII) and pneumococcal conjugate vaccine (PCV) (*79–81*) (BII) in accordance with the guidelines of the Advisory Committee on Immunization Practices (*74,76,79*) and the American Academy of Pediatrics (*80*). Children aged >2 years should also receive 23-valent PPV (BII). Revaccination with a second dose of the 23-valent PPV should usually be administered after 3–5 years to children aged ≤10 years and after 5 years to children aged >10 years (BIII).

To prevent serious bacterial infections among HIV-infected children who have hypogammaglobulinemia (IgG <400 mg/dL), clinicians should use intravenous immune globulin (IVIG) (AI). Respiratory syncytial virus (RSV) IVIG (750 mg/kg body weight), not monoclonal RSV antibody, can be substituted for IVIG during the RSV season to provide broad anti-infective protection, if RSV IVIG is available.

To prevent recurrence of serious bacterial respiratory infections, antibiotic chemoprophylaxis can be considered (BI). However, health-care providers should be cautious when using antibiotics solely for this purpose because of the potential development of drug-resistant microorganisms and drug toxicity. Administering IVIG should also be considered for HIV-infected children who have recurrent serious bacterial infections (BI), although such treatment might not provide additional benefit to children who are being administered daily TMP-SMZ. However, IVIG can be considered for children who have recurrent serious bacterial infections despite receiving TMP-SMZ or other antimicrobials (CIII) (*82*).

Pregnant Women. Pneumococcal vaccination is recommended during pregnancy for HIV-infected patients who have not been vaccinated during the previous 5 years (BIII). Among nonpregnant adults, vaccination has been associated with a transient burst of HIV replication. Whether the transient viremia can increase the risk for perinatal HIV transmission is unknown. Because of this concern, when feasible, vaccination can be deferred until after HAART has been initiated to prevent perinatal HIV transmission (CIII).

Bacterial Enteric Infections

Preventing Exposure

Food. Health-care providers should advise HIV-infected persons not to eat raw or undercooked eggs, including specific foods that might contain raw eggs (e.g., certain preparations of hollandaise sauce, Caesar and other salad dressings, certain mayonnaises, uncooked cookie and cake batter, and egg nog); raw or undercooked poultry, meat, seafood (raw shellfish in particular); unpasteurized dairy products; unpasteurized fruit juices; and raw seed sprouts (e.g., alfalfa sprouts or mung bean sprouts). Poultry and meat are safest when adequate cooking is confirmed by thermometer (i.e., internal temperature of 180ºF for poultry and 165ºF for red meats). If a thermometer is not used, the risk for illness is decreased by consuming poultry and meat that have no trace of pink color. Color change of the meat (e.g., absence of pink) does not always correlate with internal temperature (BIII). Produce should be washed thoroughly before being eaten (BIII).

Health-care providers should advise HIV-infected persons to avoid cross-contamination of foods. Uncooked meats, including hot dogs, and their juices should not come into contact with other foods. Hands, cutting boards, counters, knives, and other utensils should be washed thoroughly after contact with uncooked foods (BIII).

Health-care providers should advise HIV-infected persons that, although the incidence of listeriosis is low, it is a serious disease that occurs with unusually high frequency among severely immunosuppressed HIV-infected persons. An immunosuppressed, HIV-infected person who wishes to reduce the risk for acquiring listeriosis as much as possible can choose to do the following (CIII): 1) avoid soft cheeses (e.g., feta, Brie, Camembert, blue-veined, and such Mexican-style cheese as queso fresco). Hard cheeses, processed cheeses, cream cheese (including slices and spreads), cottage cheese, or yogurt need not be avoided; 2) cook leftover foods or ready-to-eat foods (e.g., hot dogs) until steaming hot before eating; 3) avoid foods from delicatessen counters (e.g., prepared salads, meats, cheeses) or heat/reheat these foods until steaming before eating; 4) avoid refrigerated pâtés and other meat spreads, or heat/reheat these foods until steaming. Canned or shelf-stable pâté and meat spreads need not be avoided; 5) avoid raw or unpasteurized milk (including goat's milk) or milk-products, or foods that contain unpasteurized milk or milk-products. (CIII).

Pets. When obtaining a new pet, HIV-infected persons should avoid animals aged <6 months (BIII). HIV-infected persons also should avoid contact with any animals that have diarrhea (BIII). HIV-infected pet owners should seek veterinary care for animals with diarrheal illness, and a fecal sample from such animals should be examined for *Cryptosporidium*, *Salmonella*, and *Campylobacter*. HIV-infected persons should wash their hands after handling pets, including before eating, and should avoid contact with pets' feces (BIII). HIV-infected persons should avoid contact with reptiles (e.g., snakes, lizards, iguanas, and turtles) as well as chicks and ducklings because of the risk for salmonellosis (BIII).

Travel. The risk for foodborne and waterborne infections among immunosuppressed, HIV-infected persons is magnified during travel to economically developing countries. Persons who travel to such countries should avoid foods and beverages that might be contaminated, including raw fruits and vegetables, raw or undercooked seafood or meat, tap water, ice made with tap water, unpasteurized milk and dairy products, and items sold by street vendors (AII). Foods and beverages that are usually safe include steaming hot foods, fruits that are peeled by the traveler, bottled (including carbonated) beverages, hot coffee and tea, beer, wine, and water brought to a rolling boil for 1 minute (AII). Treatment of water with iodine or chlorine might not be as effective as boiling but can be used when boiling is not practical (BIII).

Preventing Disease

Prophylactic antimicrobial agents are not usually recommended for travelers (DIII). The effectiveness of these agents depends on local antimicrobial-resistance patterns of gastrointestinal pathogens, which are seldom known. Moreover, these agents can elicit adverse reactions and promote the emergence of resistant organisms. However, for HIV-infected travelers, antimicrobial prophylaxis can be considered, depending on the level of immunosuppression and the region and duration of travel (CIII). Use of fluoroquinolones (e.g., ciprofloxacin, 500 mg/day) can be considered when prophylaxis is deemed necessary (CIII). As an alternative (e.g., for children, pregnant women, and persons already taking TMP-SMZ for PCP prophylaxis), TMP-SMZ might offer limited protection against traveler's diarrhea (BIII). Risk for toxicity should be considered before treatment with TMP-SMZ is initiated solely because of travel.

Antimicrobial agents (e.g., fluoroquinolones) should be administered to patients before their departure, to be taken empirically (e.g., 500 mg of ciprofloxacin twice daily for 3–7 days) if severe traveler's diarrhea occurs (BIII). Fluoroquinolones should be avoided for children aged <18 years and pregnant women, and alternative antibiotics should be considered (BIII). Travelers should consult a physician if their diarrhea is severe and does not respond to empirical therapy, if their stools contain blood, if fever is accompanied by shaking chills, or if dehydration occurs. Antiperistaltic agents (e.g., loperamide) can be used to treat mild diarrhea. However, use of these drugs should be discontinued if symptoms

persist ≥48 hours. Moreover, these agents should not be administered to patients who have a high fever or who have blood in the stool (AII).

Certain specialists recommend that HIV-infected persons who have *Salmonella* gastroenteritis be administered antimicrobial therapy to prevent extraintestinal spread of the pathogen. However, no controlled study has demonstrated a beneficial effect of such treatment, and certain studies of immunocompetent persons have indicated that antimicrobial therapy can lengthen the shedding period. The fluoroquinolones, primarily ciprofloxacin (750 mg twice daily for 14 days), can be used when antimicrobial therapy is chosen (CIII).

Preventing Recurrence

HIV-infected persons who have *Salmonella* septicemia require long-term therapy (i.e., secondary prophylaxis or chronic maintenance therapy) to prevent recurrence. Fluoroquinolones, primarily ciprofloxacin, are usually the drugs of choice for susceptible organisms (BII). Household contacts of HIV-infected persons who have salmonellosis or shigellosis should be evaluated for persistent asymptomatic carriage of *Salmonella* or *Shigella* so that strict hygienic measures or antimicrobial therapy can be instituted and recurrent transmission to the HIV-infected person can be prevented (CIII).

Special Considerations

Children. Similar to HIV-infected adults, HIV-infected children should wash their hands after handling pets, including before eating, and should avoid contact with pets' feces. Handwashing should be supervised (BIII). HIV-exposed infants aged <3 months and all HIV-infected children who have severe immunosuppression should be administered treatment for *Salmonella* gastroenteritis to prevent extraintestinal spread of the pathogen (CIII). Choices of antibiotics include TMP-SMZ, ampicillin, cefotaxime, ceftriaxone, or chloramphenicol; fluoroquinolones should be used with caution and only if no alternatives exist. HIV-infected children who have *Salmonella* septicemia should be offered long-term therapy to prevent recurrence (CIII). TMP-SMZ is the drug of choice; ampicillin or chloramphenicol can be used if the organism is susceptible. Fluoroquinolones should be used with caution and only if no alternative exists. Antiperistaltic drugs are not recommended for children (DIII).

Pregnant Women. Because both pregnancy and HIV infection confer a risk for listeriosis, pregnant HIV-infected women should heed recommendations regarding listeriosis (BII). Because extraintestinal spread of *Salmonella* during pregnancy might lead to infection of the placenta and amniotic fluid and result in pregnancy loss similar to that seen with *Listeria monocytogenes*, pregnant women with *Salmonella* gastroenteritis should receive treatment (BIII). Choices for treatment include ampicillin, cefotaxime, ceftriaxone, or TMP-SMZ. Fluoroquinolones should not be used during pregnancy. TMP-SMZ might offer limited protection against traveler's diarrhea.

Bartonellosis

Preventing Exposure

HIV-infected persons, specifically those who are severely immunosuppressed, are at unusually high risk for experiencing relatively severe disease caused by infection with *Bartonella*, which can be transmitted from cats. These persons should consider the potential risks of cat ownership (CIII). Persons who acquire a cat should adopt or purchase an animal aged >1 year and in good health (BII). Although declawing is not usually advised, HIV-infected persons should avoid rough play with cats and situations in which scratches are likely (BII). Any cat-associated wound should be washed promptly (CIII). Cats should not be allowed to lick open wounds or cuts of HIV-infected persons (BIII). Care of cats should include flea control (CIII). No evidence indicates any benefits to cats or their owners from routine culture or serologic testing of the pet for *Bartonella* infection (DII).

Preventing Disease

No data support chemoprophylaxis for *Bartonella*-associated disease (CIII).

Preventing Recurrence

Relapse or reinfection with *Bartonella* has sometimes followed a course of primary treatment. Although no firm recommendation can be made regarding prophylaxis in this situation, long-term suppression of infection with erythromycin or doxycycline should be considered (CIII).

Special Considerations

Children. Risks of cat ownership for HIV-infected children who are severely immunocompromised should be discussed with parents and caretakers (CIII).

Pregnant Women. If long-term suppression of *Bartonella* infection is required, erythromycin should be used. Tetracycline should not be used during pregnancy.

Candidiasis

Preventing Exposure

Candida organisms are common on mucosal surfaces and skin. No measures are available to reduce exposure to these fungi.

Preventing Disease

Data from prospective controlled trials indicate that fluconazole can reduce the risk for mucosal (e.g., oropharyngeal, esophageal, and vaginal) candidiasis and cryptococcosis among patients with advanced HIV disease (*76–78*). However, routine primary prophylaxis is not recommended because of the effectiveness of therapy for acute disease, the low mortality associated with mucosal candidiasis, the potential for resistant *Candida* organisms to develop, the possibility of drug interactions, and the cost of prophylaxis (DIII).

Preventing Recurrence

Certain HIV specialists do not recommend chronic prophylaxis of recurrent oropharyngeal or vulvovaginal candidiasis for the same reasons that they do not recommend primary prophylaxis. However, if recurrences are frequent or severe, health-care providers might consider administering an oral azole (fluconazole [CI] [*83–85*] or itraconazole solution [CI]). Other factors that influence choices related to such therapy include impact of recurrences on the patient's well-being and quality of life, need for prophylaxis for other fungal infections, cost, toxicities, drug interactions, and potential to induce drug resistance among *Candida* and other fungi. Prolonged use of systemically absorbed azoles, specifically among patients with low $CD4^+$ T lymphocyte counts (i.e., <100 cells/µL), increases the risk for experiencing azole resistance. Adults or adolescents who have a history of documented esophageal candidiasis, including multiple episodes, should be considered candidates for chronic suppressive therapy. Fluconazole at a dose of 100–200 mg daily is appropriate (BI). However, potential azole resistance should be taken into account when long-term azoles are considered.

Special Considerations

Children. Primary prophylaxis of candidiasis among HIV-infected infants is not indicated (DIII). Suppressive therapy with systemic azoles should be considered for infants who have severe recurrent mucocutaneous candidiasis (CIII), including those who have esophageal candidiasis (BIII).

Pregnant Women. Experience with using systemic antifungal drugs during human pregnancy is limited. Four cases of infants born with craniofacial and skeletal abnormalities after prolonged in utero exposure to fluconazole have been reported (*86,87*). In addition, itraconazole is embryotoxic and teratogenic in animal systems (*88*). These same potential risks for teratogenicity are presumed to apply to other systemically absorbed azole antifungals (e.g., ketoconazole). Therefore, chemoprophylaxis against oropharyngeal, esophageal, or vaginal candidiasis using systemically absorbed azoles should not be initiated during pregnancy (DIII), and azoles should be discontinued for HIV-infected women who become pregnant (DIII). Effective birth control measures should be recommended to all HIV-infected women on azole therapy for candidiasis (AIII).

Cryptococcosis

Preventing Exposure

HIV-infected persons cannot completely avoid exposure to *Cryptococcus neoformans*. No evidence exists that exposure to pigeon droppings is associated with an increased risk for acquiring cryptococcosis.

Preventing Disease

Routine testing of asymptomatic persons for serum cryptococcal antigen is not recommended because of low probability that the results will affect clinical decisions (DIII). Prospective controlled trials indicate that fluconazole and itraconazole can reduce the frequency of cryptococcal disease among patients who have advanced HIV disease. However, the majority of HIV specialists recommend that antifungal prophylaxis not be used routinely to prevent cryptococcosis because of the relative infrequency of cryptococcal disease, lack of survival benefits associated with prophylaxis, possibility of drug interactions, potential antifungal drug resistance, and cost. Need for prophylaxis or suppressive therapy for other fungal infections (e.g., candidiasis, histoplasmosis, or coccidioidomycosis) should be considered when making decisions concerning prophylaxis for cryptococcosis. If used, fluconazole at doses of 100–200 mg daily is reasonable for patients whose $CD4^+$ T lymphocyte counts are <50 cellsµL (CI) (*83*).

Preventing Recurrence

Patients who have completed initial therapy for cryptococcosis should be administered lifelong suppressive treatment (i.e., secondary prophylaxis or chronic maintenance therapy) (AI), unless immune reconstitution occurs as a consequence of HAART (see the following recommendation). Fluconazole is superior to itraconazole for preventing relapse of cryptococcal disease and is the preferred drug (AI) (*89–91*).

Discontinuing Secondary Prophylaxis (Chronic Maintenance Therapy). Apparently, adult and adolescent patients are at low risk for recurrence of cryptococcosis when they have successfully completed a course of initial therapy for cryptococcosis, remain asymptomatic with regard to signs and symptoms of cryptococcosis, and have a sustained increase (e.g., ≥6 months) in their CD4$^+$ T lymphocyte counts to >100–200 cells/µL after HAART. The numbers of patients who have been evaluated remain limited (*92,93*). On the basis of these observations and inference from more extensive data regarding safety of discontinuing secondary prophylaxis for other OIs during advanced HIV disease, discontinuing chronic maintenance therapy among such patients is a reasonable consideration, although recurrences can occur (CIII). Certain HIV specialists would perform a lumbar puncture to determine if the cerebrospinal fluid (CSF) is culture-negative before stopping therapy, even if patients have been asymptomatic; other specialists do not believe this is necessary.

Restarting Secondary Prophylaxis. Maintenance therapy should be reinitiated if the CD4$^+$ T lymphocyte count decreases to 100–200 cells/µL (AIII).

Special Considerations

Children. No data exist on which to base specific recommendations for children, but lifelong suppressive therapy with fluconazole after an episode of cryptococcosis is appropriate (AIII).

Pregnant Women. Prophylaxis with fluconazole or itraconazole should not be initiated during pregnancy because of the low incidence of cryptococcal disease, lack of a recommendation for primary prophylaxis against cryptococcosis among nonpregnant adults, and potential teratogenic effects of these drugs during pregnancy (DIII) (*86,87*). For patients who conceive while being administered primary prophylaxis and who elect to continue their pregnancy, prophylaxis should be discontinued. The occurrence of craniofacial and skeletal abnormalities among infants after prolonged in utero exposure to fluconazole should be considered when assessing the therapeutic options for HIV-infected women who become pregnant and are receiving secondary prophylaxis (chronic maintenance therapy) for cryptococcosis (*86,87*). If a woman meets the criteria for discontinuing secondary prophylaxis as discussed previously, discontinuing therapy during pregnancy as long as the CD4$^+$ T lymphocyte count remains >100–200 cells/µL should be strongly considered. For patients requiring therapy, amphotericin B might be preferred, including during the first trimester. Effective birth control measures should be recommended to all HIV-infected women on azole therapy for cryptococcosis (AIII).

Histoplasmosis

Preventing Exposure

Although HIV-infected persons living in or visiting histoplasmosis-endemic areas cannot completely avoid exposure to *Histoplasma capsulatum*, those whose CD4$^+$ T lymphocyte counts are <200 cells/µL should avoid activities known to be associated with increased risk (e.g., creating dust when working with surface soil; cleaning chicken coops that are heavily contaminated with droppings; disturbing soil beneath bird roosting sites; cleaning, remodeling, or demolishing old buildings; and exploring caves) (CIII).

Preventing Disease

Routine skin testing with histoplasmin and serologic testing for antibody or antigen in histoplasmosis-endemic areas are not predictive of disease and should not be performed (DII). Data from a prospective randomized controlled trial indicate that itraconazole can reduce the frequency of histoplasmosis among patients who have advanced HIV infection and who live in histoplasmosis-endemic areas (*94*). However, no survival benefit was observed among persons receiving itraconazole. Prophylaxis with itraconazole can be considered for patients with CD4$^+$ T lymphocyte counts <100 cells/µL who are at high risk because of occupational exposure or who live in a community with a hyperendemic rate of histoplasmosis (≥10 cases/100 patient-years) (CI).

Preventing Recurrence

Patients who complete initial therapy for histoplasmosis should be administered lifelong suppressive treatment (i.e., secondary prophylaxis or chronic maintenance therapy) with itraconazole (200 mg twice daily) (AI) (*95*).

Discontinuing Secondary Prophylaxis (Chronic Maintenance Therapy). Although patients receiving secondary prophylaxis (chronic maintenance therapy) might be at low risk for recurrence of systemic mycosis when their CD4$^+$ T lymphocyte counts increase to >100 cells/µL in response to HAART, the number of patients who have been evaluated is insufficient to warrant a recommendation to discontinue prophylaxis.

Special Considerations

Children. Because primary histoplasmosis can lead to disseminated infection among children, a reasonable option is to administer lifelong suppressive therapy after an acute episode of the disease (AIII).

Pregnant Women. Because of the embryotoxicity and teratogenicity of itraconazole in animal systems, primary prophylaxis against histoplasmosis should not be offered

during pregnancy (DIII) (*81*). These data as well as observation of craniofacial and skeletal abnormalities among infants after prolonged in utero exposure to fluconazole (*86,87*) should be considered when assessing the need for chronic maintenance therapy among HIV-infected pregnant women with histoplasmosis. For such patients, therapy with amphotericin B might be preferred, chiefly during the first trimester. For women receiving HAART with a sustained rise in $CD4^+$ T lymphocyte counts >100 cells/µL, discontinuing azole prophylaxis, chiefly during the first trimester, should be considered. Effective birth control measures should be recommended to all HIV-infected women on azole therapy for histoplasmosis (AIII).

Coccidioidomycosis

Preventing Exposure

Although HIV-infected persons living in or visiting areas in which coccidioidomycosis is endemic cannot completely avoid exposure to *Coccidioides immitis*, they should, when possible, avoid activities associated with increased risk (e.g., those involving extensive exposure to disturbed native soil, for example, at building excavation sites or during dust storms) (CIII).

Preventing Disease

Routine skin testing with coccidioidin (spherulin) in coccidioidomycosis-endemic areas is not predictive of disease and should not be performed (DII). Within the endemic area, a positive serologic test might indicate an increased risk for active infection; however, routine testing does not appear to be useful and should not be performed (DIII). Primary prophylaxis for HIV-infected persons who live in coccidioidomycosis-endemic areas is not routinely recommended.

Preventing Recurrence

Patients who complete initial therapy for coccidioidomycosis should be administered lifelong suppressive therapy (i.e., secondary prophylaxis or chronic maintenance therapy) (AII) using either 400 mg of fluconazole by mouth daily or 200 mg of itraconazole twice daily (*96*). Treatment for patients with meningeal disease requires consultation with a specialist.

Discontinuing Secondary Prophylaxis (Chronic Maintenance Therapy). Although patients receiving secondary prophylaxis (chronic maintenance therapy) might be at low risk for recurrence of systemic mycosis when their $CD4^+$ T lymphocyte counts increase to >100 cells/µL, in response to HAART, the numbers of patients who have been evaluated are insufficient to warrant a recommendation to discontinue prophylaxis.

Special Considerations

Children. Although no specific data are available regarding coccidioidomycosis among HIV-infected children, a reasonable option is to administer lifelong suppressive therapy after an acute episode of the disease (AIII).

Pregnant Women. The potential teratogenicity of fluconazole (*86,87*) and itraconazole (*81*) should be considered when assessing the therapeutic options for HIV-infected women who become pregnant while receiving chronic maintenance therapy for coccidioidomycosis. For such patients, therapy with amphotericin B might be preferred, chiefly during the first trimester. For women receiving HAART with a sustained rise in $CD4^+$ T lymphocyte counts >100 cells/µL, discontinuing azole prophylaxis, chiefly during the first trimester, should be considered. Effective birth control measures should be recommended for all HIV-infected women on azole therapy for coccidioidomycosis (AIII).

Cytomegalovirus Disease

Preventing Exposure

HIV-infected persons who belong to groups at risk with relatively low rates of seropositivity for cytomegalovirus (CMV) and who therefore cannot be presumed to be seropositive should be tested for antibody to CMV (BIII). These groups include patients who have not had contact with men who have sex with men or used injection drugs. HIV-infected adolescents and adults should be advised that CMV is shed in semen, cervical secretions, and saliva and that latex condoms must always be used during sexual contact to reduce the risk for exposure to CMV and to other sexually transmitted pathogens (AII).

HIV-infected adults and adolescents who are child-care providers or parents of children in child-care facilities should be informed that they are at increased risk for acquiring CMV infection (BI). Similarly, parents and other caretakers of HIV-infected children should be advised of the increased risk to children at these centers (BIII). Risk for acquiring CMV infection can be diminished by optimal hygienic practices (e.g., hand-washing) (AII).

HIV-exposed infants and infected children, adolescents, and adults who are seronegative for CMV and require blood transfusion should be administered only CMV antibody-negative or leukocyte-reduced cellular blood products in nonemergency situations (BIII).

Preventing Disease

Prophylaxis with oral ganciclovir can be considered for HIV-infected adults and adolescents who are CMV-seropositive and who have a $CD4^+$ T lymphocyte count of <50 cells/µL (CI)

(*97,98*). Ganciclovir-induced neutropenia, anemia, conflicting reports of efficacy, lack of proven survival benefit, risk for experiencing ganciclovir-resistant CMV, and cost are among the concerns that should be addressed when deciding whether to institute prophylaxis in individual patients. Acyclovir is not effective in preventing CMV disease, and valacyclovir is not recommended because of an unexplained trend toward increased deaths among persons with AIDS who were administered valacyclovir for CMV prophylaxis (*99*). Therefore, neither acyclovir nor valacyclovir should be used for this purpose (EI). The primary method for preventing severe CMV disease is recognition of the early manifestations of the disease. Early recognition of CMV retinitis probably occurs when the patient has been educated regarding this topic. Patients should be made aware of the importance of increased floaters in the eye and should be advised to assess their visual acuity regularly by using simple techniques (e.g., reading newsprint) (BIII). Regular funduscopic examinations performed by an ophthalmologist are recommended by certain specialists for patients with low (e.g., <50 cells/µL) CD4$^+$ T lymphocyte counts (CIII).

Preventing Recurrence

CMV disease is not cured with courses of available antiviral agents (e.g., ganciclovir, foscarnet, cidofovir, or fomivirsen). After induction therapy, secondary prophylaxis (chronic maintenance therapy) is recommended for life (AI), unless an immune reconstitution occurs as a consequence of HAART (see the following recommendation). Regimens demonstrated to be effective for chronic suppression in randomized, controlled clinical trials include parenteral or oral ganciclovir, parenteral foscarnet, combined parenteral ganciclovir and foscarnet, parenteral cidofovir, and (for retinitis only) ganciclovir administration via intraocular implant or repetitive intravitreous injections of fomivirsen (AI) (*100–108*). Oral valganciclovir has been approved by the Food and Drug Administration (FDA) for both acute induction therapy and for maintenance therapy, although substantial data have not been published. Repetitive intravitreous injections of ganciclovir, foscarnet, and cidofovir have been reported to be effective for secondary prophylaxis of CMV retinitis related to uncontrolled case series (*109,110*). Intraocular therapy alone does not provide protection to the contralateral eye or to other organ systems and typically is combined with oral ganciclovir (*100*). The choice of a chronic maintenance regimen for patients treated for CMV disease should be made in consultation with a specialist. For patients with retinitis, this decision should be made in consultation with an ophthalmologist and should take into consideration the anatomic location of the retinal lesion, vision in the contralateral eye, the immunologic and virologic status of the patient, and the patient's response to HAART (BIII).

Discontinuing Secondary Prophylaxis (Chronic Maintenance Therapy). Multiple case series have reported that maintenance therapy can be discontinued safely among adult and adolescent patients with CMV retinitis whose CD4$^+$ T lymphocyte counts have indicated a sustained (e.g., ≥6 months) increase to >100–150 cells/µL in response to HAART (*111–116*). These patients have remained disease-free for >30–95 weeks, whereas during the pre-HAART era, retinitis typically reactivated in ≤6–8 weeks after stopping CMV therapy. Plasma HIV RNA levels were variable among these patients, demonstrating that the CD4$^+$ T lymphocyte count is the primary determinant of immune recovery to CMV. Discontinuing prophylaxis should be considered for patients with a sustained (e.g., ≥6 months) increase in CD4$^+$ T lymphocyte counts to >100–150 cells/µL in response to HAART (BII). Such decisions should be made in consultation with an ophthalmologist and should take into account such factors as magnitude and duration of CD4$^+$ T lymphocyte increase, anatomic location of the retinal lesion, vision in the contralateral eye, and the feasibility of regular ophthalmologic monitoring (BII). All patients who have had anti-CMV maintenance therapy discontinued should continue to undergo regular ophthalmologic monitoring for early detection of CMV relapse as well as for immune reconstitution uveitis (AIII). CMV viral load or other markers of CMV infection (e.g., antigenemia or viral deoxyribonucleic acid [DNA] tests) are not well-standardized; their role in predicting relapse remains to be defined (*117,118*). Relapses have been reported rarely among patients with CD4$^+$ T lymphocyte counts of >100–150 cells/µL (*119*).

Restarting Secondary Prophylaxis. Relapse of CMV retinitis occurs among patients whose anti-CMV maintenance therapies have been discontinued and whose CD4$^+$ T lymphocyte counts have decreased to <50 cells/µL (*109*). Therefore, reinstitution of secondary prophylaxis should occur when the CD4$^+$ T lymphocyte count has decreased to <100–150 cells/µL (AIII). Relapse has been reported among patients whose CD4$^+$ T lymphocyte counts are >100 cells/µL, but such reports are rare (*119*).

Special Considerations

Children. Certain HIV specialists recommend obtaining a CMV urine culture for all HIV-infected or exposed infants at birth or at an early postnatal visit to identify those infants with congenital CMV infection (CIII). In addition, beginning at age 1 year, CMV antibody testing on an annual basis can be considered for CMV-seronegative and culture-negative HIV-infected infants and children who are severely

immunosuppressed (Table 9) (CIII). Annual testing will allow identification of children who have acquired CMV infection and might benefit from screening for retinitis.

HIV-infected children who are CMV-infected and severely immunosuppressed might benefit from a dilated retinal examination performed by an ophthalmologist every 4–6 months (CIII). In addition, older children should be counseled to be aware of floaters in the eye, similar to the recommendation for adults (BIII).

Oral ganciclovir results in reduced CMV shedding among CMV-infected children and can be considered for primary prophylaxis against CMV disease among CMV-infected children who are severely immunosuppressed (e.g., $CD4^+$ T lymphocyte count <50 cells/μL) (CII). Patients with a history of CMV disease should be administered lifelong prophylaxis to prevent recurrence (AII). For children with CMV disease, no data are available to guide decisions concerning discontinuing secondary prophylaxis (chronic maintenance therapy) when the $CD4^+$ T lymphocyte count has increased in response to HAART.

Pregnant Women. Indications for prophylaxis are the same for pregnant women as for nonpregnant women. Choice of agents to be used during pregnancy should be individualized after consultation with a specialist.

Herpes Simplex Virus Disease

Preventing Exposure

HIV-infected persons should use latex condoms during every act of sexual intercourse to reduce the risk for exposure to herpes simplex virus (HSV) and to other sexually transmitted pathogens (AII). They should specifically avoid sexual contact when herpetic lesions (genital or orolabial) are evident (AII).

Preventing Disease

Antiviral prophylaxis after exposure to HSV, or to prevent initial episodes of HSV disease among persons with latent infection, is not recommended (DIII).

Preventing Recurrence

Because episodes of HSV disease can be treated successfully, chronic therapy with acyclovir is not required after lesions resolve. However, persons who have frequent or severe recurrences can be administered daily suppressive therapy with oral acyclovir or oral famciclovir (AI) (*120,121*). Valacyclovir also is an option (CIII). Intravenous foscarnet or cidofovir can be used to treat infection caused by acyclovir-resistant isolates of HSV, which are routinely resistant to ganciclovir as well (AII).

Special Considerations

Children. Recommendations for preventing initial disease and recurrence among adults and adolescents apply to children as well.

Pregnant Women. Oral acyclovir prophylaxis during late pregnancy is a controversial strategy recommended by certain specialists to prevent neonatal herpes transmission. However, such prophylaxis is not routinely recommended. For patients who have frequent, severe recurrences of genital HSV disease, acyclovir prophylaxis might be indicated (BIII). No pattern of adverse pregnancy outcomes has been reported after acyclovir exposures (*122*).

Varicella-Zoster Virus Disease

Preventing Exposure

HIV-infected children and adults who are susceptible to varicella-zoster virus (VZV) (i.e., those who have no history of chickenpox or shingles or are seronegative for VZV) should avoid exposure to persons with chickenpox or shingles (AII). Household contacts, specifically children, of susceptible HIV-infected persons should be vaccinated against VZV if they have no history of chickenpox and are seronegative for HIV, so that they will not transmit VZV to their susceptible HIV-infected contacts (BIII).

Preventing Disease

Limited data regarding the safety and efficacy of using varicella vaccine among HIV-infected adults are available, and no recommendation for its use can be made for this population (see Special Considerations/Children for information regarding use of varicella vaccine among children). For prophylaxis against chickenpox, HIV-infected children and adults who are susceptible to VZV (i.e., those who have no history of chickenpox or shingles or who have no detectable antibody against VZV) should be administered varicella-zoster immune globulin (VZIG) as soon as possible but in ≤96 hours after close contact with a person who has chickenpox or shingles (AIII). Data are lacking regarding the effectiveness of acyclovir for preventing chickenpox among susceptible HIV-infected children or adults. No preventive measures are available for shingles.

Preventing Recurrence

No drug has been proven to prevent the recurrence of shingles among HIV-infected persons.

Special Considerations

Children. HIV-infected children who are asymptomatic and not immunosuppressed (i.e., in immunologic category 1,

Table 9) should receive live-attenuated varicella vaccine at age ≥12–15 months (BII). Varicella vaccine should not be administered to other HIV-infected children because of the potential for disseminated viral infection (EIII).

Pregnant Women. VZIG is recommended for VZV-susceptible, HIV-infected pregnant women in ≤96 hours after exposure to VZV (AIII). If oral acyclovir is used, VZV serology should be performed so that the drug can be discontinued if the patient is seropositive for VZV (BIII).

HHV-8 Infection (Kaposi Sarcoma-Associated Herpes Virus)

Preventing Exposure

Persons coinfected with HIV and HHV-8 are at risk for experiencing Kaposi sarcoma (KS), and evidence exists that progression to KS might be accelerated among persons who seroconvert to HHV-8 after being infected with HIV. Thus, preventing acquisition of HHV-8 infections among those already HIV-infected is important (*123–125*). Apparently, the three major routes of HHV-8 transmission are oral (i.e., the virus infects oral epithelial cells; infection was associated with deep kissing in one study), semen (HHV-8 is less frequently detected in semen than in saliva), and through blood by sharing needles (*126–128*). Patients should be counseled that deep kissing and sexual intercourse with persons who have high risk for being infected with HHV-8 (e.g., persons who have KS or who are HIV-infected) might lead to acquisition of the agent that causes KS (CIII). Although efficacy of condom use for preventing HHV-8 exposure has not been established, HIV-infected persons should use latex condoms during every act of sexual intercourse to reduce exposure to sexually transmitted pathogens (AII). HIV-infected injection-drug users should be counseled not to share drug-injection equipment, even if both users are already HIV-infected, because of the chance of becoming infected with HHV-8 or other bloodborne pathogens (BIII).

Preventing Disease

Because clinical use of routine serologic testing to identify HHV-8 infection has not been established, no recommendation for serologic testing can be made at this time. Lower rates of KS have been observed among AIDS patients treated with ganciclovir or foscarnet for CMV retinitis (*99*). HHV-8 replication in vitro is inhibited by ganciclovir, foscarnet, and cidofovir. However, because the efficacy and clinical use of these drugs in preventing KS have not been established, no recommendation can be made concerning use of these or other drugs to prevent KS among persons coinfected with HIV and HHV-8. Potent antiretroviral drug combinations that suppress HIV replication reduce the frequency of KS among HIV-infected persons (*129*) and should be considered for all persons who qualify for such therapy (BII).

Preventing Recurrence

Effective suppression of HIV replication with antiretroviral drugs among HIV-infected patients with KS might prevent KS progression or occurrence of new lesions and should be considered for all persons with KS (BII).

Special Considerations

Children. In parts of the world where HHV-8 is endemic, mother-to-child transmission of HHV-8 has been reported (*130–133*), and horizontal transmission among young children, possibly through saliva occurs. However, no recommendations are available for preventing HHV-8 transmission from child to child.

Human Papillomavirus Infection

Preventing Exposure

HIV-infected persons should use latex condoms during every act of sexual intercourse to reduce the risk for exposure to sexually transmitted pathogens (AII), although limited evidence exists to demonstrate that condoms reduce the risk for infection with human papillomavirus (HPV).

Preventing Disease

HPV-Associated Genital Epithelial Cancers Among HIV-Infected Women. After a complete history of previous cervical disease has been obtained, HIV-infected women should have a pelvic examination and a Papanicolaou (Pap) smear. In accordance with the recommendation of the Agency for Health Care Policy and Research, the Pap smear should be obtained twice during the first year after diagnosis of HIV infection and, if the results are normal, annually thereafter (AII). If the results of the Pap smear are abnormal, care should be provided according to the Interim Guidelines for Management of Abnormal Cervical Cytology published by a National Cancer Institute Consensus Panel and briefly summarized in the following recommendations (*134*).

For patients whose Pap smears are interpreted as atypical squamous cells of undetermined significance (ASCUS), different management options are available; the choice depends in part on whether the interpretation of ASCUS is qualified by a statement indicating that a neoplastic process is suspected. Follow-up by Pap tests without colposcopy is acceptable, including when the diagnosis of ASCUS is not qualified further or the cytopathologist suspects a reactive process. In such

situations, Pap tests should be repeated every 4–6 months for 2 years until three consecutive smears have been negative. If a second report of ASCUS occurs in the 2-year follow-up period, the patient should be considered for colposcopic evaluation (BIII).

Women who have a diagnosis of unqualified ASCUS associated with severe inflammation should be evaluated for an infectious process. If specific infections are identified, reevaluation should be performed after appropriate treatment, preferably after 2–3 months (BIII). If the diagnosis of ASCUS is qualified by a statement indicating that a neoplastic process is suspected, the patient should be managed as if a low-grade squamous intraepithelial lesion (LSIL) were present (see the following recommendation) (BIII). If a patient who has a diagnosis of ASCUS is at high risk (i.e., previous positive Pap tests or suboptimal adherence to follow-up), the option of colposcopy should be considered (BIII).

Different management options are available for patients who have LSIL. Follow-up with Pap tests every 4–6 months is used by certain clinicians and is being used in countries outside the United States as an established management method. Patients managed in this way must be carefully selected and considered reliable for follow-up. If repeat smears indicate persistent abnormalities, colposcopy and directed biopsy are indicated (BIII). Colposcopy and directed biopsy of any abnormal area on the ectocervix constitute another appropriate option (BIII). Women who have cytologic diagnosis of high-grade squamous intraepithelial lesions (HSILs) or squamous cell carcinoma should undergo colposcopy and directed biopsy (AII). No data are available to demonstrate that these guidelines to prevent cervical disease should be modified for women on HAART.

HPV-Associated Anal Intraepithelial Neoplasia and Anal Cancer Among HIV-Infected Men Who Have Sex With Men and Among Women. Evidence from multiple studies demonstrates that HPV-positive men who have sex with men and HPV-infected women are at increased risk for anal HSILs and might be at increased risk for anal cancer. In view of this evidence, coupled with a recent cost-effectiveness analysis projecting that screening and treatment for anal HSILs provide clinical benefits comparable to other measures to prevent OIs among HIV-infected persons (*131*), anal cytology screening of HIV-infected men who have sex with men and cytology screening of women might become useful preventive measures. However, studies of screening and treatment programs for anal HSILs need to be implemented before recommendations for anal cytology screening can be made.

Preventing Recurrence

Risks for recurrence of squamous intraepithelial lesions and cervical cancer after conventional therapy are increased among HIV-infected women. Preventing illness associated with recurrence depends on careful follow-up of patients after treatment. Patients should be monitored with frequent cytologic screening and, when indicated, colposcopic examination for recurrent lesions (AI) (*134,135*). In one recent study of HIV-infected women treated for HSILs by using standard therapy, low-dose intravaginal 5-fluorouracil (i.e., 2 grams twice weekly for 6 months) reduced the short-term risk for recurrence and possibly the grade recurrence (*136*). However, clinical experience with this therapy is too limited to provide a recommendation for use.

Special Considerations

Pregnant Women. Using intravaginal 5-fluorouracil to prevent recurrent dysplasia is not recommended during pregnancy.

HCV Infection

Preventing Exposure

The primary route of HCV transmission in the United States is injection-drug use. Because injection-drug use is a complex behavior, clinicians should assess the patient's readiness to change this practice and encourage efforts to provide patient education and support directed at recovery. Patients who inject drugs should be advised to (*137–139*)

- stop using injection drugs (AIII); and
- enter and complete a substance-abuse treatment program, including a relapse prevention program (AIII).

If they continue to inject drugs (BIII), patients should be advised to

- never reuse or share syringes, needles, rinse water, or drug-preparation equipment; if, nonetheless, injection equipment that has been used by other persons is shared, the equipment should be cleaned before reuse with bleach and water as is recommended for HIV prevention;
- use only sterile syringes obtained from a reliable source (e.g., pharmacies or syringe-exchange programs);
- use sterile (e.g., boiled) water to prepare drugs, and if this is not possible, to use clean water from a reliable source (e.g., fresh tap water);
- use a new or disinfected container (i.e., cooker) and a new filter (i.e., cotton) to prepare drugs;
- clean the injection site with a new alcohol swab before injection; and
- safely dispose of syringes after one use.

Persons considering tattooing or body-piercing should be informed of potential risks for acquiring bloodborne infections, which could be transmitted if equipment is not sterile or if proper infection control procedures are not followed (e.g., washing hands, using latex gloves, and cleaning and disinfecting surfaces) (*139*) (BIII). To reduce risks for acquiring bloodborne infections, patients should be advised not to share dental appliances, razors, or other personal care articles (BIII).

Although efficiency of sexual transmission of HCV is low, safe-sex practices should be encouraged for all HIV-infected persons, and barrier precautions (e.g., latex condoms) are recommended to reduce the risk for exposure to sexually transmitted pathogens (AII).

Preventing Disease

All HIV-infected patients should be screened for HCV infection (BIII). Screening is recommended because certain HIV-infected patients (e.g., injection-drug users and patients with hemophilia) are at increased risk for HCV infection and HCV-related disease, and because knowledge of HCV status is critical for management of all HIV-infected patients (e.g., to interpret and manage elevated liver-related tests). Screening should be performed by using enzyme immunoassays (EIAs) licensed for detection of antibody to HCV (anti-HCV) in blood (BIII). Positive anti-HCV results should be verified with additional testing (i.e., recombinant immunoblot assay [RIBA] or reverse transcriptase-polymerase chain reaction [RT-PCR] for HCV RNA). The presence of HCV RNA in blood might also be assessed for HIV-infected persons with undetectable antibody but other evidence of chronic liver disease (e.g., unexplained elevated liver-specific enzymes) or when acute HCV infection is suspected (CIII).

Persons coinfected with HIV and HCV should be advised not to drink excessive amounts of alcohol (AII). Avoiding alcohol altogether might be prudent because whether even occasional alcohol use (e.g., <12 ounces of beer or <10 grams of alcohol/day) increases the incidence of cirrhosis among HCV-infected persons is unclear (CIII).

Patients with chronic HCV should be vaccinated against hepatitis A because 1) apparently, the risk for fulminant hepatitis associated with hepatitis A is increased among such patients; 2) hepatitis A vaccine is safe for HIV-infected persons; and 3) although immunogenicity is reduced among patients with advanced HIV infection, 66%–75% of patients experience protective antibody responses (BIII). Prevaccination screening for total (IgG and immunoglobulin M [IgM]) antibody to hepatitis A virus is cost-effective and therefore recommended when >30% prevalence of hepatitis A virus antibody is expected among the population being screened (e.g., persons aged >40 years) (*140*). Patients should also be vaccinated for hepatitis B virus if they are susceptible (BIII).

HIV- and HCV-coinfected patients might experience HCV-associated liver disease in a shorter time course than patients infected with HCV alone (*139,141–143*) and should be evaluated for chronic liver disease and the possible need for treatment. Limited data indicate that HCV treatment can be safely provided to patients coinfected with HIV and HCV. Because the optimal means of treating coinfected patients has not been established and certain HIV-infected patients have conditions that complicate therapy (e.g., depression), this care should occur during a clinical trial or be coordinated by health-care providers with experience treating both HIV and HCV infections (BIII).

In certain studies, the incidence of antiretroviral-associated liver enzyme elevations has been increased among patients coinfected with HIV and HCV (*141*); such increases might not require treatment modifications. Thus, although liver enzymes should be carefully monitored, HAART should not be routinely withheld from patients coinfected with HIV and HCV (DIII). However, coinfected patients initiating HAART might have an inflammatory reaction that mimics an exacerbation of underlying liver disease. In this situation, careful monitoring of liver function is required.

Preventing Recurrence

If the serum HCV RNA level becomes undetectable during HCV therapy and remains undetectable for 6 months after HCV therapy is stopped (i.e., sustained virologic response), >90% of HIV-uninfected patients with HCV will remain HCV RNA-negative for >5 years and have improved liver histology (*144*). For HIV- and HCV-coinfected patients, durability of treatment response and requirement for maintenance therapy are unknown.

Special Considerations

Children. Transmission of HCV from mother to child appears to be more frequent for mothers coinfected with HIV and HCV than for those infected with HCV alone. Therefore, children born to women coinfected with HIV and HCV should be tested for HCV infection (*137*) (BI). Because maternal HCV antibody can persist for ≤18 months, testing should be performed at age ≥2 years. If earlier diagnosis is desired, RT-PCR for HCV RNA can be performed after age 1 month and should be repeated at a subsequent time. The average rate of HCV infection among infants born to coinfected women is approximately 15% (range: 5%–36%) (*145*). Data are limited regarding the natural history of HCV infection and treatment of chronic HCV among children.

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TABLE 1. Prophylaxis to prevent first episode of opportunistic disease among adults and adolescents infected with human immunodeficiency virus (HIV)

Pathogen	Preventive regimen		
	Indication	First choice	Alternative
I. Strongly recommended as standard of care			
Pneumocystis carinii[*]	$CD4^+$ counts of <200/µL or oropharyngeal candidiasis	Trimethoprim-sulfamethoxazole (TMP-SMZ), 1 double-strength tablet (DS) by mouth, daily (AI) or TMP-SMZ, 1 single-strength tablet (SS) by mouth daily (AI)	Dapsone, 50 mg by mouth, twice daily or 100 mg by mouth daily (BI); dapsone, 50 mg by mouth daily plus pyrimethamine, 50 mg by mouth weekly plus leucovorin, 25 mg by mouth weekly (BI); dapsone, 200 mg by mouth plus pyrimethamine, 75 mg by mouth plus leucovorin, 25 mg by mouth weekly (BI); aerosolized pentamidine, 300 mg monthly via Respirgard II™ nebulizer (manufactured by Marquest, Englewood, Colorado) (BI); atovaquone, 1,500 mg by mouth daily (BI); TMP-SMZ, 1 DS by mouth three times weekly (BI)
Mycobacterium tuberculosis, Isoniazid-sensitive[†]	Tuberculin skin test (TST) reaction ≥5 mm or prior positive TST result without treatment or contact with person with active tuberculosis, regardless of TST result (BIII)	Isoniazid, 300 mg by mouth plus pyridoxine, 50 mg by mouth daily for 9 mos (AII) or isoniazid, 900 mg by mouth plus pyridoxine, 100 mg by mouth, twice weekly for 9 mos (BII)	Rifampin, 600 mg by mouth daily (BIII) for 4 mos or rifabutin 300 mg by mouth daily (CIII) for 4 mos; pyrazinamide, 15–20 mg/kg body weight by mouth daily for 2 mos plus either rifampin, 600 mg by mouth daily (BI) for 2 mos or rifabutin, 300 mg by mouth daily (CIII) for 2 mos
Isoniazid-resistant	Same as previous pathogen; increased probability of exposure to isoniazid-resistant tuberculosis	Rifampin, 600 mg by mouth daily (AIII) or rifabutin, 300 mg by mouth (BIII) daily for 4 mos	Pyrazinamide, 15–20 mg/kg body weight by mouth daily for 2 mos plus either rifampin, 600 mg by mouth daily (BI) for 2 mos or rifabutin, 300 mg by mouth daily (CIII) for 2 mos
Multidrug-resistant (isoniazid and rifampin)	Same as previous pathogen; increased probability of exposure to multidrug-resistant tuberculosis	Choice of drugs requires consultation with public health authorities; depends on susceptibility of isolate from source patient	—
Toxoplasma gondii[§]	Immunoglobulin G (µgG) antibody to *Toxoplasma* and $CD4^+$ count of <100/µL	TMP-SMZ, 1 DS by mouth daily (AII)	TMP-SMZ, 1 SS by mouth daily (BIII); dapsone, 50 mg by mouth daily plus pyrimethamine, 50 mg by mouth weekly plus leucovorin, 25 mg by mouth weekly (BI); dapsone, 200 mg by mouth plus pyrimethamine, 75 mg by mouth plus leucovorin, 25 mg by mouth weekly (BI); atovaquone, 1,500 mg by mouth daily with or without pyrimethamine, 25 mg by mouth daily plus leucovorin, 10 mg by mouth daily (CIII)
Mycobacterium avium complex[¶]	$CD4^+$ count of <50/µL	Azithromycin, 1,200 mg by mouth weekly (AI) or clarithromycin,[¶] 500 mg by mouth twice daily (AI)	Rifabutin, 300 mg by mouth daily (BI); azithromycin, 1,200 mg by mouth daily plus rifabutin, 300 mg by mouth daily (CI)

TABLE 1. (*Continued*) Prophylaxis to prevent first episode of opportunistic disease among adults and adolescents infected with human immunodeficiency virus (HIV)

Pathogen	Preventive regimen		
	Indication	First choice	Alternative
Varicella-zoster virus (VZV)	Substantial exposure to chickenpox or shingles for patients who have no history of either condition or, if available, negative antibody to VZV	Varicella-zoster immune globulin (VZIG), 5 vials (1.25 mL each) intramuscularly, administered ≤96 hours after exposure, ideally in ≤48 hours (AIII)	—
II. Usually recommended			
*Streptococcus pneumoniae***	$CD4^+$ count of ≥200/µL	23-valent polysaccharide vaccine, 0.5 mL intramuscularly (BII)	—
Hepatitis B virus[†† §§]	All susceptible patients (i.e., antihepatitis B core antigen-negative)	Hepatitis B vaccine: 3 doses (BII)	—
Influenza virus[†† ¶¶]	All patients (annually, before influenza season)	Inactivated trivalent influenza virus vaccine: one annual dose (0.5 mL) intramuscularly (BII)	Oseltamivir, 75 mg by mouth daily (influenza A or B) (CIII); rimantadine, 100 mg by mouth twice daily (CIII), or amantadine, 100 mg by mouth twice daily (CIII) (influenza A only)
Hepatitis A virus[†† §§]	All susceptible patients at increased risk for hepatitis A infection (i.e., antihepatitis A virus-negative) (e.g., illegal drug users, men who have sex with men, hemophiliacs) or patients with chronic liver disease, including chronic hepatitis B or C	Hepatitis A vaccine: two doses (BIII)	—
III. Evidence for efficacy but not routinely indicated			
Bacteria	Neutropenia	Granulocyte-colony-stimulating factor (G-CSF), 5-10 µg/kg body weight subcutaneously daily for 2–4 weeks or granulocyte-macrophage colony-stimulating factor (GM-CSF), 250 µg/m^2 subcutaneously for 2–4 weeks (CII)	—
Cryptococcus neoformans	$CD4^+$ count of <50/µL	Fluconazole, 100–200 mg by mouth daily (CI)	Itraconazole capsule, 200 mg by mouth daily (CIII)
*Histoplasma capsulatum****	$CD4^+$ count of <100/µL, endemic geographic area	Itraconazole capsule, 200 mg by mouth (CI)	—
Cytomegalovirus (CMV)[†††]	$CD4^+$ count of <50/µL and CMV antibody positivity	Oral ganciclovir, 1 gm by mouth three times daily (CI)	—

TABLE 1. (*Continued*) Prophylaxis to prevent first episode of opportunistic disease among adults and adolescents infected with human immunodeficiency virus (HIV)

Notes: Information included in these guidelines might not represent Food and Drug Administration (FDA) approval or approved labeling for products or indications. Specifically, the terms *safe* and *effective* might not be synonymous with the FDA-defined legal standards for product approval. Letters and Roman numerals in parentheses after regimens indicate the strength of the recommendation and the quality of evidence supporting it (see Box).

* Prophylaxis should also be considered for persons with a $CD4^+$ percentage of <14%, for persons with a history of an AIDS-defining illness, and possibly for those with $CD4^+$ counts of >200 but <250 cells/iL. TMP-SMZ also reduces the frequency of toxoplasmosis and some bacterial infections. Patients receiving dapsone should be tested for glucose-6 phosphate dehydrogenase deficiency. A dosage of 50 mg daily is probably less effective than 100 mg daily. Efficacy of parenteral pentamidine (e.g., 4 mg/kg body weight/month) is uncertain. Fansidar (sulfadoxine-pyrimethamine) is rarely used because of severe hypersensitivity reactions. Patients who are being administered therapy for toxoplasmosis with sulfadiazine-pyrimethamine are protected against *Pneumocystis carinii* pneumonia (PCP) and do not need additional prophylaxis against PCP.

† Directly observed therapy is recommended for isoniazid (e.g., 900 mg twice weekly); isoniazid regimens should include pyridoxine to prevent peripheral neuropathy. If rifampin or rifabutin are administered concurrently with protease inhibitors or nonnucleoside reverse transcriptase inhibitors, careful consideration should be given to potential pharmacokinetic interactions (**Source:** CDC. Updated guidelines for the use of rifabutin or rifampin for the treatment and prevention of tuberculosis among HIV-infected patients taking protease inhibitors or nonnucleoside reverse transcriptase inhibitors [Notice to readers]. MMWR 2000; 49:183–9) (see discussion of rifamycin interactions in text). Reports exist of fatal and severe liver injury associated with treatment of latent tuberculosis infection among HIV-uninfected persons treated with the 2-month regimen of daily rifampin and pyrazinamide; therefore, using regimens that do not contain pyrazinamide among HIV-infected persons whose completion of treatment can be ensured is prudent (**Source:** CDC. Update: Fatal and severe liver injuries associated with rifampin and pyrazinamide for latent tuberculosis infection and revisions in American Thoracic Society/CDC recommendations—United States, 2001 MMWR 2001;50:733–5). Exposure to multidrug-resistant tuberculosis might require prophylaxis with two drugs; consult public health authorities. Possible regimens include pyrazinamide plus either ethambutol or a fluoroquinolone.

§ Protection against toxoplasmosis is provided by TMP-SMZ, dapsone plus pyrimethamine, and possibly atovaquone. Atovaquone can be used with or without pyrimethamine. Pyrimethamine alone probably provides limited, if any, protection.

¶ See text for discussion of drug interactions and CDC. Prevention and treatment of tuberculosis among patients infected with human immunodeficiency virus: principles of therapy and revised recommendations. MMWR 1998;47;(RR-20):1–51 and CDC. Updated guidelines for the use of rifabutin or rifampin for the treatment and prevention of tuberculosis among HIV-infected patients taking protease inhibitors or nonnucleoside reverse transcriptase inhibitors. MMWR 2000; 49:185–9. During pregnancy, azithromycin is preferred over clarithromycin because of teratogenicity of clarithromycin among animals.

** Vaccination can be offered to persons who have a $CD4^+$ T lymphocyte count of <200 cells/µL, although the efficacy is probably diminished. Revaccination ≥5 years after the first dose is considered optional, as is revaccination sooner if the initial vaccination was administered when the $CD4^+$ count was <200 cells/µL and the $CD4^+$ counts has increased to >200 cells/µL while on highly active antiretroviral therapy (HAART). Certain authorities are concerned that vaccinations might stimulate the replication of HIV.

†† Although data demonstrating clinical benefit of these vaccines among HIV-infected persons are not available, assuming that those patients who develop antibody responses will derive a certain amount of protection is reasonable. Researchers are concerned that vaccinations might stimulate HIV replication, although for influenza vaccination, an observational study of HIV-infected persons in clinical care reported no adverse effect of this vaccine, including multiple doses, on patient survival (personal communication, John W. Ward, M.D., CDC). Also, this concern might be less relevant in the setting of HAART. However, because of the theoretical concern that increases in HIV plasma ribonucleic acid (RNA) after vaccination during pregnancy might increase the risk for perinatal transmission of HIV, health-care providers can defer vaccination for such patients until after HAART is initiated.

§§ Hepatitis B vaccine has been recommended for all children and adolescents and for all adults with risk factors for hepatitis B virus (HBV). For persons requiring vaccination against both hepatitis A and B, a combination vaccine is now available. For additional information regarding vaccination against hepatitis A and B, see CDC. Hepatitis B virus: a comprehensive strategy for eliminating transmission in the United States through universal childhood vaccination: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1991;40(No. RR-13):1–19.

¶¶ Oseltamivir is appropriate during outbreaks of either influenza A or B. Rimantadine or amantadine are appropriate during outbreaks of influenza A, although neither rimantadine nor amantadine is recommended during pregnancy. Dosage reduction for antiviral chemoprophylaxis against influenza might be indicated for decreased renal or hepatic function, and for persons with seizure disorders. Physicians should consult the drug package inserts and the annual CDC influenza guidelines for more specific information concerning adverse effects and dosage adjustments. For additional information regarding vaccination, antiviral chemoprophylaxis and therapy against influenza, see CDC. Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2002;51(No. RR-3):1–31.

*** In a limited number of occupational or other circumstances, prophylaxis should be considered; a specialist should be consulted.

††† Acyclovir is not protective against CMV. Valacyclovir is not recommended because of an unexplained trend toward increased mortality observed among persons with AIDS who were being administered this drug for prevention of CMV disease.

TABLE 2. Prophylaxis to prevent recurrence of opportunistic disease, after chemotherapy for acute disease, among adults and adolescents infected with human immunodeficiency virus (HIV)

Pathogen	Preventive regimen		
	Indication	First choice	Alternative
I. Recommended as standard of care			
Pneumocystis carinii	Prior *P. carinii* pneumonia (PCP)	Trimethoprim-sulfamethoxazole (TMP-SMZ), 1 double-strength tablet (DS) by mouth daily (AI); TMP-SMZ 1 single-strength tablet (SS) by mouth daily (AI)	Dapsone, 50 mg by mouth twice daily or 100 mg by mouth daily (BI); dapsone, 50 mg by mouth daily plus pyrimethamine, 50 mg by mouth weekly plus leucovorin, 25 mg by mouth weekly (BI); dapsone, 200 mg by mouth plus pyrimethamine, 75 mg by mouth plus leucovorin, 25 mg by mouth weekly (BI); aerosolized pentamidine, 300 mg every month via Respirgard II™ nebulizer (manufactured by Marquest, Englewood, Colorado) (BI); atovaquone, 1,500 mg by mouth daily (BI); TMP-SMZ, 1 DS by mouth three times weekly (CI)
Toxoplasma gondii[*]	Prior toxoplasmic encephalitis	Sulfadiazine, 500–1,000 mg by mouth four times daily plus pyrimethamine, 25–50 mg by mouth daily plus leucovorin, 10–25 mg by mouth daily (AI)	Clindamycin, 300–450 mg by mouth every 6–8 hours plus pyrimethamine, 25–50 mg by mouth daily plus leucovorin 10–25 mg by mouth daily (BI); atovaquone, 750 mg by mouth every 6–12 hours with or without pyrimethamine, 25 mg by mouth daily plus leucovorin, 10 mg by mouth daily (CIII)
Mycobacterium avium complex[†]	Documented disseminated disease	Clarithromycin,[†] 500 mg by mouth twice daily (AI) plus ethambutol, 15 mg/kg body weight by mouth daily (AII); with or without rifabutin, 300 mg by mouth daily (CI)	Azithromycin, 500 mg by mouth daily (AII) plus ethambutol, 15 mg/kg body weight by mouth daily(AII); with or without rifabutin, 300 mg by mouth daily (CI)
Cytomegalovirus	Prior end-organ disease	Ganciclovir, 5–6 mg/kg body weight/day intravenously 5–7 days weekly or 1,000 mg by mouth three times daily (AI); or foscarnet, 90–120 mg/kg body weight intravenously daily (AI); or for retinitis, ganciclovir, sustained-release implant every 6–9 months plus ganciclovir, 1.0–1.5 gm by mouth three times daily (AI)	Cidofovir, 5 mg/kg body weight intravenously every other week with probenecid 2 gm by mouth 3 hours before the dose followed by 1 gm by mouth 2 hours after the dose, and 1 gm by mouth 8 hours after the dose (total of 4 gm) (AI). Fomivirsen 1 vial (330 µg) injected into the vitreous, then repeated every 2–4 weeks (AI); valganciclovir 900 mg by mouth daily (BI)
Cryptococcus neoformans	Documented disease	Fluconazole, 200 mg by mouth daily (AI)	Amphotericin B, 0.6–1.0 mg/kg body weight intravenously weekly–three times weekly (AI); itraconazole, 200-mg capsule by mouth daily (BI)
Histoplasma capsulatum	Documented disease	Itraconazole capsule, 200 mg by mouth twice daily (AI)	Amphotericin B, 1.0 mg/kg body weight intravenously weekly (AI)
Coccidioides immitis	Documented disease	Fluconazole, 400 mg by mouth daily (AII)	Amphotericin B, 1.0 mg/kg body weight intravenously weekly (AI); itraconazole, 200-mg capsule by mouth twice daily (AII)

TABLE 2. (*Continued*) Prophylaxis to prevent recurrence of opportunistic disease, after chemotherapy for acute disease, among adults and adolescents infected with human immunodeficiency virus (HIV)

Pathogen	Preventive regimen		
	Indication	First choice	Alternative
Salmonella species, (nontyphi)[§]	Bacteremia	Ciprofloxacin, 500 mg by mouth twice daily for ≥2 months (BII)	Antibiotic chemoprophylaxis with another active agent (CIII)
II. Recommended only if subsequent episodes are frequent or severe			
Herpes simplex virus	Frequent/severe recurrences	Acyclovir, 200 mg by mouth three times daily or 400 mg by mouth twice daily (AI); famciclovir, 250 mg by mouth twice daily (AI)	Valacyclovir, 500 mg by mouth twice daily (CIII)
Candida (oropharyngeal or vaginal)	Frequent or severe recurrences	Fluconazole, 100–200 mg by mouth daily (CI)	Itraconazole solution, 200 mg by mouth daily (CI)
Candida (esophageal)	Frequent or severe recurrences	Fluconazole, 100–200 mg by mouth daily (BI)	Itraconazole solution, 200 mg by mouth daily (BI)

Notes: Information included in these guidelines might not represent Food and Drug Administration (FDA) approval or approved labeling for products or indications. Specifically, the terms *safe* and *effective* might not be synonymous with the FDA-defined legal standards for product approval. Letters and Roman numerals in parentheses after regimens indicate the strength of the recommendation and the quality of evidence supporting it (see Box).

* Pyrimethamine-sulfadiazine confers protection against PCP as well as toxoplasmosis; clindamycin-pyrimethamine does not offer protection against PCP.

† Certain multidrug regimens are not well-tolerated. Drug interactions (e.g., those observed with clarithromycin and rifabutin) can be problematic; rifabutin has been associated with uveitis, chiefly when administered at daily doses of >300 mg or concurrently with fluconazole or clarithromycin (see discussion of rifamycin interactions in text) (**Source:** CDC. Updated guidelines for the use of rifabutin or rifampin for the treatment and prevention of tuberculosis among HIV-infected patients taking protease inhibitors or nonnucleoside reverse transcriptase inhibitors [Notice to readers]. MMWR 2000; 49:185–9). During pregnancy, azithromycin is recommended instead of clarithromycin because clarithromycin is teratogenic among animals.

§ Efficacy for eradication of *Salmonella* has been demonstrated only for ciprofloxacin.

TABLE 3. Effects of food on drugs used to prevent opportunistic infections

Drug	Food effect	Recommendation
Atovaquone	Bioavailability increased ≤3-fold with high-fat meal	Administer with food
Ganciclovir (capsules)	High-fat meal results in 22% (ganciclovir) or 30% (valganciclovir) increase in area under the blood concentration curve	High-fat meal might increase toxicity of valganciclovir
Itraconazole	Grapefruit juice results in 30% decrease in area under the blood concentration curve	Avoid concurrent grapefruit juice
Itraconazole (capsules)	Substantial increase in bioavailability when taken with a full meal	Administer with food
Itraconazole (solution)	31% increase in area under the blood concentration curve when taken under fasting conditions	Take without food, if possible

TABLE 4. Effects of medications on drugs used to prevent opportunistic infections

Affected drug	Interacting drug(s)	Mechanism/effect	Recommendation
Atovaquone	Rifampin	Induction of metabolism; decreased drug levels	Concentrations might not be therapeutic; avoid combination or increase atovaquone dose
Atovaquone	Lopinavir-ritonavir	Potential for induction of metabolism; decreased drug levels	Concentrations might not be therapeutic; might require increase of atovaquone dose, but data are insufficient to make specific recommendation
Clarithromycin	Efavirenz	Induction of metabolism; decrease in clarithromycin area under the blood concentration curve (AUC) by 39%; increase in AUC of 14-OH clarithromycin by 34%	Clarithromycin efficacy is uncertain
Clarithromycin	Ritonavir	Inhibition of metabolism; increased clarithromycin drug levels by 77%	Dose adjustment of clarithromycin necessary only if renal dysfunction is present; for creatinine clearance (CrCl) <60 mL/min, reduce clarithromycin dose by 50%; for CrCl <30 mL/min, reduce dose by 75%
Clarithromycin	Lopinavir-ritonavir	Inhibition of metabolism; increased clarithromycin drug levels	Dose adjustment of clarithromycin necessary only if renal dysfunction is present; for CrCl <60 mL/min, reduce clarithromycin dose by 50%; for CrCl <30 mL/min, reduce dose by 75%
Clarithromycin	Nevirapine	Induction of metabolism; decrease in clarithromycin AUC by 35%; increase in AUC of 14-OH clarithromycin by 27%	Efficacy of *Mycobacterium avium* complex prophylaxis might be decreased; monitor closely
Ketoconazole	Lopinavir-ritonavir	Inhibition of metabolism; increased ketoconazole AUC	Use with caution at ketoconazole doses >200 mg/day
Ketoconazole	Antacids, didanosine, (but not didanosine enteric-coated tablets), buffered products, H2-blockers, proton pump inhibitors	Increase in gastric pH that impairs absorption of ketoconazole	Avoid using ketoconazole with pH-raising agents or use alternative antifungal drug
Quinolone antibiotics (ciprofloxacin, levofloxacin, gatifloxacin, moxifloxacin)	Didanosine (but not didanosine enteric-coated tablets), antacids, iron products, calcium products, sucralfate (cation preparations)	Chelation results in marked decrease in quinolone drug levels	Administer cation preparation ≥2 hours after quinolone
Rifabutin	Fluconazole	Inhibition of metabolism; marked increase in rifabutin drug levels	Monitor for rifabutin toxicities (e.g., uveitis, nausea, or neutropenia)
Rifabutin	Efavirenz	Induction of metabolism; substantial decrease in rifabutin AUC	Increase rifabutin dose to 450–600 mg daily or 600 mg twice weekly.*
Rifabutin	Ritonavir, lopinavir-ritonavir, ritonavir-saquinavir	Inhibition of metabolism; marked increase in rifabutin drug levels	Decrease rifabutin to 150 mg every other day or three times weekly
Rifabutin	Indinavir, nelfinavir, amprenavir	Inhibition of metabolism; marked increase in rifabutin drug levels	Decrease rifabutin to 150 mg daily or 300 mg three times weekly

* Appropriate dose of efavirenz is uncertain if a protease inhibitor is used with efavirenz plus rifabutin.

TABLE 5. Effects of opportunistic infection medications on anti-infective drugs commonly administered to persons infected with human immunodeficiency virus (HIV)*

Affected drug	Interacting drug(s)	Mechanism/effect	Recommendation
Amprenavir, delavirdine, indinavir, lopinavir-ritonavir, nelfinavir, saquinavir	Rifampin	Induction of metabolism; marked decrease in protease inhibitor or delavirdine drug levels	Avoid concomitant use
Efavirenz, ritonavir, ritonavir-saquinavir, nevirapine	Rifampin	Induction of metabolism; decrease in protease inhibitor or nevirapine levels	Combinations could possibly be used, but clinical experience is limited; consider efavirenz 800 mg daily when used with rifampin
Delavirdine	Rifabutin	Induction of metabolism; 50%–60% decrease in delavirdine levels	Avoid concomitant use
Indinavir, nelfinavir, amprenavir*	Rifabutin	Induction of metabolism; 50% decrease in protease inhibitor levels	Consider increase in indinavir dose to 1,000 mg every 8 hours; if indinavir is the sole protease inhibitor, decrease rifabutin dose to 150 mg daily
Ritonavir, ritonavir-saquinavir, lopinavir-ritonavir	Rifabutin	Induction of metabolism of ritonavir	No dosage change for protease inhibitors; consider rifabutin 150 mg every other day or three times weekly
Efavirenz	Rifabutin	Potential for decreased efavirenz levels	No dosage change necessary for efavirenz; adjust rifabutin dose to 450–600 mg daily or 600 mg twice weekly
Saquinavir	Rifabutin	Potential for decreased saquinavir levels	Limited data
Didanosine	Ganciclovir (by mouth)	Increased didanosine area under the blood concentration curve by approximately 100%	Clinical significance unknown; monitor for didanosine-related adverse effects

* Data are limited regarding use of rifamycin drugs with ritonavir-boosting protease inhibitor regimens, except for ritonavir-saquinavir and ritonavir-lopinavir; therefore, concomitant use of rifamycins with these regimens must be approached cautiously.

TABLE 6. Adverse effects of drugs used in preventing opportunistic infections

Adverse effect	Drug(s)
Bone marrow suppression	Cidofovir, dapsone, ganciclovir, pyrimethamine, rifabutin, sulfadiazine, trimethoprim-sulfamethoxazole
Diarrhea	Atovaquone, clindamycin
Hepatotoxicity	Clarithromycin, fluconazole, isoniazid, itraconazole, ketoconazole, pyrazinamide, rifabutin, rifampin, trimethoprim-sulfamethoxazole
Nephrotoxicity	Amphotericin B, cidofovir, foscarnet, pentamidine, high-dose acyclovir
Ocular effects	Cidofovir, ethambutol, rifabutin
Pancreatitis	Pentamidine, trimethoprim-sulfamethoxazole
Peripheral neuropathy	Isoniazid
Neurotoxicity	High-dose acyclovir, quinolones
Skin rash	Atovaquone, dapsone, pyrimethamine, sulfadiazine, trimethoprim-sulfamethoxazole, ribavirin

TABLE 7. Dosing of drugs for primary prevention or maintenance therapy for opportunistic infections related to renal insufficiency

Drug	Normal dose	Renal dysfunction: Creatinine clearance (CrCl) (mL/min/1.73 m^2)	Adjusted dose	
Acyclovir	200 mg by mouth three times daily or 400 mg every 12 hrs	<10 Hemodialysis	200 mg every 12 hrs 200 mg every 12 hrs; administer the first daily dose after dialysis	
Cidofovir	5 mg/kg body weight intravenously every other week (administer with probenecid and hydration)	Reduce from 5 mg/kg body weight to 3 mg/kg body weight for an increase in serum creatinine of 0.3–0.4 above baseline; discontinue for an increase in creatinine ≥0.5 above baseline or development of 3+ proteinuria; not recommended for patients with baseline serum creatinine ≥1.5, CrCl ≤55 mL/min,		
Ciprofloxacin	500 mg by mouth every 12 hrs	30–50 <30 Hemodialysis	250–500 mg every 12 hrs 250–500 mg every 18 hrs 250–500 mg after each dialysis	
Clarithromycin	500 mg twice daily	Reduce dose by one half or double interval if creatinine clearance is <30 mL/min		
Famciclovir	250–500 mg every 12 hr	20–39 <20 Hemodialysis	125–250 mg every 12 hrs 125–250 mg every 24 hrs 125 mg after each dialysis	
Fluconazole	50–400 mg daily	<50 (not on dialysis) Hemodialysis	½ dose Full dose after each dialysis	
			Low dose	**High dose**
Foscarnet*	90–120 mg/kg body weight daily	>1.4* 1.0–1.4 0.8–1.0 0.6–0.8 0.5–0.6 0.4–0.5 <0.4	90 mg every 24 hrs 70 mg every 24 hrs 50 mg every 24 hrs 80 mg every 48 hrs 60 mg every 48 hrs 50 mg every 48 hrs Not recommended	120 mg every 24 hrs 90 mg every 24 hrs 65 mg every 24 hrs 104 mg every 48 hrs 80 mg every 48 hrs 65 mg every 48 hrs Not recommended
			Capsules	**Intravenously**
Ganciclovir	1 gm by mouth three times daily (capsules); or 5 mg/kg body weight intravenously daily or 6 mg/kg body weight intravenously daily for 5 days/week	50–69 25–49 10–24 <10 Hemodialysis	1,500 mg by mouth daily or 500 mg three times daily 1,000 mg by mouth daily or 500 mg twice daily 500 mg daily 500 mg three times weekly 500 mg after each dialysis	2.5 mg/kg body weight every 24 hrs 1.25 mg/kg body weight every 24 hrs 0.625 mg/kg body weight every 24 hrs 0.625 mg/kg body weight three times weekly 0.625 mg/kg body weight after each dialysis
Levofloxacin	500 mg daily	20–49 10–19 Hemodialysis	500 mg loading dose, then 250 mg every 24 hrs 500 mg loading dose, then 250 mg every 48 hrs 250 mg after each dialysis	
Trimethoprim-sulfamethoxazole	1 double-strength tablet daily; or 1 double-strength tablet three times weekly; or 1 single-strength tablet daily	15–30 <15 Hemodialysis	½ dose ½ dose or use alternative agent ½ dose; administer scheduled dose after each dialysis	
Valacyclovir	500 mg–1 gm every 24 hrs	<30 Hemodialysis	500 mg every 24–48 hrs 500 mg after each dialysis	
Valganciclovir	900 mg daily	40–59 25–39 10–24 <10 Dialysis	450 mg daily 450 mg daily 450 mg twice weekly Not recommended Not recommended	

*Creatinine clearance for foscarnet is expressed as mL/min/kg body weight.

TABLE 8. Wholesale acquisition costs of agents recommended for preventing opportunistic infections among adults infected with human immunodeficiency virus

Pathogen	Drug or vaccine	Dose	Estimated annual cost/patient (US$)
Pneumocystis carinii	Trimethoprim-sulfamethoxazole	160/800 mg daily	135
	Dapsone	100 mg daily	72
	Aerosolized pentamidine	300 mg every morning	1,185
	Atovaquone	1500 mg daily	11,627
Mycobacterium avium complex	Clarithromycin	500 mg twice daily	2,843
	Azithromycin	1,200 mg weekly	3,862
	Rifabutin	300 mg daily	3,352
Cytomegalovirus	Ganciclovir (by mouth)	1,000 mg three times daily	17,794
	Ganciclovir implant*	—	5,000
	Ganciclovir (intravenous)	5 mg/kg body weight daily	13,093
	Foscarnet (intravenous)	90–120 mg/kg body weight daily	27,770–37,027
	Cidofovir (intravenous)	375 mg every other week	20,904
	Fomivirsen (intravitreal)	1 vial every 4 weeks	12,000
	Valganciclovir	900 mg daily	21,582
Mycobacterium tuberculosis	Isoniazid†	300 mg daily	23/9 months
	Rifampin	600 mg daily	294/2 months
	Pyrazinamide	1,500 mg daily	194/2 months
Fungi	Fluconazole	200 mg daily	4,603
	Itraconazole capsules	200 mg daily	5,340
	Itraconazole solution	200 mg daily	5,673
	Ketoconazole	200 mg daily	1,230
Herpes simplex virus	Acyclovir	400 mg twice daily	1,384
	Famciclovir	500 mg twice daily	5,311
	Valacyclovir	500 mg twice daily	2,538
Toxoplasma gondii	Pyrimethamine	50 mg weekly	49
	Leucovorin	25 mg weekly	988
	Sulfadiazine	500 mg four times daily	1,490
Streptococcus pneumoniae	23-valent pneumococcal vaccine	1 0.5-mL dose intramuscularly	13
Influenza virus	Inactivated trivalent influenza vaccine	1 0.5-mL dose intramuscularly	3
Hepatitis A virus	Hepatitis A vaccine	2 1.0-mL doses intramuscularly	124
Hepatitis B virus	Recombinant hepatitis B vaccine	3 10–20-µg doses intramuscularly	70
Bacterial infections	granulocyte-colony-stimulating factor, intravenously	300 µg three times weekly	29,406
Varicella-zoster virus	varicella-zoster immune globulin	5, 6.25-mL vials	562

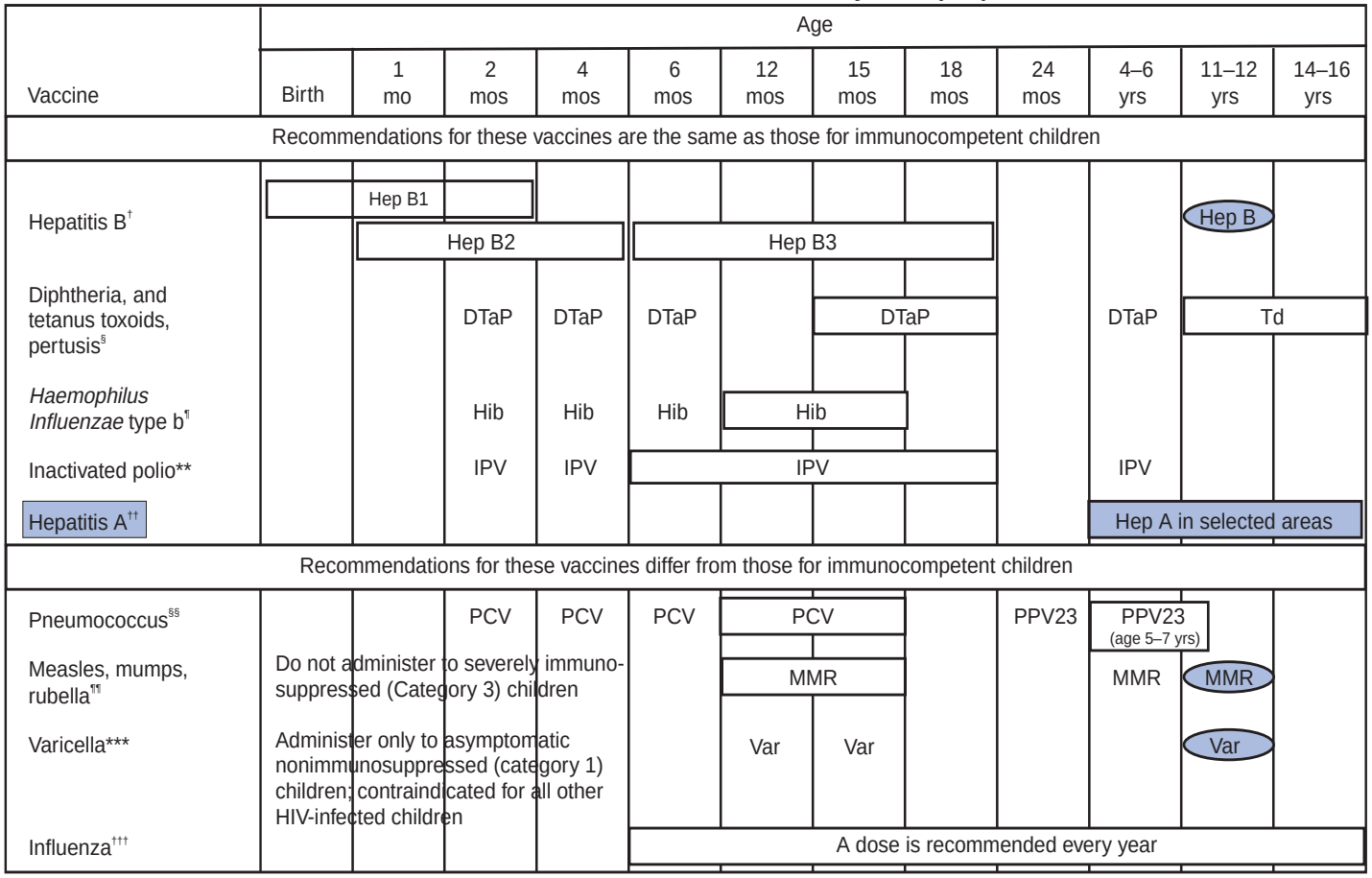
Source: Medical Economics Company. Drug topics red book. Montvale, NJ: Medical Economics, Inc., 2000.
* Implant typically lasts 6–9 months.
† Cost/9 months of therapy.

TABLE 9. Immunologic categories for human immunodeficiency virus-infected children, based on age-specific CD4+ T lymphocyte counts and percentage of total lymphocytes*

Immunologic category	Age (yrs)		
	≤12 mos cells/µL (%)	1–5 cells/µL (%)	6–12 cells/µL (%)
No evidence of suppression	≥1,500 (≥25)	≥1,000 (≥25)	≥500 (≥25)
Evidence of moderate suppression	750–1,499 (15–24)	500–999 (15–24)	200–499 (15–24)
Severe suppression	<750 (<15)	<500 (<15)	<200 (<15)

* Adapted from CDC. 1994 revised classification system for human immunodeficiency virus infection in children less than 13 years of age. MMWR 1994;43(No. RR-12):1–10.

TABLE 10. Recommended immunization schedule for human immunodeficiency virus (HIV)-infected children*



* This schedule indicates the recommended ages for routine administration of licensed childhood vaccines as of November 1, 2000, for children aged birth–18 years. Additional vaccines might be licensed and recommended during the year. Licensed combination vaccines might be used whenever any components of the combination are indicated and the vaccine's other components are not contraindicated. Providers should consult the manufacturer's package inserts for detailed recommendations.

† Infants born to hepatitis B surface antigen (HBsAg)-negative mothers should receive the first dose of hepatitis B vaccine (Hep B) at birth and no later than age 2 months. The second dose should be administered ≥1 months after the first dose. The third dose should be administered ≥4 months after the first dose and ≥2 months after the second dose, but not before age 6 months. Infants born to HBsAg-positive mothers should receive Hep B and 0.5 mL hepatitis B immune globulin (HBIG) ≤12 hours after birth at separate sites. The second dose is recommended at age 1–2 months and the third dose at age 6 months. Infants born to mothers whose HBsAg status is unknown should receive Hep B ≤12 hours after birth. Maternal blood should be drawn at delivery to determine the mother's HBsAg status; if the HBsAg test is positive, the infant should receive HBIG as soon as possible (no later than age 1 week). All children and adolescents (through age 18 years) who have not been immunized against hepatitis B should begin the series during any visit. Providers should make special efforts to immunize children who were born in, or whose parents were born in, areas of the world where hepatitis B virus infection is moderately or highly endemic.

§ The fourth dose of diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP) can be administered as early as age 12 months, provided 6 months have elapsed since the third dose and the child is unlikely to return at age 15–18 months. Vaccination with tetanus and diphtheria toxoids (Td) is recommended at age 11–12 years if ≥5 years have elapsed since the last dose of diphtheria and tetanus toxoids and pertussis vaccine (DTP), DTaP, or diphtheria and tetanus toxoids (DT). Subsequent routine Td boosters are recommended every 10 years.

¶ Three *Haemophilus influenzae* type b (Hib) conjugate vaccines are licensed for infant use. If Hib conjugate vaccine (polyribosylribitol phosphate-meningococcal outer membrane protein [PRP-OMP]) (PedvaxHIB® or ComVax™ [Merck and Company, Inc., Whitehouse Station, New Jersey]) is administered at ages 2 and 4 months, a dose at age 6 months is not required. Because clinical studies among infants have demonstrated that using certain combination products might induce a lower immune response to the Hib vaccine component, DTaP/Hib combination products should not be used for primary immunization among infants at ages 2, 4, or 6 months, unless approved by the Food and Drug Administration for these ages.

** An all-inactivated poliovirus vaccine (IPV) schedule is recommended for routine childhood polio vaccination in the United States. All children should receive four doses of IPV at age 2 months, age 4 months, ages 6–18 months, and ages 4–6 years. Oral poliovirus vaccine should not be administered to HIV-infected persons or their household contacts.

†† Hepatitis A vaccine (Hep A) is recommended for use in selected states or regions and for certain persons at high risk (e.g., those with Hepatitis B or C infection). Information is available from local public health authorities.

§§ Heptavalent pneumococcal conjugate vaccine (PCV) is recommended for all HIV-infected children aged 2–59 months. Children aged ≥2 years should also receive the 23-valent pneumococcal polysaccharide vaccine; a single revaccination with the 23-valent vaccine should be offered to children after 3–5 years. Refer to the Advisory Committee on Immunization Practices recommendations (see CDC. Preventing pneumococcal disease among infants and young children: recommendations of the Advisory Committee on Immunization Practices [ACIP]. MMWR 2000;49[No. RR-9]:1–38) for dosing intervals for children starting the vaccination schedule after age 2 months.

¶¶ Measles, mumps, and rubella (MMR) should not be administered to severely immunocompromised (category 3) children. HIV-infected children without severe immunosuppression would routinely receive their first dose of MMR as soon as possible after reaching their first birthdays. Consideration should be given to administering the second dose of MMR at age 1 month (i.e., a minimum of 28 days) after the first dose rather then waiting until school entry.

*** Varicella-zoster virus vaccine should be administered only to asymptomatic, nonimmunosuppressed children. Eligible children should receive two doses of vaccine with a ≥3-month interval between doses. The first dose can be administered at age 12 months.

††† Inactivated split influenza virus vaccine should be administered to all HIV-infected children aged ≥6 months each year. For children aged 6 months–<9 years who are receiving influenza vaccine for the first time, two doses administered 1 month apart are recommended. For specific recommendations, see CDC. Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2002;51(No. RR-4):1–32.

TABLE 11. Prophylaxis to prevent first episode of opportunistic disease among infants and children infected with human immunodeficiency virus

Pathogen	Preventive regimen		
	Indication	First choice	Alternative
I. Strongly recommended as standard of care			
*Pneumocystis carinii**	HIV-infected or HIV-indeterminate, infants aged 1–12 mos; HIV-infected children aged 1–5 yrs with $CD4^+$ count of <500/µL or $CD4^+$ percentages of <15%; HIV-infected children aged 6–12 yrs with $CD4^+$ count of <200/µL or $CD4^+$ percentages of <15%	Trimethoprim-sulfamethoxazole (TMP-SMZ), 150/750 mg/m^2/day in 2 divided doses by mouth three times weekly on consecutive days (AII); acceptable alternative dosage schedules: (AII) single dose by mouth three times weekly on consecutive days; 2 divided doses by mouth daily; or 2 divided doses by mouth three times weekly on alternate days	Dapsone (children aged ≥1 mos), 2 mg/kg body weight (max 100 mg) by mouth daily or 4 mg/kg body weight (max 200 mg) by mouth weekly (CII); aerosolized pentamidine (children aged ≥5 yrs), 300 mg every month via Respirgard II™ (manufactured by Marquest, Englewood, Colorado) nebulizer (CIII); atovaquone (children aged 1–3 mos and >24 mos, 30 mg/kg body weight by mouth daily; children aged 4–24 mos, 45 mg/kg body weight by mouth daily) (CII)
Mycobacterium tuberculosis			
Isoniazid-sensitive	Tuberculin skin test (TST) reaction, ≥5 mm or prior positive TST result without treatment; or contact with any person with active tuberculosis, regardless of TST result	Isoniazid, 10–15 mg/kg body weight (max 300 mg) by mouth daily for 9 mos (AII); or 20–30 mg/kg body weight (max 900 mg) by mouth twice weekly for 9 months (BII)	Rifampin, 10–20 mg/kg body weight (max 600 mg) by mouth daily for 4–6 mos (BIII)
Isoniazid-resistant	Same as previous pathogen; increased probability of exposure to isoniazid-resistant tuberculosis	Rifampin, 10–20 mg/kg body weight (max 600 mg) by mouth daily for 4–6 mos (BIII)	Uncertain
Multidrug-resistant (isoniazid and rifampin)	Same as previous pathogen; increased probability of exposure to multidrug-resistant tuberculosis	Choice of drugs requires consultation with public health authorities and depends on susceptibility of isolate from source patient	—
Mycobacterium avium complex†	For children aged ≥6 yrs with $CD4^+$ count of <50/µL; aged 2–6 yrs with $CD4^+$ count of <75/µL; aged 1–2 yrs with $CD4^+$ count of <500/µL; aged <1 yr with $CD4^+$ count of <750/µL	Clarithromycin, 7.5 mg/kg body weight (max 500 mg) by mouth twice daily (AII), or azithromycin, 20 mg/kg body weight (max 1,200 mg) by mouth weekly (AII)	Azithromycin, 5 mg/kg body weight (max 250 mg) by mouth daily (AII); children aged ≥6 yrs, rifabutin, 300 mg by mouth daily (BI)
Varicella-zoster virus§	Substantial exposure to varicella or shingles with no history of chickenpox or shingles	Varicella zoster immune globulin (VZIG), 1 vial (1.25 mL)/10 kg body weight (max 5 vials) intramuscularly, administered ≤96 hrs after exposure, ideally in ≤48 hrs (AII)	—
Vaccine-preventable pathogens¶	HIV exposure/infection	Routine immunizations (see Table 10)	—
II. Usually recommended			
*Toxoplasma gondii***	Immunoglobulin G (IgG) antibody to *Toxoplasma* and severe immunosuppression	TMP-SMZ, 150/750 mg/m^2/day in 2 divided doses by mouth daily (BIII)	Dapsone (children aged ≥1 mos), 2 mg/kg body weight or 15 mg/m^2 (max 25 mg) by mouth daily plus pyrimethamine, 1 mg/kg body weight by mouth daily plus leucovorin, 5 mg by mouth every 3 days (BIII); atovaquone, children aged 1–3 mos and >24 mos, 30 mg/kg body weight by mouth daily; children aged 14–24 mos, 45 mg/kg body weight by mouth daily (CIII)

TABLE 11. (*Continued*) Prophylaxis to prevent first episode of opportunistic disease among infants and children infected with human immunodeficiency virus

Pathogen	Preventive regimen		
	Indication	First choice	Alternative
Varicella zoster virus	HIV-infected children who are asymptomatic and not immunosuppressed	Varicella zoster vaccine (see vaccine-preventable pathogens section of this table) (BII)	—
Influenza virus	All patients, annually, before influenza season	Inactivated split trivalent influenza vaccine (see vaccine-preventable section of this table) (BIII)	Oseltamivir (during outbreaks of influenza A or B) for children aged ≥13 years, 75 mg by mouth daily (CIII); rimantadine or amantadine (during outbreaks of influenza A), children aged 1–9 yrs, 5 mg/kg body weight in 2 divided doses (max 150 mg/day) by mouth daily; children aged ≥10 yrs, use adult doses (CIII)
III. Not recommended for the majority of children; indicated for use only in unusual circumstances			
Invasive bacterial infections[††]	Hypogammaglobulinemia (i.e., IgG <400 mg/dL)	Intravenous immune globulin (400 mg/kg body weight every 2–4 weeks) (AI)	—
Cryptococcus neoformans	Severe immunosuppression	Fluconazole, 3–6 mg/kg body weight by mouth daily (CII)	Itraconazole, 2–5 mg/kg body weight by mouth every 12–24 hrs (CII)
Histoplasma capsulatum	Severe immunosuppression, endemic geographic area	Itraconazole, 2–5 mg/kg body weight by mouth every 12–24 hrs (CIII)	—
Cytomegalovirus (CMV)[§§]	CMV antibody positivity and severe immunosuppression	Oral ganciclovir, 30 mg/kg body weight by mouth three times daily (CII)	—

Notes: Information included in these guidelines might not represent Food and Drug Administration (FDA) approval or approved labeling for products or indications. Specifically, the terms *safe* and *effective* might not be synonymous with the FDA-defined legal standards for product approval. Letters and Roman numerals in parentheses after regimens indicate the strength of the recommendation and the quality of the evidence supporting it (see Box).

* Daily TMP-SMZ reduces the frequency of certain bacterial infections. Apparently, TMP-SMZ, dapsone-pyrimethamine, and possibly atovaquone (with or without pyrimethamine) protect against toxoplasmosis, although data have not been prospectively collected. When compared with weekly dapsone, daily dapsone is associated with lower incidence of *Pneumocystis carinii* pneumonia (PCP) but higher hematologic toxicity and mortality (**Source:** McIntosh K, Cooper E, Xu J, et al. Toxicity and efficacy of daily vs. weekly dapsone for prevention of *Pneumocystis carinii* pneumonia in children infected with human immunodeficiency virus. ACTG 179 Study Team. AIDS Clinical Trials Group. Pediatr Infect Dis J 1999;18:432–9). The efficacy of parenteral pentamidine (e.g., 4 mg/kg body weight every 2–4 weeks) is controversial. Patients receiving therapy for toxoplasmosis with sulfadiazine-pyrimethamine are protected against PCP and do not need TMP-SMZ.

† Substantial drug interactions can occur between rifamycins (i.e., rifampin and rifabutin) and protease inhibitors and nonnucleoside reverse transcriptase inhibitors. A specialist should be consulted.

§ Children routinely being administered intravenous immune globulin (IVIG) should receive VZIG if the last dose of IVIG was administered >21 days before exposure.

¶ HIV-infected and exposed children should be immunized according to the childhood immunization schedule in this report (see Table 10), which has been adapted from the January–December 2001 schedule recommended for immunocompetent children by the Advisory Committee on Immunization Practices, the American Academy of Pediatrics, and the American Academy of Family Physicians. This schedule differs from that for immunocompetent children in that both the conjugate pneumococcal vaccine (PCV-7) and the pneumococcal polysaccharide vaccine (PPV-23) are recommended (BII) and vaccination against influenza (BIII) should be offered. Measles, mumps, and rubella should not be administered to severely immunocompromised children (DIII). Vaccination against varicella is indicated only for asymptomatic nonimmunosuppressed children (BII). After an HIV-exposed child is determined not to be HIV-infected, the schedule for immunocompetent children applies.

** Protection against toxoplasmosis is provided by the preferred antipneumocystis regimens and possibly by atovaquone. Atovaquone can be used with or without pyrimethamine. Pyrimethamine alone probably provides limited, if any, protection (for definition of severe immunosuppression, see Table 9).

†† Respiratory syncytial virus (RSV) IVIG (750 mg/kg body weight), not monoclonal RSV antibody, can be substituted for IVIG during the RSV season to provide broad anti-infective protection, if this product is available.

§§ Oral ganciclovir and perhaps valganciclovir results in reduced CMV shedding among CMV-infected children. Acyclovir is not protective against CMV.

TABLE 12. Prophylaxis to prevent recurrence of opportunistic disease, after chemotherapy for acute disease, among HIV-infected infants and children

Pathogen	Preventive regimen		
	Indication	First choice	Alternative
I. Recommended for life as standard of care			
Pneumocystis carinii	Prior *P. carinii* pneumonia (PCP)	Trimethoprim-sulfamethoxazole (TMP-SMZ), 150/750 mg/m^2/day in 2 divided doses by mouth three times weekly on consecutive days (AII); acceptable alternative schedules for same dosage (AII): single dose by mouth three times weekly on consecutive days; 2 divided doses by mouth daily; 2 divided doses by mouth three times weekly on alternate days	Dapsone (children aged ≥1 mos), 2 mg/kg body weight (max 100 mg) by mouth daily or 4 mg/kg body weight (max 200 mg) by mouth weekly (CII); aerosolized pentamidine (children aged ≥5 yrs), 300 mg every month via Respirgard II™ nebulizer (manufactured by Marquest, Englewood, Colorado) (CIII); atovaquone (children aged 1–3 mos and >24 mos, 30 mg/kg body weight by mouth daily; children aged 4–24 mos, 45 mg/kg body weight by mouth daily) (CII)
Toxoplasma gondii[*]	Prior toxoplasmic encephalitis	Sulfadiazine, 85–120 mg/kg body weight/day in 2–4 divided doses by mouth daily plus pyrimethamine, 1 mg/kg body weight or 15 mg/m^2 (max 25 mg) by mouth daily plus leucovorin, 5 mg by mouth every 3 days (AI)	Clindamycin, 20–30 mg/kg body weight/day in 4 divided doses by mouth daily plus pyrimethamine, 1 mg/kg body weight by mouth daily plus leucovorin, 5 mg by mouth every 3 days (BI)
Mycobacterium avium complex[†]	Prior disease	Clarithromycin, 7.5 mg/kg body weight (max 500 mg) by mouth twice daily (AII) plus ethambutol, 15 mg/kg body weight (max 900 mg) by mouth daily (AII); with or without rifabutin, 5 mg/kg body weight (max 300 mg) by mouth daily (CII)	Azithromycin, 5 mg/kg body weight (max 250 mg) by mouth daily (AII) plus ethambutol, 15 mg/kg body weight (max 900 mg) by mouth daily (AII); with or without rifabutin, 5 mg/kg body weight (max 300 mg) by mouth daily (CII)
Cryptococcus neoformans	Documented disease	Fluconazole, 3–6 mg/kg body weight by mouth daily (AII)	Amphotericin B, 0.5–1.0 mg/kg body weight intravenously 1–3 times weekly (AI); itraconazole, 2–5 mg/kg body weight by mouth every 12–24 hrs (BII)
Histoplasma capsulatum	Documented disease	Itraconazole, 2–5 mg/kg body weight by mouth every 12–48 hrs (AIII)	Amphotericin B, 1.0 mg/kg body weight intravenously weekly (AIII)
Coccidioides immitis	Documented disease	Fluconazole, 6 mg/kg body weight by mouth daily (AIII)	Amphotericin B, 1.0 mg/kg body weight intravenously weekly (AIII); itraconazole, 2–5 mg/kg body weight by mouth every 12–48 hrs (AIII)
Cytomegalovirus	Prior end-organ disease	Ganciclovir, 5 mg/kg body weight intravenously daily; or foscarnet, 90–120 mg/kg body weight intravenously daily (AI)	(For retinitis) Ganciclovir sustained release implant, every 6–9 mos plus ganciclovir, 30 mg/kg body weight by mouth three times daily (BIII)
Salmonella species (nontyphi)[§]	Bacteremia	TMP-SMZ, 150/750 mg/m^2 in 2 divided doses by mouth daily for ≥2 months (CIII)	Antibiotic chemoprophylaxis with another active agent (CIII)

TABLE 12. (*Continued*) Prophylaxis to prevent recurrence of opportunistic disease, after chemotherapy for acute disease, among HIV-infected infants and children

Pathogen	Preventive regimen		
	Indication	First choice	Alternative
II. Recommended only if subsequent episodes are frequent or severe			
Invasive bacterial Infections¶	>2 infections in a 1-year period	TMP-SMZ, 150/750 mg/m^2, in 2 divided doses by mouth daily (BI); or intravenous immune globulin (IVIG), 400 mg/kg body weight every 2–4 weeks (BI)	Antibiotic chemoprophylaxis with another active agent (BIII)
Herpes simplex virus	Frequent or severe recurrences	Acyclovir, 80 mg/kg body weight/day in 3–4 divided doses by mouth daily (AII)	—
Candida (oropharyngeal)	Frequent or severe recurrences	Fluconazole, 3–6 mg/kg body weight by mouth daily (CIII)	—
Candida (esophageal)	Frequent or severe recurrences	Fluconazole, 3–6 mg/kg body weight by mouth daily (BIII)\	Itraconazole solution, 5 mg/kg body weight by mouth daily (CIII)

Notes: Information included in these guidelines might not represent Food and Drug Administration (FDA) approval or approved labeling for products or indications. Specifically, the terms *safe* and *effective* might not be synonymous with the FDA-defined legal standards for product approval. Letters and Roman numerals in parentheses after regimens indicate the strength of the recommendations and the quality of evidence supporting it (see Box).

* Only pyrimethamine plus sulfadiazine confers protection against PCP as well as toxoplasmosis. Although the clindamycin plus pyrimethamine regimen is recommended for adults, it has not been tested among children. However, these drugs are safe and are used for other infections.

† Substantial drug interactions might occur between rifabutin and protease inhibitors and nonnucleoside reverse transcriptase inhibitors. A specialist should be consulted.

§ Drugs should be determined by susceptibilities of the organism isolated. Alternatives to TMP-SMZ include ampicillin, chloramphenicol, or ciprofloxacin. However, ciprofloxacin is not approved for use among persons aged <18 years; therefore, it should be used among children with caution and only if no alternatives exist.

¶ Antimicrobial prophylaxis should be chosen on the basis of microorganism and antibiotic sensitivities. TMP-SMZ, if used, should be administered daily. Health-care providers should be cautious regarding using antibiotics solely for this purpose because of the potential for development of drug-resistant microorganisms. IVIG might not provide additional benefit to children receiving daily TMP-SMZ but might be considered for children who have recurrent bacterial infections despite TMP-SMZ prophylaxis. Choice of antibiotic prophylaxis versus IVIG should also involve consideration of adherence, ease of intravenous access, and cost. If IVIG is used, respiratory syncytial virus (RSV) IVIG (750 mg/kg body weight), not monoclonal RSV antibody, can be substituted for IVIG during the RSV season to provide broad anti-infective protection, if this product is available.

TABLE 13. Criteria for starting, discontinuing, and restarting opportunistic infection prophylaxis for adults with human immunodeficiency virus infection

Opportunistic illness	Criteria for initiating primary prophylaxis	Criteria for discontinuing primary prophylaxis	Criteria for restarting primary prophylaxis	Criteria for initiating secondary prophylaxis	Criteria for discontinuing secondary prophylaxis	Criteria for restarting secondary prophylaxis
Pneumocystis carinii pneumonia	$CD4^+$ count of <200 cells/μL or oropharyngeal *Candida* (AI)	$CD4^+$ count of >200 cells/μL for ≥3 months (AI)	$CD4^+$ count of <200 cells/μL (AIII)	Prior *Pneumocystis carinii* pneumonia (AI)	$CD4^+$ count of >200 cells/μL for ≥3 months (BII)	$CD4^+$ count of <200 cells/μL (AIII)
Toxoplasmosis	Immunoglobulin G (IgG) antibody to *Toxoplasma* and $CD4^+$ count of <100 cells/μL (AI)	$CD4^+$ count of >200 cells/μL for ≥3 months (AI)	$CD4^+$ count of <100–200 cells/μL (AIII)	Prior toxoplasmic encephalitis (AI)	$CD4^+$ count of >200 cells/μL sustained (e.g., ≥6 months) and completed initial therapy and asymptomatic for *Toxoplasma* (CIII)	$CD4^+$ count of <200 cells/μL (AIII)
Disseminated *Mycobacterium avium* complex (MAC)	$CD4^+$ count of <50 cells/μL (AI)	$CD4^+$ count of >100 cells/μL for ≥3 months (AI)	$CD4^+$ count of <50–100 cells/μL (AIII)	Documented disseminated disease (AII)	$CD4^+$ count of >100 cells/μL sustained (e.g., ≥6 months) and completed 12 months of MAC therapy and asymptomatic for MAC (CIII)	$CD4^+$ count of <100 cells/μL (AIII)
Cryptococcosis	—	Not applicable	Not applicable	Documented disease (AI)	$CD4^+$ count of >100–200 cells/μL sustained (e.g., ≥6 months) and completed initial therapy and asymptomatic for cryptococcosis (CIII)	$CD4^+$ count of <100–200 cells/μL (AIII)
Histoplasmosis	—	Not applicable	Not applicable	Documented disease (AI)	No criteria recommended for stopping	Not applicable
Coccidioidomycosis	—	Not applicable	Not applicable	Documented disease (AI)	No criteria recommended for stopping	Not applicable
Cytomegalovirus retinitis	—	Not applicable	Not applicable	Documented end-organ disease (AI)	$CD4^+$ count of >100–150 cells/μL sustained (e.g., ≥6 months) and no evidence of active disease; regular ophthalmic examination (BII)	$CD4^+$ count of <100–150 cells/μL (AIII)

Appendix

Recommendations To Help Patients Avoid Exposure to or Infection from Opportunistic Pathogens*

Sexual Exposures

Patients should use a latex condom during every act of sexual intercourse to reduce the risk for acquiring cytomegalovirus, herpes simplex virus, and human papillomavirus, as well as other sexually transmitted pathogens (AII). Condom use also will, theoretically, reduce the risk for acquiring human herpesvirus 8, as well as superinfection with a strain of human immunodeficiency virus (HIV) that has become resistant to antiretroviral drugs (BIII) and will prevent transmission of HIV and other sexually transmitted pathogens to others (AII). Data regarding the use and efficacy of female condoms are incomplete, but these devices should be considered a risk-reduction strategy (BIII).

Patients should avoid sexual practices that might result in oral exposure to feces (e.g., oral-anal contact) to reduce the risk for intestinal infections (e.g., cryptosporidiosis, shigellosis, campylobacteriosis, amebiasis, giardiasis, and hepatitis A) (BIII). Latex condom use alone might not reduce the risk for acquiring these fecal-orally transmitted pathogens, chiefly those that have low infectious doses. Persons wishing to reduce their risk for exposure might consider using dental dams or similar barrier methods for oral-anal and oral-genital contact, changing condoms after anal intercourse, and wearing latex gloves during digital-anal contact. Frequent washing of hands and genitals with warm soapy water during and after activities that might bring these body parts in contact with feces might further reduce risk for illness (CIII).

Hepatitis B vaccination is recommended for all susceptible (antihepatitis B core antigen-negative) HIV-infected patients (BII). Hepatitis A vaccination is recommended for all susceptible men who have sex with men, as well as others with indications for hepatitis A virus vaccine (BIII).

Injection-Drug–Use Exposures

Injection-drug use is a complex behavior that puts HIV-infected persons at risk for hepatitis B virus and hepatitis C virus infection, additional, possibly drug-resistant strains of HIV, and other bloodborne pathogens. Providers should assess the person's readiness to change this practice and encourage efforts to provide education and support directed at recovery. Patients should be counseled to stop using injection drugs (AIII) and to enter and complete substance-abuse treatment, including relapse prevention programs (AIII).

For patients who continue to inject drugs, health-care providers should advise them to (BIII)

- never reuse or share syringes, needles, water, or drug preparation equipment; if, nonetheless, injection equipment that has been used by other persons is shared, they should first clean the equipment with bleach and water (*A-1*);
- use only sterile syringes obtained from a reliable source (e.g., pharmacies or syringe-exchange programs);
- use sterile (e.g., boiled) water to prepare drugs, and if this is not feasible, to use clean water from a reliable source (e.g., fresh tap water); to use a new or disinfected container (i.e., cooker) and a new filter (i.e., cotton) to prepare drugs;
- clean the injection site with a new alcohol swab before injection;
- safely dispose of syringes after one use.

All susceptible injection-drug users should be vaccinated against hepatitis B (BII) and hepatitis A (BIII).

Environmental and Occupational Exposures

Certain activities or types of employment might increase the risk for exposure to tuberculosis (BIII). These include volunteer work or employment in health-care facilities, correctional institutions, and shelters for the homeless, as well as other settings identified as high risk by local health authorities. Decisions regarding whether to continue with such activities should be made in conjunction with the health-care provider and should be based on such factors as the patient's specific duties in the workplace, the prevalence of tuberculosis in the community, and the degree to which precautions designed to prevent the transmission of tuberculosis are taken in the workplace (BIII). These decisions will affect the frequency with which the patient should be screened for tuberculosis.

*Letters and Roman numerals in parentheses indicate the strength of the recommendation and the quality of evidence supporting it (see Box in text).

Child-care providers and parents of children in child care are at increased risk for acquiring cytomegalovirus infection, cryptosporidiosis, and other infections (e.g., hepatitis A and giardiasis) from children. The risk for acquiring infection can be diminished by optimal hygienic practices (e.g., hand-washing) after fecal contact (e.g., during diaper changing) and after contact with urine or saliva (AII). All children in child care facilities also are at increased risk for acquiring these same infections; parents and other caretakers of HIV-infected children should be advised of this risk (BIII).

Occupations involving contact with animals (e.g., veterinary work and employment in pet stores, farms, or slaughterhouses) might pose a risk for cryptosporidiosis, toxoplasmosis, salmonellosis, campylobacteriosis, or *Bartonella* infection. However, available data are insufficient to justify a recommendation against HIV-infected persons working in such settings.

Contact with young farm animals, specifically animals with diarrhea, should be avoided to reduce the risk for cryptosporidiosis (BII). Hand-washing after gardening or other contact with soil might reduce the risk for cryptosporidiosis and toxoplasmosis (BIII). In areas endemic for histoplasmosis, patients should avoid activities known to be associated with increased risk (e.g., creating dust when working with surface soil; cleaning chicken coops that are heavily contaminated with compost droppings; disturbing soil beneath bird-roosting sites; cleaning, remodeling or demolishing old buildings; and cave exploring) (CIII). In areas endemic for coccidioidomycosis, when possible, patients should avoid activities associated with increased risk, including those involving extensive exposure to disturbed native soil (e.g., at building excavation sites or during dust storms) (CIII).

Pet-Related Exposures

Health-care providers should advise HIV-infected persons of the potential risk posed by pet ownership. However, they should be sensitive to the possible psychological benefits of pet ownership and should not routinely advise HIV-infected persons to part with their pets (DIII). Specifically, providers should advise HIV-infected patients of the following precautions (*A-2*):

General

Veterinary care should be sought when a pet develops diarrheal illness. If possible, HIV-infected persons should avoid contact with animals that have diarrhea (BIII). A fecal sample should be obtained from animals with diarrhea and examined for *Cryptosporidium*, *Salmonella*, and *Campylobacter*.

When obtaining a new pet, HIV-infected patients should avoid animals aged <6 months (or <1 year for cats; see the following section) and specifically those with diarrhea (BIII). Because the hygienic and sanitary conditions in pet-breeding facilities, pet stores, and animal shelters are highly variable, the patient should be cautious when obtaining a pet from these sources. Stray animals should be avoided. Animals aged <6 months, and specifically those with diarrhea, should be examined by a veterinarian for *Cryptosporidium*, *Salmonella*, and *Campylobacter* (BIII).

Patients should wash their hands after handling pets, including before eating, and avoid contact with pets' feces to reduce the risk for cryptosporidiosis, salmonellosis, and campylobacteriosis (BIII). Hand-washing for HIV-infected children should be supervised.

Cats

Patients should be aware that cat ownership increases their risk for toxoplasmosis and *Bartonella* infection, as well as enteric infections (CIII). Those who elect to obtain a cat should adopt or purchase an animal that is aged >1 year and in good health to reduce the risk for cryptosporidiosis, *Bartonella* infection, salmonellosis, and campylobacteriosis (BII).

Litter boxes should be cleaned daily, preferably by an HIV-negative, nonpregnant person; if the HIV-infected patient performs this task, his or her hands should be washed thoroughly afterward to reduce the risk for toxoplasmosis (BIII). To further reduce the risk for toxoplasmosis, HIV-infected patients should keep cats indoors, not allow them to hunt, and not feed them raw or undercooked meat (BIII). Although declawing is not usually advised, patients should avoid activities that might result in cat scratches or bites to reduce the risk for *Bartonella* infection (BII). Patients should also wash sites of cat scratches or bites promptly (CIII) and should not allow cats to lick the patients' open cuts or wounds (BIII).

Care of cats should include flea control to reduce the risk for *Bartonella* infection (CIII). Testing cats for toxoplasmosis (EII) or *Bartonella* infection (DII) is not recommended.

Birds

Screening healthy birds for *Cryptococcus neoformans*, *Mycobacterium avium*, or *Histoplasma capsulatum* is not recommended (DIII).

Other

Contact with reptiles (e.g., snakes, lizards, iguanas, and turtles) as well as chicks and ducklings should be avoided to reduce the risk for salmonellosis (BIII). Gloves should be used

during aquarium cleaning to reduce the risk for infection with *Mycobacterium marinum* (BIII). Contact with exotic pets (e.g., nonhuman primates) should be avoided (CIII).

Food and Water-Related Exposures

HIV-infected persons should avoid eating certain foods, including foods that might contain raw eggs (e.g., certain preparations of hollandaise sauce, Caesar and other salad dressings, certain mayonnaises, uncooked cookie and cake batter, and egg nog); raw or undercooked poultry, meat, seafood (raw shellfish in particular); and unpasteurized dairy products; unpasteurized fruit juice; and raw seed sprouts (e.g., alfalfa sprouts or mung bean sprouts). Poultry and meat are safest when adequate cooking is confirmed with a thermometer (internal temperature of 180°F for poultry and 165°F for red meats). If a thermometer is not used, the risk for illness is decreased by consuming poultry and meat that have no trace of pink. However, color change of meat (e.g., absence of pink) does not always correlate with internal temperature. Produce should be washed thoroughly before being eaten (BIII).

Cross-contamination of foods should be avoided. Uncooked meats should not be allowed to come in contact with other foods; hands, cutting boards, counters, and knives and other utensils should be washed thoroughly after contact with uncooked foods (BIII).

Although incidence of listeriosis is low, it is a serious disease that occurs unusually frequently among HIV-infected persons who are severely immunosuppressed. An immunosuppressed, HIV-infected person who wishes to reduce the risk for acquiring listeriosis as much as possible can choose to do the following:

1. avoid soft cheeses (e.g., feta, Brie, Camembert, blue-veined, and Mexican queso fresco cheese). Hard cheeses, processed cheeses, cream cheese, including slices and spreads, cottage cheese, or yogurt need not be avoided;
2. cook leftover foods or ready-to-eat foods (e.g., hot dogs) until steaming hot before eating;
3. avoid foods from delicatessen counters (e.g., prepared salads, meats, cheeses) or heat/reheat these foods until steaming before eating;
4. avoid refrigerated pâtés and other meat spreads, or heat/reheat these foods until steaming if eaten; canned or shelf-stable pâté and meat spreads need not be avoided;
5. avoid raw or unpasteurized milk, including goat's milk, or milk products, or foods that contain unpasteurized milk or milk products (CIII).

Patients should not drink water directly from lakes or rivers because of the risk for cryptosporidiosis and giardiasis (AIII). Waterborne infection might also result from swallowing water during recreational activities. Patients should avoid swimming in water that is probably contaminated with human or animal waste and should avoid swallowing water during swimming (BII).

During outbreaks or in other situations in which a community boil-water advisory is issued, boiling water for ≥1 minutes will eliminate the risk for acquiring cryptosporidiosis (AI). Using submicron, personal-use water filters (home/office types) or drinking bottled water might also reduce the risk (see text) (CIII). Available data are inadequate to support a recommendation that all HIV-infected persons boil or otherwise avoid drinking tap water in nonoutbreak settings. However, persons who wish to take independent action to reduce their risk for waterborne cryptosporidiosis might choose to take precautions similar to those recommended during outbreaks. Such decisions are best made in conjunction with a health-care provider. Persons who opt for a personal-use filter or bottled water should be aware of the complexities involved in selecting the appropriate products, the lack of enforceable standards for destruction or removal of oocysts, product cost, and the difficulty of using these products consistently. Patients taking precautions to avoid acquiring cryptosporidiosis from drinking water should be advised that ice made from contaminated tap water also can be a source of infection (BII). Such persons should be aware that fountain beverages served in restaurants, bars, theaters, and other public places might also pose a risk, because these beverages, as well as the ice they might contain, are made from tap water. Nationally distributed brands of bottled or canned carbonated soft drinks are safe to drink. Commercially packaged noncarbonated soft drinks and fruit juices that do not require refrigeration until after they are opened (i.e., those that can be stored unrefrigerated on grocery shelves) also are safe. Nationally distributed brands of frozen fruit juice concentrate are safe if they are reconstituted by the user with water from a safe source. Fruit juices that must be kept refrigerated from the time they are processed to the time of consumption might be either fresh (i.e., unpasteurized) or heat-treated (i.e., pasteurized); only juices labeled as pasteurized should be considered free of risk from *Cryptosporidium*. Other pasteurized beverages and beers are also considered safe to drink (BII). No data are available concerning survival of *Cryptosporidium* oocysts in wine.

Travel-Related Exposures

Travel, specifically to developing countries, might result in substantial risks for the exposure of HIV-infected persons to opportunistic pathogens, including for patients who are severely immunosuppressed. Consultation with health-care

providers or specialists in travel medicine should help patients plan itineraries (BIII).

During travel to developing countries, HIV-infected persons are at a higher risk for foodborne and waterborne infections than they are in the United States. Foods and beverages, specifically raw fruits and vegetables, raw or undercooked seafood or meat, tap water, ice made with tap water, unpasteurized milk and dairy products, and items purchased from street vendors, might be contaminated (AII). Items that are usually safe include steaming hot foods, fruits that are peeled by the traveler, bottled (including carbonated) beverages, hot coffee or tea, beer, wine, and water brought to a rolling boil for ≥1 minutes (AII). Treating water with iodine or chlorine might not be as effective as boiling but can be used, perhaps in conjunction with filtration, when boiling is not practical (BIII).

Waterborne infections might result from swallowing water during recreational activities. To reduce the risk for cryptosporidiosis and giardiasis, patients should avoid swallowing water during swimming and should not swim in water that might be contaminated (e.g., with sewage or animal waste) (BII).

Antimicrobial prophylaxis for traveler's diarrhea is not recommended routinely for HIV-infected persons traveling to developing countries (DIII). Such preventive therapy can have adverse effects and can promote the emergence of drug-resistant organisms. Nonetheless, studies (none involving an HIV-infected population) have reported that prophylaxis can reduce the risk for diarrhea among travelers (*A-3*). Under selected circumstances (e.g., those in which the risk for infection is high and the period of travel brief), the health-care provider and patient might weigh the potential risks and benefits and decide that antibiotic prophylaxis is warranted (CIII). For those persons to whom prophylaxis is offered, fluoroquinolones (e.g., ciprofloxacin [500 mg daily]) can be considered (CIII), although fluoroquinolones should not be administered to children or pregnant women. Trimethoprim-sulfamethoxazole (TMP-SMZ) (one double-strength tablet daily) also has been demonstrated to be effective, but resistance to this drug has become common in tropical areas. Persons already taking TMP-SMZ as prophylaxis against *Pneumocystis carinii* pneumonia (PCP) might gain protection against traveler's diarrhea. For HIV-infected persons who are not already taking TMP-SMZ, health-care providers should be cautious in prescribing this agent for prophylaxis of diarrhea because of increased rates of adverse reactions and possible need for the agent for other purposes (e.g., PCP prophylaxis) in the future.

All HIV-infected travelers to developing countries should carry a sufficient supply of an antimicrobial agent to be taken empirically if diarrhea occurs (BIII). One appropriate regimen is 500 mg of ciprofloxacin twice daily for 3–7 days. Alternative antibiotics (e.g., TMP-SMZ) should be considered as empirical therapy for use by children and pregnant women (CIII). Travelers should consult a physician if their diarrhea is severe and does not respond to empirical therapy, if their stools contain blood, if fever is accompanied by shaking chills, or if dehydration occurs. Antiperistaltic agents (e.g., diphenoxylate and loperamide) are used for treating diarrhea; however, they should not be used by patients with high fever or with blood in the stool, and their use should be discontinued if symptoms persist >48 hours (AII). Antiperistaltic agents are not recommended for children (DIII).

Travelers should be advised concerning other preventive measures appropriate for anticipated exposures (e.g., chemoprophylaxis for malaria, protection against arthropod vectors, treatment with immune globulin, and vaccination) (AII). They should avoid direct contact of the skin with soil or sand (e.g., by wearing shoes and protective clothing and by using towels on beaches) in areas where fecal contamination of soil is likely (BIII).

Typically, live-virus vaccines should be avoided (EII). One exception is measles vaccine, which is recommended for nonimmune persons. However, measles vaccine is not recommended for persons who are severely immunosuppressed (DIII); immune globulin should be considered for measles-susceptible, severely immunosuppressed persons who are anticipating travel to measles-endemic countries (BIII). Another exception is varicella vaccine, which can be administered to asymptomatic nonimmunosuppressed children (BII). Inactivated (killed) poliovirus vaccine should be used instead of oral (live) poliovirus vaccine, which is contraindicated for HIV-infected persons. Persons at risk for exposure to typhoid fever should be administered an inactivated parenteral typhoid vaccine instead of the live-attenuated oral preparation. Yellow fever vaccine is a live-virus vaccine with uncertain safety and efficacy among HIV-infected persons. Travelers with asymptomatic HIV infection 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 of the risk, instructed in methods for avoiding the bites of vector mosquitoes, and provided with a vaccination waiver letter.

Usually, killed and recombinant vaccines (e.g., diphtheria-tetanus, rabies, hepatitis A, hepatitis B, Japanese encephalitis vaccines) should be used for HIV-infected persons just as they would be used for non-HIV–infected persons anticipating travel (BIII). Preparation for travel should include a review and updating of routine vaccinations, including diphtheria-

tetanus for adults and all routine immunizations for children. The available cholera vaccine is not recommended for persons after a routine tourist itinerary, even if travel includes countries reporting cases of cholera (DII).

Travelers should be informed regarding other area-specific risks and instructed in ways to reduce those risks (BIII). Geographically focal infections that pose an increased risk to HIV-infected persons include visceral leishmaniasis (a protozoan infection transmitted by the sandfly) and different fungal infections (e.g., *Penicillium marneffei* infection, coccidioidomycosis, and histoplasmosis). Certain tropical and developing areas have high rates of tuberculosis.

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List of Abbreviations Used in This Report

AIDS	acquired immunodeficiency syndrome
ASCUS	atypical squamous cells of undetermined significance
ATIS	HIV/AIDS Treatment Information Service
BCG	bacille Calmette-Guérin
CMV	cytomegalovirus
CSF	cerebrospinal fluid
CYP450	cytochrome P450
DNA	deoxyribonucleic acid
EIA	enzyme immunoassays
FDA	Food and Drug Administration
G-CSF	granulocyte-colony-stimulating factor
HAART	highly active antiretroviral therapy
HCV	hepatitis C virus
HHV-8	human herpesvirus 8
Hib	*Haemophilus influenzae* type B
HIV	human immunodeficiency virus
HPV	human papillomavirus
HSIL	high-grade squamous intraepithelial lesions
HSV	herpes simplex virus
IDSA	Infectious Diseases Society of America
IgG	immunoglobulin G
IgM	immunoglobulin M
IVIG	intravenous immune globulin
KS	Kaposi sarcoma
LSIL	low-grade squamous intraepithelial lesion
MAC	*Mycobacterium avium* complex
NNRTI	nonnucleoside reverse transcriptase inhibitor
OI	opportunistic infection
Pap	Papanicolaou
PCP	*Pneumocystis carinii* pneumonia
PCV	pneumococcal conjugate vaccine
PPV	polysaccharide pneumococcal vaccine
PI	protease inhibitor
PPD	purified protein derivative
RIBA	recombinant immunoblot assay
RNA	ribonucleic acid
RSV	respiratory syncytial virus
RT-PCR	reverse transcriptase-polymerase chain reaction
TB	tuberculosis
TST	tuberculin skin test
TE	toxoplasmic encephalitis
TMP-SMZ	trimethoprim-sulfamethoxazole
USPHS	U.S. Public Health Service
VZIG	varicella-zoster immune globulin
VZV	varicella-zoster virus