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Recommendations and Reports

Inside: Continuing Education Examination

1999 USPHS/IDSA Guidelines for the Prevention of Opportunistic Infections in Persons Infected with Human Immunodeficiency Virus

U.S. Public Health Service (USPHS)

and

Infectious Diseases Society of America (IDSA)

U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES
Centers for Disease Control and Prevention (CDC)
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USPHS/IDSA Prevention of Opportunistic Infections Working Group

1999 USPHS/IDSA Guidelines for the Prevention of Opportunistic Infections in Persons Infected with Human Immunodeficiency Virus

U.S. Public Health Service (USPHS)
and
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PREFACE

In 1995, the U.S. Public Health Service (USPHS) and the Infectious Diseases Society of America (IDSA) developed guidelines for preventing opportunistic infections (OIs) in persons infected with human immunodeficiency virus (HIV) (*1–3*). These guidelines, written for health-care providers and patients, were revised in 1997 and published in the *MMWR* (*4*), *Clinical Infectious Diseases* (*5*), the *Annals of Internal Medicine* (*6*), the *American Family Physician* (*7*), and *Pediatrics* (*8*); an accompanying editorial appeared in *JAMA* (*9*). Response to these guidelines (e.g., the many requests for reprints and observations from health-care providers) suggests they have served as a valuable reference for HIV care providers. Because the 1995 and 1997 guidelines included ratings indicating the strength of each recommendation and the quality of supporting evidence, readers were able to assess the relative importance of each recommendation.

Since AIDS was first recognized nearly 20 years ago, remarkable progress has been made in improving the quality and duration of life of HIV-infected persons. During the first decade of the epidemic, this improvement occurred because of better recognition of opportunistic disease processes, better therapy for acute and chronic complications, and the introduction of chemoprophylaxis against *Pneumocystis carinii* pneumonia (PCP), toxoplasmosis, *Mycobacterium avium* complex disease, and bacterial infections. Trimethoprim-sulfamethoxazole was shown to reduce not only the incidence of PCP but also of toxoplasmosis and bacterial infections.

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 individual OIs. HAART has reduced the incidence of OIs and extended life substantially (*10*). HAART is the most effective approach to preventing OIs and should be considered for all HIV-infected persons who qualify for such therapy. However, some patients are not ready or able to take HAART, and others have tried HAART regimens, but therapy has failed. Such patients will benefit from prophylaxis against OIs. In addition, prophylaxis against specific OIs continues to provide survival benefits even among persons who are receiving HAART (*11*).

Because important new data concerning the prevention of opportunistic diseases have emerged since 1997, the USPHS and the IDSA reconvened the Prevention of Opportunistic Infections Working Group on March 4 and 5, 1999, to determine which recommendations warranted revision. Participants included representatives from federal agencies, universities, and professional societies, as well as community

health-care providers and patient advocates. Much attention was focused on recent data related to the advisability of discontinuing OI prophylaxis (primary prophylaxis and prophylaxis against recurrence) among persons whose CD4+ T-lymphocyte counts have increased to above prophylaxis thresholds because of HAART. The OI Working Group also addressed two pathogens not previously considered — human herpesvirus type 8 and hepatitis C virus. In addition, working group members reviewed data concerning the prevention of all common HIV-associated OIs. In revising these current guidelines, as in earlier editions of the guidelines, the group considered factors such as incidence of disease; severity of disease in terms of morbidity and mortality; level of immunosuppression at which disease is most likely to occur; feasibility, efficacy, and cost of preventive measures; impact of intervention on quality of life; and drug toxicities, drug interactions, and the potential for drug resistance to develop.

During the development of these revised guidelines, working group members reviewed published manuscripts as well as abstracts and material presented at professional meetings if complete manuscripts providing data were available for review. A review of the data that served as the basis for the revisions and additional information discussed at the meeting but not deemed sufficient to justify a revision of the recommendations will be published separately in *Clinical Infectious Diseases*.

Primary Changes in the Recommendations

Primary changes in the disease-specific recommendations that follow include

- The addition of statements concerning discontinuation of prophylaxis against specific OIs when the CD4+ T-lymphocyte count increases in response to HAART.
- New recommendations regarding human herpesvirus type 8 and hepatitis C virus.
- New recommendations concerning injection drug users.
- New recommendations about short-course chemoprophylaxis against tuberculosis in HIV-infected persons with positive tuberculin skin tests.
- Changes in secondary prophylaxis (chronic maintenance therapy) recommended to prevent the recurrence of *Mycobacterium avium* complex and cytomegalovirus disease.
- Caution against using fluconazole during pregnancy.
- Statements concerning the use of varicella and rotavirus vaccines among HIV-infected infants.

These guidelines developed by the OI Working Group were made available for public comment through announcements in the *Federal Register* and the *MMWR*. The final document is endorsed by the USPHS and IDSA as well as by the Infectious Diseases Society of Obstetrics and Gynecology and the National Foundation for Infectious Diseases.

How to Use the Information in This Report

For each of the 19 diseases covered in this report, specific recommendations are provided that address a) prevention of exposure to the opportunistic pathogen, b) prevention of the first episode of disease, and c) prevention of disease recurrence. Recommendations are rated by a revised version of the IDSA rating system (see Box) (*12*). In this system, the letters A through E signify the strength of the recommendation for or against a preventive modality, and Roman numerals I through III indicate the quality of evidence supporting the recommendation.

Because of their length and complexity, the tables in this report are grouped together, following the references. The tables appear in the following order: dosages for prophylaxis to prevent first episode of opportunistic disease in HIV-infected adults

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

Rating	Strength of the 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 generally 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. **Optional.**
D	Moderate evidence for lack of efficacy or for adverse outcome supports a recommendation against use. **Should generally not be offered.**
E	Good evidence for lack of efficacy or for adverse outcome supports a recommendation against use. **Should never be offered.**
	Quality of evidence supporting the recommendation
I	Evidence from at least one properly randomized, controlled trial.
II	Evidence from at least one well-designed clinical trial 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 expert committees.

*Modified from Gross PA, Barrett TL, Dellinger EP, et al., 1994 (*12*).

and adolescents (Table 1); dosages for prophylaxis to prevent recurrence of opportunistic disease in HIV-infected adults and adolescents (Table 2); effects of food on drugs used to treat OIs (Table 3); effects of medications on drugs used to treat OIs (Table 4); effects of OI medications on drugs commonly administered to HIV-infected persons (Table 5); adverse effects of drugs used to manage HIV infection (Table 6); dosages of drugs for prevention of OIs for persons with renal insufficiency (Table 7); costs of agents recommended for the prevention of OIs in adults with HIV infection (Table 8); immunologic categories for HIV-infected children (Table 9); immunization schedule for HIV-infected children (Table 10); dosages for prophylaxis to prevent first episode of opportunistic disease in HIV-infected infants and children (Table 11); dosages for prophylaxis to prevent recurrence of opportunistic disease in HIV-infected infants and children (Table 12); and criteria for discontinuing and restarting OI prophylaxis for adult patients with HIV infection (Table 13). Recommendations advising patients how to prevent exposure to opportunistic pathogens appear in the appendix at the end of this report.

This report is oriented toward the prevention of specific opportunistic infections in HIV-infected persons in the United States and other industrialized countries. Recommendations for use of antiretroviral therapy, which is designed to prevent immunologic deterioration and delay the need for many of the chemoprophylactic strategies described in this report, are published elsewhere (*10*) as are integrated approaches to the care of HIV-infected persons (*13*).

Single copies of this report can be obtained from the AIDS Treatment Information Service (ATIS) by calling (800) 448-0440, (301) 217-0023 (international), or (800) 243-7012 (TTY), and the report can be downloaded from the ATIS website at <www.hivatis.org>. In addition, pamphlets for patients are available from ATIS and also can be accessed on CDC's Division of HIV/AIDS Prevention homepage at <www.cdc.gov/hiv>.

New data on prevention of OIs in HIV-infected persons are emerging, and randomized controlled trials addressing some unresolved issues in OI prophylaxis are ongoing. The OI Working Group has therefore developed a mechanism for routinely and periodically reviewing emerging data and for updating these guidelines on a regular basis. The most recent information will be available from the ATIS website at <www.hivatis.org>.

DISEASE-SPECIFIC RECOMMENDATIONS

Pneumocystis carinii Pneumonia

Prevention of Exposure

1. Although some authorities recommend that persons with human immunodeficiency virus (HIV) infection who are at risk for *P. carinii* pneumonia (PCP) not share a hospital room with a patient who has PCP, data are insufficient to support this recommendation as standard practice (CIII).

Prevention of Disease

Initiation of Primary Prophylaxis

2. Adults and adolescents who have HIV infection (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) (*14*). Persons who have a CD4+ T-lymphocyte percentage of <14% or history of an acquired immunodeficiency syndrome (AIDS)-defining illness but do not otherwise qualify should be considered for prophylaxis (BII) (*15,16*). When monitoring the CD4+ T-lymphocyte count at least every 3 months is not possible, initiation of chemoprophylaxis at a CD4+ T-lymphocyte count of >200 but <250 cells/μL also should be considered (BII) (*15*).

3. Trimethoprim-sulfamethoxazole (TMP-SMZ) is the recommended prophylactic agent (AI) (*16–18*). One double-strength tablet per day is the preferred regimen (AI) (*17*). However, one single-strength tablet per day (*19*) is also effective and might be better tolerated (AI). One double-strength tablet three times per week is also effective (BI) (*20*). TMP-SMZ at a dose of one double-strength tablet per day confers cross-protection against toxoplasmosis (*21*) and some common respiratory bacterial infections (*17,22*). 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, reinstitution of TMP-SMZ should be strongly considered after the adverse event has resolved (AII). Patients who have experienced adverse events, especially fever and rash, might better tolerate reintroduction of the drug with a gradual increase in dose (desensitization) as per published regimens (BI) (*23,24*) or reintroduction of TMP-SMZ at a reduced dose or frequency (CIII); up to 70% of patients can tolerate such reinstitution of therapy (*22*).

4. If TMP-SMZ cannot be tolerated, prophylactic regimens that can be recommended as alternatives include dapsone (BI) (*17*), dapsone plus pyrimethamine plus leucovorin (BI) (*25,26*), aerosolized pentamidine administered by the Respirgard II™ nebulizer (Marquest, Englewood, Colorado) (BI) (*18*), and atovaquone (BI) (*27,28*). Atovaquone appears to be as effective as aerosolized pentamidine (*28*) or dapsone (BI) (*27*) 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) (*25,26*) or atovaquone with or without pyrimethamine (CIII). The following regimens generally cannot be recommended as alternatives because data regarding their efficacy for PCP prophylaxis are insufficient for a firm recommendation: aerosolized pentamidine administered by other nebulization devices, intermittently administered parenteral pentamidine, oral pyrimethamine plus sulfadoxine, oral clindamycin plus primaquine, and intravenous trimetrexate. However, clinicians may consider using these agents in unusual situations in which the recommended agents cannot be administered (CIII).

Discontinuation of Primary Prophylaxis

5. Initial reports from three prospective observational studies (*29–31*), one retrospective review (*32*), and one randomized trial (*33*) suggest that PCP prophylaxis can

be safely discontinued in patients responding to HAART with a sustained increase in CD4+ T-lymphocyte counts from <200 cells/μL to >200 cells/μL. Such reports have mostly included patients receiving primary prophylaxis (no prior episode of PCP) and protease inhibitor-containing regimens. In these studies, median follow-up ranged from 6 to 12 months and the median CD4+ T-lymphocyte count at the time prophylaxis was discontinued was >300 cell/μL. At the time PCP prophylaxis was discontinued, many patients had sustained suppression of HIV plasma RNA levels below detection limits of the available assays. Although optimal criteria for discontinuing PCP prophylaxis are still being assessed, providers may wish to discontinue prophylaxis when patients have sustained a CD4+ T-lymphocyte count of >200 cells/μL for at least 3–6 months (CII). Additional criteria might include sustained reduction in viral load for at least 3–6 months (CIII).

Restarting Primary Prophylaxis

6. No data are available to guide recommendations for reinstituting primary prophylaxis. Pending the availability of such data, a reasonable approach would be to use the criteria for initiating prophylaxis described on page 5 (CIII).

Prevention of Recurrence

7. Adults and adolescents who have a history of PCP should be administered chemoprophylaxis (i.e., secondary prophylaxis or chronic maintenance therapy) with the regimens described on page 5 in order to prevent recurrence (AI) (*16*).

Discontinuation of Secondary Prophylaxis (Chronic Maintenance Therapy)

8. Although patients receiving secondary prophylaxis (prior episode of PCP) might also be at low risk for PCP when their CD4+ T-lymphocyte counts increase to >200 cells/μL, inadequate numbers of patients have been evaluated to warrant a recommendation to discontinue prophylaxis in such patients.

Special Considerations

Children

9. Children born to HIV-infected mothers should be administered prophylaxis with TMP-SMZ beginning at 4–6 weeks of age (*34*) (AII). Prophylaxis should be discontinued for children who are subsequently found 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. The 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 in HIV-infected children receiving HAART has not been studied.

10. Children who have a history of PCP should be administered lifelong chemoprophylaxis to prevent recurrence (AI) (*34*).

Pregnant Women

11. 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, providers may choose to withhold prophylaxis during the first trimester. In such cases, aerosolized pentamidine may 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

Prevention of Exposure

1. 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 *Toxoplasma gondii* (BIII).

2. All HIV-infected persons, but particularly those who lack IgG antibody to *Toxoplasma*, should be counseled about the various sources of toxoplasmic infection. They should be advised not to eat raw or undercooked meat, particularly undercooked pork, lamb, or venison (BIII). Specifically, meat should be cooked to an internal temperature of 150 F (65.5 C); meat cooked until it is no longer pink inside generally has an internal temperature of 165 F (73.8 C) and therefore 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, the patient should wash the 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).

Prevention of Disease

Initiation of Primary Prophylaxis

3. *Toxoplasma*-seropositive patients who have a CD4+ T-lymphocyte count of <100/μL should be administered prophylaxis against toxoplasmic encephalitis (TE) (AII) (*21*). The double-strength tablet daily dose of TMP-SMZ recommended as the preferred regimen for PCP prophylaxis appears to be effective against TE as well and is therefore recommended (AII) (*21*). If patients cannot tolerate TMP-SMZ, the recommended alternative is dapsone-pyrimethamine, which is also effective against PCP (BI) (*25,26*). Atovaquone with or without pyrimethamine also may be considered (CIII). Prophylactic monotherapy with dapsone, pyrimethamine, azithromycin, or clarithromycin cannot be recommended on the basis of current data (DII). Aerosolized pentamidine does not protect against TE and is not recommended (EI) (*17,21*).

4. *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 count declines below 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 above (AII).

Discontinuation of Primary Prophylaxis

5. Limited data suggest that discontinuing prophylaxis for patients whose CD4+ T-lymphocyte counts increase to >100 cells/μL in response to HAART is associated with a low risk for TE. However, the numbers of patients who have been evaluated are insufficient to recommend routine discontinuation of prophylaxis in such patients. Persons whose CD4+ T-lymphocyte count remains <200 cells/μL or who have a history of PCP or oropharyngeal candidiasis still require prophylaxis against PCP, as noted previously.

Prevention of Recurrence

6. Patients who have had TE should be administered lifelong suppressive therapy (secondary prophylaxis or chronic maintenance therapy) with drugs active against *Toxoplasma* to prevent relapse (AI) (*35,36*). The combination of pyrimethamine plus sulfadiazine and leucovorin is highly effective for this purpose (AI) (*35,36*). A commonly used regimen for patients who cannot tolerate sulfa drugs is pyrimethamine plus clindamycin (BI); however, only the combination of pyrimethamine plus sulfadiazine appears to provide protection against PCP as well (AII).

Discontinuation of Secondary Prophylaxis (Chronic Maintenance Therapy)

7. The numbers of patients who have stopped maintenance therapy after responding to HAART are insufficient to warrant recommending discontinuation of maintenance therapy.

Special Considerations

Children

8. 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 found to be seropositive for *Toxoplasma* should be administered prophylaxis for both PCP and toxoplasmosis (i.e., dapsone plus pyrimethamine) (BIII).

Pregnant Women

9. 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, the health-care provider and clinician should be well informed about the benefit of lifelong therapy and the concerns about teratogenicity of pyrimethamine. Most clinicians favor lifelong therapy for the mother, given the high likelihood that disease will recur promptly if therapy is stopped (AIII).

10. 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

Prevention of Exposure

1. HIV-infected persons should be educated and counseled about the many 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.

2. 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).

3. HIV-infected persons should be advised that newborn and very young pets might pose a small risk for transmitting cryptosporidial infection, but they should not be advised to destroy or give away healthy pets. Persons contemplating the acquisition of 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 small 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).

4. HIV-infected persons should avoid exposure to calves and lambs and to premises where these animals are raised (BII).

5. HIV-infected persons should not drink water directly from lakes or rivers (AIII).

6. Waterborne infection also might result from swallowing water during recreational activities. HIV-infected persons should be aware that many lakes, rivers, and salt-water beaches and some 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).

7. Several outbreaks of cryptosporidiosis have been linked to municipal water supplies. During outbreaks or in other situations in which a community "boil-water" advisory is issued, boiling water for 1 minute will eliminate the risk for cryptosporidiosis (AI). Use of submicron personal-use water filters* (home/office types)

*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 many filters in this category might not be capable of removing 99% of oocysts.

and/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 current 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 may 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 products, the lack of enforceable standards for the destruction or removal of oocysts, the cost of the products, and the logistic difficulty of using these products consistently.

8. 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 (unpasteurized) or heat-treated (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.

9. HIV-infected persons should avoid eating raw oysters because cryptosporidial oocysts can survive in oysters for more than 2 months and have been found in oysters taken from some commercial oyster beds (BIII). *Cryptosporidium*-infected patients should not work as food handlers, especially if the food to be handled is intended to be eaten without cooking (BII). Because most 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.

10. 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, some experts recommend that HIV-infected persons, especially those who are severely immunocompromised, should not share a room with a patient with cryptosporidiosis (CIII).

[†]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 free of cryptosporidial oocysts. 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 nearly the same level of protection. Use of nominal 1-μm filters by bottlers as the only barrier to *Cryptosporidia* might not result in the removal of 99% of oocysts.

Prevention of Disease

11. No agents have been proven to be effective as chemoprophylaxis against cryptosporidiosis. Rifabutin or clarithromycin, when taken for *Mycobacterium avium* complex prophylaxis, were associated with a reduced risk for cryptosporidiosis in one study (*37*), but data are insufficient to warrant a recommendation for using these drugs.

Prevention of Recurrence

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

Special Considerations

Children

13. At present, no data indicate that formula-preparation practices for infants should be altered in an effort to prevent cryptosporidiosis (CIII). However, in the event of a "boil-water" advisory, similar precautions for the preparation of infant formula should be taken as for drinking water for adults (AII).

Microsporidiosis

Prevention of Exposure

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

Prevention of Disease

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

Prevention of Recurrence

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

Tuberculosis

Prevention of Exposure

1. HIV-infected persons should be advised that certain activities and occupations might increase the likelihood of exposure to tuberculosis (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 about whether to continue with activities in these settings should be made in conjunction with the health-care provider and should be based on factors such as the patient's specific duties in the workplace, the prevalence of tuberculosis in the community, and the degree to which precautions are taken to prevent the transmission of tuberculosis in the workplace (BIII). Whether the patient

continues with such activities might affect the frequency with which screening for tuberculosis needs to be conducted.

Prevention of Disease

2. 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, there are selected situations in which anergy evaluation might assist in guiding individual decisions about preventive therapy (*38*).

3. 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 tuberculosis. HIV-infected persons who have symptoms suggestive of tuberculosis should promptly undergo chest radiography and clinical evaluation regardless of their TST status (AII).

4. All HIV-infected persons, regardless of age, who have a positive TST result yet have no evidence of active tuberculosis and no history of treatment or prophylaxis for tuberculosis should be administered preventive chemotherapy. Options include isoniazid daily (AII) or twice weekly (BI) for 9 months or 2 months of therapy with either rifampin and pyrazinamide (AI) or rifabutin and pyrazinamide (BIII) (*38*). Because HIV-infected persons are at risk for peripheral neuropathy, those receiving isoniazid should also receive pyridoxine (BIII). A decision to use a regimen containing either rifampin or rifabutin should be made after careful consideration of potential drug interactions, especially those related to protease inhibitors and nonnucleoside reverse transcriptase inhibitors (see Special Considerations/Drug Interactions, page 13). Directly observed therapy should be used with intermittent dosing regimens (AI) and when otherwise operationally feasible (BIII) (*38*).

5. HIV-infected persons who are close contacts of persons who have infectious tuberculosis should be administered preventive therapy — regardless of their TST results, age, or prior courses of chemoprophylaxis — after the diagnosis of active tuberculosis has been excluded (AII) (*38*). 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.

6. For persons exposed to isoniazid- and/or rifampin-resistant TB, the decision to use chemoprophylactic antimycobacterial agents other than isoniazid 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).

7. TST-negative, HIV-infected persons from risk groups or geographic areas with a high prevalence of *Mycobacterium tuberculosis* infection might be at increased risk for primary or reactivation tuberculosis. However, the efficacy of preventive therapy in this group has not been demonstrated. Decisions concerning the use of chemoprophylaxis in these situations must be considered individually.

8. Although the reliability of the 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 there is a substantial risk for exposure to *M. tuberculosis* (BIII). Clinicians also may consider repeating TSTs for persons whose immune function has improved because

of HAART (i.e., those whose CD4+ T-lymphocyte count has increased to >200 cells/μL) (CIII). In addition to confirming tuberculous 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.

9. The administration of bacille Calmette-Guérin (BCG) vaccine to HIV-infected persons is contraindicated because of its potential to cause disseminated disease (EII).

Prevention of Recurrence

10. Chronic suppressive therapy for a patient who has successfully completed a recommended regimen of treatment for tuberculosis is not necessary (DII).

Special Considerations

Drug Interactions

11. Rifampin should not be administered with protease inhibitors or nonnucleoside reverse transcriptase inhibitors (EI) (*38*). Rifabutin is an acceptable alternative but should not be used with the protease inhibitor hard-gel saquinavir; caution is also advised if the drug is coadministered with soft-gel saquinavir, but data are lacking. Rifabutin can be administered at one half the usual daily dose (i.e., reduce from 300 mg to 150 mg per 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. Similarly, rifabutin should not be used with the nonnucleoside reverse transcriptase inhibitor delavirdine. Pharmacokinetic data suggest that rifabutin at an increased dose can be administered with efavirenz; a dose of 450 mg per day has been suggested (*38*). Information is lacking regarding coadministration of rifabutin with nevirapine.

Children

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

Pregnant Women

13. Chemoprophylaxis for tuberculosis is recommended during pregnancy for HIV-infected patients who have either a positive TST or a history of exposure to active tuberculosis, after active tuberculosis has been excluded (AIII). A chest radiograph should be obtained before treatment and appropriate abdominal/pelvic lead apron shields should be used to minimize radiation exposure to the embryo/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, providers may 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 experience with rifampin has not been associated with adverse pregnancy outcomes. Pyrazinamide should generally be avoided, particularly in the first trimester because of lack of information concerning fetal effects.

Disseminated Infection with *Mycobacterium avium* Complex

Prevention of Exposure

1. Organisms of the *M. avium* complex (MAC) are common in environmental sources such as food and water. Current information does not support specific recommendations regarding avoidance of exposure.

Prevention of Disease

Initiation of Primary Prophylaxis

2. 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) (*4*). Clarithromycin (*39,40*) or azithromycin (*41*) 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) (*39*). 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) (*41*). 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 (BI) (*39,41,42*). Tolerance, cost, and drug interactions are among the issues that should be considered in decisions regarding the choice of prophylactic agents for MAC disease. Particular attention to interactions with antiretroviral protease inhibitors and nonnucleoside reverse transcriptase inhibitors is warranted (see Special Considerations/Drug Interactions, page 15). 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 the development of resistance to rifampin in persons who have active tuberculosis, active tuberculosis should also be excluded before rifabutin is used for prophylaxis.

3. Although the detection of MAC organisms in the respiratory or gastrointestinal tract might predict the development of disseminated MAC infection, no data are available on the efficacy of prophylaxis with clarithromycin, azithromycin, rifabutin, or other drugs in 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).

Discontinuation of Primary Prophylaxis

4. Information from observational studies suggested a low rate of disseminated infection with MAC among persons who responded to HAART with an increase in

CD4+ T-lymphocyte count from <50 cells/μL to >100 cells/μL (*32,43*). Although the optimal criteria for discontinuing MAC prophylaxis remain to be defined, a reasonable option would be to consider discontinuing prophylaxis in patients with a CD4+ T-lymphocyte count of >100 cells/μL for a sustained period (e.g., >3–6 months) and sustained suppression of HIV plasma RNA for a similar period (CII).

Restarting Primary Prophylaxis

5. No data are available on which to base recommendations for reinstituting prophylaxis. Pending the availability of such data, a reasonable approach would be to use the criteria for initiating prophylaxis described on page 14 (CIII).

Prevention of Recurrence

6. Patients who have been treated for disseminated MAC disease should continue to receive full therapeutic doses of antimycobacterial agents for life (i.e., secondary prophylaxis or chronic maintenance therapy) (AII) (*42*). Unless good clinical or laboratory evidence of macrolide resistance exists, the use of a macrolide (clarithromycin or, alternatively, azithromycin) is recommended in combination with ethambutol (AII) with or without rifabutin (CI) (*44,45*). Treatment of MAC disease with clarithromycin in a dose of 1,000 mg twice a day is associated with a higher mortality rate than has been observed with clarithromycin administered at 500 mg twice a day; thus, the higher dose should not be used (EI) (*46,47*). Clofazimine has been associated with an adverse clinical outcome in the treatment of MAC disease and should not be used (DII) (*47,48*).

Discontinuation of Secondary Prophylaxis (Chronic Maintenance Therapy)

7. Although patients receiving chronic maintenance therapy for MAC might be at low risk for recurrence of MAC when their CD4+ T-lymphocyte counts increase to >100 cells/μL following 6–12 months of HAART, the numbers of patients who have been evaluated are insufficient to warrant a recommendation to discontinue maintenance therapy in such patients.

Special Considerations

Drug Interactions

8. Rifabutin should not be administered with certain protease inhibitors or nonnucleoside reverse transcriptase inhibitors (see Special Considerations/Drug Interactions in Tuberculosis section, page 13). Although protease inhibitors might also increase clarithromycin levels, no recommendation to adjust the dose of either clarithromycin or protease inhibitors can be made on the basis of existing data.

Children

9. HIV-infected children aged <13 years who have advanced immunosuppression also can develop disseminated MAC infections, and prophylaxis should be offered to high-risk children 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. The safety of discontinuing MAC prophylaxis in children whose CD4+ T-lymphocyte counts have increased in response to HAART has not been studied.

Pregnant Women

10. Chemoprophylaxis for MAC disease should be administered to pregnant women as is done for other adults and adolescents (AIII). However, because of general concerns about administering drugs during the first trimester of pregnancy, some providers may choose to withhold prophylaxis during the first trimester. Animal studies and anecdotal evidence of safety in humans suggest that of the available agents, azithromycin is the drug of choice (BIII) (*49*). Experience with rifabutin is limited. Clarithromycin has been demonstrated to be a teratogen in animals and should be used with caution during pregnancy (*50*). For secondary prophylaxis (chronic maintenance therapy), azithromycin plus ethambutol are the preferred drugs (BIII).

Bacterial Respiratory Infections

Prevention of Exposure

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

Prevention of Disease

2. As soon as feasible after HIV infection is diagnosed, 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 if they have not had this vaccine during the previous 5 years (BII) (*51,52*). For persons who have a CD4+ T-lymphocyte count of <200 cells/μL, vaccination can be offered, although the humoral response and clinical efficacy are likely to be diminished (CIII). The recommendation to vaccinate is increasingly pertinent because of the increasing incidence of invasive infections with drug-resistant (including TMP-SMZ-, macrolide-, penicillin-, and beta-lactam–resistant) strains of *S. pneumoniae*. Limited data suggest that administration of certain bacterial vaccines might transiently increase HIV replication and plasma HIV-1 RNA levels in a minority of HIV-infected persons. However, there is no evidence that adverse clinical outcomes are associated with this transient increase. Most experts believe that the benefit of pneumococcal vaccination outweighs the potential risk.

3. The duration of the protective effect of primary pneumococcal vaccination is unknown. Periodic revaccination may 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 (*53*). In addition, revaccination one time should also be considered if the initial vaccination was given when the CD4+ T-lymphocyte count was <200 cells/μL and if the CD4+ T-lymphocyte count has increased to >200 cells/μL as a result of HAART (CIII).

4. The incidence of *H. influenzae* type B infection in adults is low. Therefore, *H. influenzae* type B vaccine is not generally recommended for adult use (DIII).

5. TMP-SMZ, when administered daily for PCP prophylaxis, reduces the frequency of bacterial respiratory infections; this should be considered in the selection of an agent for PCP prophylaxis (AII). However, indiscriminate use of this drug (when not indicated for PCP prophylaxis or other specific reasons) might promote the 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 the selection of an agent for prophylaxis against MAC disease (BII). However, these drugs should not be prescribed solely for preventing bacterial respiratory infection (DIII).

6. 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, providers may consider taking steps to reverse neutropenia, either by stopping myelosuppressive drugs (CII) or by administering granulocyte-colony–stimulating factor (G-CSF) (CII).

Prevention of Recurrence

7. Some clinicians may administer antibiotic chemoprophylaxis to HIV-infected patients who have very 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, providers should be cautious about 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

8. Children who have HIV infection should be administered *H. influenzae* type b vaccine in accordance with the guidelines of the Advisory Committee on Immunization Practices (*54*) and the American Academy of Pediatrics (*55*) (AII). Children aged >2 years also should be administered 23-valent polysaccharide pneumococcal vaccine (BII). Revaccination with pneumococcal vaccine generally should be offered after 3–5 years to children aged <10 years and after 5 years to children aged ≥10 years (BIII).

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

10. To prevent recurrence of serious bacterial respiratory infections, antibiotic chemoprophylaxis may be considered (BI). However, providers should be cautious about using antibiotics solely for this purpose because of the potential development of drug-resistant microorganisms and drug toxicity. The administration of 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 may be considered

for children who have recurrent serious bacterial infections despite receiving TMP-SMZ or other antimicrobials (CIII).

Pregnant Women

11. Pneumococcal vaccination is recommended during pregnancy for HIV-infected patients who have not been vaccinated during the previous 5 years (BIII). Among non-pregnant 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 may be deferred until after antiretroviral therapy has been initiated to prevent perinatal HIV transmission (CIII).

Bacterial Enteric Infections

Prevention of Exposure

Food

1. Health-care providers should advise HIV-infected persons not to eat raw or undercooked eggs (including foods that might contain raw eggs [e.g., some preparations of hollandaise sauce, Caesar and other salad dressings, and mayonnaise]); raw or undercooked poultry, meat, or seafood; or unpasteurized dairy products. Poultry and meat should be well cooked and should not be pink in the middle (internal temperature >165 F [73.8 C]). Produce should be washed thoroughly before being eaten (BIII).

2. Health-care providers should advise HIV-infected persons to avoid cross-contamination of foods. Uncooked meats 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).

3. 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 HIV-infected persons who are severely immunosuppressed. Such persons may choose to avoid soft cheeses because some studies have shown an association between these foods and listeriosis. These studies also have documented an association between ready-to-eat foods (e.g., hot dogs and cold cuts from delicatessen counters) and listeriosis. An immunosuppressed, HIV-infected person who wishes to reduce the risk for foodborne disease as much as possible may choose to reheat such foods until they are steaming hot before eating them (CIII).

Pets

4. When obtaining a new pet, HIV-infected persons should avoid animals aged <6 months, especially those that have diarrhea (BIII).

5. HIV-infected persons should avoid contact with 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*.

6. HIV-infected persons should wash their hands after handling pets (especially before eating) and should avoid contact with pets' feces (BIII).

7. HIV-infected persons should avoid contact with reptiles (e.g., snakes, lizards, iguanas, and turtles) because of the risk for salmonellosis (BIII).

Travel

8. The risk for foodborne and waterborne infections among immunosuppressed, HIV-infected persons is magnified during travel to developing countries. Persons who travel to such countries should avoid foods and beverages that might be contaminated, particularly 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 generally safe include steaming-hot foods, fruits that are peeled by the traveler, bottled (especially 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).

Prevention of Disease

9. Prophylactic antimicrobial agents are not generally 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 can promote the emergence of resistant organisms. However, for HIV-infected travelers, antimicrobial prophylaxis may be considered, depending on the level of immunosuppression and the region and duration of travel (CIII). The use of fluoroquinolones such as ciprofloxacin (500 mg per day) can be considered when prophylaxis is deemed necessary (BIII). As an alternative (e.g., for children, pregnant women, and persons already taking TMP-SMZ for PCP prophylaxis), TMP-SMZ might offer some protection against traveler's diarrhea (BIII). The risk of toxicity should be considered before treatment with TMP-SMZ is initiated solely because of travel.

10. Antimicrobial agents such as fluoroquinolones should be given to patients before their departure, to be taken empirically (e.g., 500 mg of ciprofloxacin twice a day for 3–7 days) should traveler's diarrhea develop (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 develops. Antiperistaltic agents (e.g., diphenoxylate and loperamide) can be used to treat mild diarrhea. However, the use of these drugs should be discontinued if symptoms persist beyond 48 hours. Moreover, these agents should not be administered to patients who have a high fever or who have blood in the stool (AII).

11. Some experts 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 some studies of immunocompetent persons have suggested that antimicrobial therapy can lengthen the shedding period. The fluoroquinolones — primarily ciprofloxacin (750 mg twice a day for 14 days) — can be used when antimicrobial therapy is chosen (CIII).

Prevention of Recurrence

12. 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).

13. 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 and/or antimicrobial therapy can be instituted and recurrent transmission to the HIV-infected person can be prevented (CIII).

Special Considerations

Children

14. Like HIV-infected adults, HIV-infected children should wash their hands after handling pets (especially before eating) and should avoid contact with pets' feces. Hand washing should be supervised (BIII).

15. 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.

16. 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.

17. Antiperistaltic drugs are not recommended for children (DIII).

Pregnant Women

18. Because both pregnancy and HIV infection confer a risk for listeriosis, pregnant HIV-infected women should heed recommendations regarding listeriosis (BII).

19. 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 be avoided.

20. Fluoroquinolones should not be used during pregnancy. TMP-SMZ might offer some protection against traveler's diarrhea.

Infection with *Bartonella* (Formerly *Rochalimaea*)

Prevention of Exposure

1. HIV-infected persons, particularly those who are severely immunosuppressed, are at unusually high risk for developing relatively severe disease due to 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 that is in good health (BII).

2. Although declawing is not generally 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).

3. Care of cats should include flea control (CIII).

4. No evidence indicates any benefits to cats or their owners from routine culture or serologic testing of the pet for *Bartonella* infection (DII).

Prevention of Disease

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

Prevention of Recurrence

6. 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

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

Pregnant Women

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

Candidiasis

Prevention of Exposure

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

Prevention of Disease

2. Data from prospective controlled trials indicate that fluconazole can reduce the risk for mucosal (oropharyngeal, esophageal, and vaginal) candidiasis and cryptococcosis as well in patients with advanced HIV disease (*56–58*). 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).

Prevention of Recurrence

3. Many experts 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,

providers may consider administering an oral azole (fluconazole [CI] [*56*] or itraconazole solution [CI]). Other factors that influence choices about such therapy include the impact of the recurrences on the patient's well-being and quality of life, the need for prophylaxis for other fungal infections, cost, toxicities, drug interactions, and the potential to induce drug resistance among *Candida* and other fungi. Prolonged use of systemically absorbed azoles, particularly in patients with low CD4+ T-lymphocyte counts (i.e., <100 cells/μL), increases the risk for the development of azole resistance.

4. Adults or adolescents who have a history of documented esophageal candidiasis, particularly multiple episodes, should be considered candidates for chronic suppressive therapy. Fluconazole at a dose of 100–200 mg daily is appropriate (BI). However, the potential development of azole resistance should be taken into account when long-term azoles are considered.

Special Considerations

Children

5. Primary prophylaxis of candidiasis in HIV-infected infants is not indicated (DIII).

6. Suppressive therapy with systemic azoles should be considered for infants who have severe recurrent mucocutaneous candidiasis (CIII) and particularly for those who have esophageal candidiasis (BIII).

Pregnant Women

7. Experience is limited with the use of systemic antifungal drugs during human pregnancy. Four cases of infants born with craniofacial and skeletal abnormalities following prolonged in utero exposure to fluconazole have been reported (*59,50*). In addition, itraconazole is embryotoxic and teratogenic in animal systems (*61*). These same potential risks of teratogenicity are presumed to apply to other systemically absorbed azole antifungals, such as 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

Prevention of Exposure

1. 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.

Prevention of Disease

2. Routine testing of asymptomatic persons for serum cryptococcal antigen is not recommended because of the low probability that the results will affect clinical decisions (DIII).

3. Prospective controlled trials indicate that fluconazole and itraconazole can reduce the frequency of cryptococcal disease among patients who have advanced HIV

disease. However, most experts recommend that antifungal prophylaxis not be used routinely to prevent cryptococcosis because of the relative infrequency of cryptococcal disease, the lack of survival benefits associated with prophylaxis, the possibility of drug interactions, the potential development of antifungal drug resistance, and cost. The need for prophylaxis or suppressive therapy for other fungal infections (e.g., candidiasis, histoplasmosis, or coccidioidomycosis) should be considered in making decisions about prophylaxis for cryptococcosis. If used, fluconazole at doses of 100–200 mg daily is reasonable for patients whose CD4+ T-lymphocyte counts are <50 cells/μL (CI) (*56–58*).

Prevention of Recurrence

4. Patients who complete initial therapy for cryptococcosis should be administered lifelong suppressive treatment (i.e., secondary prophylaxis or chronic maintenance therapy). Fluconazole is superior to itraconazole in preventing relapse of cryptococcal disease and is the preferred drug (AI).

Discontinuation of Secondary Prophylaxis (Chronic Maintenance Therapy)

5. 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 on HAART, the numbers of patients who have been evaluated are insufficient to warrant a recommendation to discontinue prophylaxis.

Special Considerations

Children

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

Pregnant Women

7. Prophylaxis with fluconazole or itraconazole should not be initiated during pregnancy because of the low incidence of cryptococcal disease, the lack of a recommendation for primary prophylaxis against cryptococcosis in nonpregnant adults, and potential teratogenic effects of these drugs during pregnancy (DIII) (*59–61*). 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 in infants following 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 (*59,60*). For such patients, therapy with amphotericin B may be preferred, especially during the first trimester. Effective birth control measures should be recommended to all HIV-infected women on azole therapy for cryptococcosis (AIII).

Histoplasmosis

Prevention of Exposure

1. 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).

Prevention of Disease

2. 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).

3. 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 *H. capsulatum*-endemic areas (*62*). However, no survival benefit was observed among persons receiving itraconazole. Prophylaxis with itraconazole may be considered in patients with CD4+ T-lymphocyte counts <100 cells/μL who are at especially high risk because of occupational exposure or who live in a community with a hyperendemic rate of histoplasmosis (≥10 cases per 100 patient-years) (CI).

Prevention of Recurrence

4. 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 a day) (AI) (*63*).

Discontinuation of Secondary Prophylaxis (Chronic Maintenance Therapy)

5. 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 on HAART, the numbers of patients who have been evaluated are insufficient to warrant a recommendation to discontinue prophylaxis.

Special Considerations

Children

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

Pregnant Women

7. Because of the embryotoxicity and teratogenicity of itraconazole in animal systems, primary prophylaxis against histoplasmosis should not be offered during pregnancy (DIII). These data as well as the observation of craniofacial and skeletal

abnormalities in infants following prolonged in utero exposure to fluconazole should be considered when assessing the need for chronic maintenance therapy in HIV-infected pregnant women with histoplasmosis. For such patients, therapy with amphotericin B may be preferred, especially during the first trimester. Effective birth control measures should be recommended to all HIV-infected women on azole therapy for histoplasmosis (AIII).

Coccidioidomycosis

Prevention of Exposure

1. 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).

Prevention of Disease

2. 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).

3. Primary prophylaxis for HIV-infected persons who live in coccidioidomycosis-endemic areas is not routinely recommended.

Prevention of Recurrence

4. 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 each day or 200 mg of itraconazole twice a day (*64*). Patients with meningeal disease require consultation with an expert.

Discontinuation of Secondary Prophylaxis (Chronic Maintenance Therapy)

5. 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 on HAART, the numbers of patients who have been evaluated are insufficient to warrant a recommendation to discontinue prophylaxis.

Special Considerations

Children

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

Pregnant Women

7. The potential teratogenicity of fluconazole and itraconazole should be considered when assessing the therapeutic options for HIV-infected women who become pregnant while receiving chronic maintenance therapy for coccidiodomycosis. For such patients, therapy with amphotericin B may be preferred, especially during the first trimester. Effective birth control measures should be recommended for all HIV-infected women on azole therapy for coccidioidomycosis (AIII).

Cytomegalovirus Disease

Prevention of Exposure

1. HIV-infected persons who belong to risk groups 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 male homosexual contact or used injection drugs.

2. 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).

3. 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). The risk for acquiring CMV infection can be diminished by good hygienic practices such as hand washing (AII).

4. HIV-exposed infants and HIV-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).

Prevention of Disease

5. Prophylaxis with oral ganciclovir may 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) (*65,66*). Ganciclovir-induced neutropenia, anemia, conflicting reports of efficacy, lack of proven survival benefit, the risk for developing ganciclovir-resistant CMV, and cost are among the issues that should be considered 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 (*67*). Therefore, neither acyclovir nor valacyclovir should be used for this purpose (EI). The most important method for preventing severe CMV disease is recognition of the early manifestations of the disease. Early recognition of CMV retinitis is most likely when the patient has been educated on this topic. Patients should be made aware of the significance of increased floaters in the eye and should be advised to assess their visual acuity regularly by using simple techniques such as reading newsprint (BIII). Regular funduscopic examinations

performed by an ophthalmologist are recommended by some experts for patients with low (e.g., <50 cells/μL) CD4+ T-lymphocyte counts (CIII).

Prevention of Recurrence

6. CMV disease is not cured with courses of the currently available antiviral agents (e.g., ganciclovir, foscarnet, or cidofovir). Following induction therapy, secondary prophylaxis (chronic maintenance therapy) is recommended for life (AI). Regimens that are effective for chronic suppression include parenteral or oral ganciclovir, parenteral foscarnet, combined parenteral ganciclovir and foscarnet, parenteral cidofovir, and (for retinitis only) ganciclovir administration via intraocular implant plus oral ganciclovir (AI) (*68–72*). The intraocular implant alone does not provide protection to the contralateral eye or to other organ systems. The choice of a chronic maintenance regimen for patients treated for CMV disease should be made in consultation with an expert. 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).

Discontinuation of Secondary Prophylaxis (Chronic Maintenance Therapy)

7. Several studies have found that maintenance therapy can be discontinued in patients with CMV retinitis whose CD4+ T-lymphocyte counts have increased to >100–150 cells/μL and whose HIV plasma RNA levels have been suppressed in response to HAART (*73–75*). These patients largely have remained disease-free for >30–90 weeks, whereas in the pre-HAART era, retinitis typically recurred in 6–8 weeks. Discontinuation of prophylaxis may be considered in patients with a sustained (e.g., >3–6 month) increase in CD4+ T-lymphocyte count to >100–150 cells/μL on HAART (CIII). 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, magnitude and duration of viral load suppression, anatomic location of the retinal lesion, vision in the contralateral eye, and the feasibility of regular ophthalmic monitoring (CII) (*73–75*).

Restarting Secondary Prophylaxis

8. No data exist to guide recommendations for reinstituting secondary prophylaxis. Pending the availability of such data, a reasonable approach would be to restart prophylaxis when the CD4+ T-lymphocyte count has decreased to <50–100 cells/μL (CIII).

Special Considerations

Children

9. Some experts recommend obtaining a CMV urine culture on 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 1 year of age, CMV antibody testing on an annual basis may 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.

10. 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).

11. Oral ganciclovir results in reduced CMV shedding in CMV-infected children and may be considered for primary prophylaxis against CMV disease in CMV-infected children who are severely immunosuppressed (e.g., CD4+ T-lymphocyte count <50 cells/μL) (CII).

12. For children with CMV disease, no data are available to guide decisions concerning discontinuation of secondary prophylaxis (chronic maintenance therapy) when the CD4+ T-lymphocyte count has increased in response to HAART.

Pregnant Women

13. Because of the lack of a recommendation for routine use of ganciclovir among nonpregnant adults and the lack of experience with this drug during pregnancy, ganciclovir is not recommended for primary prophylaxis against CMV disease during pregnancy (DIII). Ganciclovir should be discontinued for patients who conceive while being administered primary prophylaxis. Because of the risks to maternal health, prophylaxis against recurrent CMV disease is indicated during pregnancy (AIII). The choice of agents to be used in pregnancy should be individualized after consultation with experts.

Herpes Simplex Virus Disease

Prevention of Exposure

1. 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).

Prevention of Disease

2. Prophylaxis of initial episodes of HSV disease is not recommended (DIII).

Prevention of Recurrence

3. Because acute episodes of HSV infection 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 famciclovir (AI) (*76,77*). Valacyclovir also is an option (CIII). Intravenous foscarnet or cidofovir can be used to treat infection due to acyclovir-resistant isolates of HSV, which are routinely resistant to ganciclovir as well (AII).

Special Considerations

Children

4. The recommendations for preventing initial disease and recurrence among adults and adolescents apply to children as well.

Pregnant Women

5. Oral acyclovir prophylaxis during late pregnancy is a controversial strategy recommended by some experts 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 (*78*).

Varicella-Zoster Virus Infection

Prevention of Exposure

1. 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 (especially 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).

Prevention of Disease

2. Very little data regarding the safety and efficacy of varicella vaccine in HIV-infected adults are available, and no recommendation for its use can be made for this population. (See Special Considerations/Children, below, for information about the use of varicella vaccine in children.)

3. For the prophylaxis of 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 within 96 hours after close contact with a patient who has chickenpox or shingles (AIII). Data are lacking on the effectiveness of acyclovir for preventing chickenpox in susceptible HIV-infected children or adults.

4. No preventive measures are currently available for shingles.

Prevention of Recurrence

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

Special Considerations

Children

6. HIV-infected children who are asymptomatic and not immunosuppressed (i.e., in immunologic category 1, Table 9) should receive live attenuated varicella vaccine at 12–15 months of age or later (BII). Varicella vaccine should not be administered to other HIV-infected children because of the potential for disseminated viral infection (EIII).

Pregnant Women

7. VZIG is recommended for VZV-susceptible, HIV-infected pregnant women within 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).

Human Herpesvirus 8 Infection

Prevention of Exposure

1. The mechanism of transmitting human herpesvirus 8 (HHV-8), the herpesvirus associated with Kaposi's sarcoma (KS), is not known. Epidemiologic evidence suggests that sexual transmission is likely among men who have sex with men and can occur among heterosexuals as well. However, the virus has been detected more frequently in saliva than in semen from HHV-8–seropositive HIV-infected persons. Although the efficacy of condom use for preventing HHV-8 infection has not been established, HIV-infected persons should use latex condoms during every act of sexual intercourse to reduce the risk for exposure to sexually transmitted pathogens (AII).

Prevention of Disease

2. 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.

3. Lower rates of KS have been observed among AIDS patients treated with ganciclovir or foscarnet for CMV retinitis (*68*). 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 the use of these or other drugs to prevent KS in individuals coinfected with HIV and HHV-8.

4. Potent antiretroviral drug combinations that suppress HIV replication reduce the frequency of KS in HIV-infected persons and should be considered for all persons who qualify for such therapy (BII).

Prevention of Recurrence

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

Special Considerations

Children

6. In parts of the world where HHV-8 is endemic, horizontal transmission might occur among young children, possibly via saliva. However, no recommendations are currently available for preventing HHV-8 transmission from child to child.

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MORBIDITY AND MORTALITY WEEKLY REPORT

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Recommendations and Reports

Continuing Education Activity Sponsored by CDC

1999 USPHS/IDSA Guidelines for the Prevention of Opportunistic Infections in Persons Infected with Human Immunodeficiency Virus

U.S. Public Health Service (USPHS) and Infectious Diseases Society of America (IDSA)

OBJECTIVE

This *MMWR* provides recommendations regarding the prevention of opportunistic infections (OIs) in persons infected with human immunodeficiency virus (HIV). These recommendations were developed by CDC staff members and members of the U.S. Public Health Service/Infectious Diseases Society of America Prevention of Opportunistic Infections Working Group. This report is intended to guide clinical practice and policy development related to the prevention of OIs in persons infected with HIV. Upon completion of this educational activity, the reader should be able to 1) describe disease-specific methods for preventing exposure to the opportunistic pathogen, first episode of disease, and recurrence of disease; 2) identify adverse reactions, drug interactions, and toxicities that can result from administering medications used to manage OIs in HIV-infected persons; 3) describe special considerations for HIV-infected children and pregnant women; and 4) identify recommendations regarding the discontinuation of chemoprophylaxis in persons whose CD4+ T-lymphocyte counts have increased in response to highly active antiretroviral therapies.

ACCREDITATION

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EXPIRATION — August 20, 2000

The response form must be completed and returned electronically, by fax, or by mail, **postmarked no later than 1 year from the publication date of this report**, for eligibility to receive continuing education credit.

INSTRUCTIONS

1. Read this *MMWR* (Vol. 48, RR-10), which contains the correct answers to the questions beginning on the next page.
2. Complete all registration information on the response form, including your name, mailing address, phone number, and e-mail address, if available.
3. Indicate whether you are registering for Continuing Medical Education (CME) credit, Continuing Education Unit (CEU) credit, or Continuing Nursing Education (CNE) credit.
4. Select your answers to the questions, and mark the corresponding letters on the response form. To receive continuing education credit, you must answer *all* of the questions. Questions with more than one correct answer will instruct you to "indicate all that are true."
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If you answer all of the questions, you will receive an award letter for 3 hours of CME credit, 0.3 hour of CEU credit, or 3.3 hours of CNE credit within 90 days. No fees are charged for participating in this continuing education activity.

U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES

To receive continuing education credit, please answer all of the following questions.

1. Indications for chemoprophylaxis against *Pneumocystis carinii* pneumonia (PCP) in HIV-infected adults and adolescents might include each of the following except

A. CD4+ T-lymphocyte count <200 cells/uL.
B. CD4+ T-lymphocyte count <250 cells/uL.
C. CD4+ T-lymphocyte percentage <14%.
D. HIV plasma RNA (viral load) >10,000 copies/mL.
E. history of AIDS-defining illness.
F. history of oropharyngeal candidiasis (thrush).

2. The preferred drug regimen for chemoprophylaxis against PCP in HIV-infected adults and adolescents is

A. trimethoprim-sulfamethoxazole (TMP-SMZ), 1 double-strength tablet three times a week.
B. TMP-SMZ, 1 double-strength tablet two times a day.
C. TMP-SMZ, 1 double-strength tablet daily.
D. dapsone, 100 mg daily.
E. atovaquone, 1500 mg daily.

3. Criteria for chemoprophylaxis against toxoplasmic encephalitis in HIV-infected adults and adolescents are

A. CD4+ T-lymphocyte count <200 cells/uL.
B. CD4+ T-lymphocyte count <200 cells/uL and positive anti-*Toxoplasma* antibody.
C. CD4+ T-lymphocyte count <100 cells/uL.
D. CD4+ T-lymphocyte count <100 cells/uL and positive anti-*Toxoplasma* antibody.
E. CD4+ T-lymphocyte count <50 cells/uL and positive anti-*Toxoplasma* antibody.

4. Criteria for chemoprophylaxis against disseminated *Mycobacterium avium* complex (MAC) disease in HIV-infected adults and adolescents are

A. CD4+ T-lymphocyte count <100/uL.
B. CD4+ T-lymphocyte count <75/uL.
C. CD4+ T-lymphocyte count <50/uL.
D. HIV plasma RNA (viral load) >10,000 copies/uL.
E. positive skin test for MAC antigens.

5. Acceptable chemoprophylactic regimens to prevent tuberculosis in HIV-infected adults and adolescents, after active tuberculosis has been excluded, include each of the following except

A. isoniazid, 300 mg daily, plus pyridoxine, 50 mg daily for 9 months.
B. rifampin, 600 mg daily, plus pyrazinamide, 20 mg/kg daily for 2 months.
C. rifabutin, 300 mg daily, plus pyrazinamide, 20 mg/kg daily for 2 months.
D. rifampin, 600 mg daily, plus ethambutol, 900 mg daily for 2 months.

6. Each of the following statements regarding drug interactions between rifamycin drugs (rifampin and rifabutin) and antiretroviral drugs is true except

A. Rifampin should not be coadministered with protease inhibitors.
B. Rifampin should not be coadministered with nonnucleoside reverse transcriptase inhibitors (NNRTIs).
C. Rifabutin can be coadministered with protease inhibitors and NNRTIs; no dose adjustments are necessary.
D. Rifabutin can be coadministered with some protease inhibitors and NNRTIs but might require adjustment of the dose of rifabutin.

7. The following vaccinations should be considered for HIV-infected adults and adolescents except

A. vaccination against *Streptococcus pneumoniae*.
B. vaccination against varicella zoster virus.
C. vaccination against influenza.
D. vaccination against hepatitis B virus.

8. Recommendations regarding vaccination of HIV-exposed or HIV-infected children differ from recommendations regarding vaccination of immunocompetent children for each of the following vaccinations except

A. rotavirus vaccination.
B. varicella zoster virus vaccination.
C. oral poliovirus vaccination.
D. diphtheria-pertussis-tetanus vaccination.
E. measles vaccination.

9. Secondary prophylaxis (chronic maintenance therapy) is recommended to prevent recurrent disease after successful treatment of acute disease, in both adults and children, for each of the following diseases except

A. PCP.
B. toxoplasmic encephalitis.
C. histoplasmosis.
D. disseminated MAC disease.
E. tuberculosis.

10. Indicate your work setting.

A. State/local health department.
B. Other public health setting.
C. Hospital clinic/private practice.
D. Managed care organization.
E. Academic institution.
F. Other.

11. Which best describes your professional activities?

A. Infectious diseases – adult.
B. Infectious diseases – pediatric.
C. Internal medicine.
D. Pediatrics.
E. Family practice.
F. Obstetrics/gynecology.
G. Other.

12. I plan to use these guidelines as the basis for . . . ***(Indicate all that apply.)***

A. health education materials.
B. insurance reimbursement policies.
C. local practice guidelines.
D. public policy.
E. other.

13. Each month, approximately how many HIV-infected patients do you treat?

A. None.
B. 1-5.
C. 6-20.
D. 21-50.
E. 51-100.
F. >100.

14. How much time did you spend reading this report and completing the exam?

A. More than 2½ hours but fewer than 3 hours.
B. 3 to 3½ hours.
C. More than 3½ hours but fewer than 4 hours.
D. 4 hours or more.

15. After reading this report, I am confident I can describe disease-specific methods for preventing exposure to the opportunistic pathogen, first episode of disease, and recurrence of disease.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

16. After reading this report, I am confident I can identify adverse reactions, drug interactions, and toxicities that can result from administering medications used to manage OIs in HIV-infected persons.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

17. After reading this report, I am confident I can describe special considerations for HIV-infected children and pregnant women.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

18. After reading this report, I am confident I can identify recommendations regarding the discontinuation of chemoprophylaxis in persons whose CD4+ T-lymphocyte counts have increased in response to highly active antiretroviral therapies.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

19. The objectives are relevant to the purpose of this report.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

20. The tables are useful.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

21. Overall, the presentation of the report enhanced my ability to understand the material.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

22. These recommendations will affect my practice.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

Correct answers for questions 1–9

1. D; 2. C; 3. D; 4. C; 5. D; 6. C; 7. B; 8. D; 9. E.

MMWR Response Form for Continuing Education Credit
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1999 USPHS/IDSA Guidelines for the Prevention of Opportunistic Infections in Persons Infected with Human Immunodeficiency Virus

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Human Papillomavirus Infection

Prevention of Exposure

1. 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 little evidence exists to suggest that condoms reduce the risk for infection with human papillomavirus (HPV).

Prevention of Disease

HPV-associated Genital Epithelial Cancers in HIV-infected Women

2. After a complete history of previous cervical disease has been obtained, HIV-infected women should have a pelvic examination and a Pap smear. In accordance with the recommendation of the Agency for Health Care Policy and Research, the Pap smear should be obtained twice in the first year after diagnosis of HIV infection and, if the results are normal, annually thereafter (AII).

3. 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 Recommendations 4–8, which follow (*79*).

4. For patients whose Pap smears are interpreted as atypical squamous cells of undetermined significance (ASCUS), several 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, particularly 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).

5. 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).

6. 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 Recommendation 7, which follows) (BIII). If a patient who has a diagnosis of ASCUS is at high risk (i.e., previous positive Pap tests or poor adherence to follow-up), the option of colposcopy should be considered (BIII).

7. Several management options are available for patients who have LSIL. Follow up with Pap tests every 4–6 months is used by many clinicians and is currently used in countries outside the United States as an established method of management. Patients managed in this way must be carefully selected and considered reliable for follow-up. If repeat smears show 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).

8. Women who have cytologic diagnosis of high-grade squamous intraepithelial lesions (HSILs) or squamous cell carcinoma should undergo colposcopy and directed biopsy (AII).

9. No data are available to suggest that these guidelines to prevent cervical disease should be modified for women on HAART.

HPV-associated Anal Intraepithelial Neoplasia and Anal Cancer in HIV-infected, Men Who Have Sex With Men

10. Evidence from several studies shows that HPV-positive men who have sex with men 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 in HIV-infected persons (*80*), anal cytology screening of HIV-infected men who have sex with men might become a useful preventive measure in the near future. However, further studies of screening and treatment programs for anal HSILs need to be carried out before recommendations for routine anal cytology screening can be made.

Prevention of Recurrence

11. The risks for recurrence of squamous intraepithelial lesions and cervical cancer after conventional therapy are increased among HIV-infected women. The prevention of illness associated with recurrence depends on careful follow-up of patients after treatment. Patients should be monitored with frequent cytologic screening and, when indicated, with colposcopic examination for recurrent lesions (AI) (*79*).

12. In one recent study of HIV-infected women treated for HSILs using standard therapy, low-dose intravaginal 5-fluorouracil (2 grams twice a week for 6 months) reduced the short-term risk for recurrence and possibly the grade of recurrence (*81*). However, clinical experience with this therapy is too limited to provide a recommendation for routine use.

Special Considerations

Pregnant Women

13. Use of intravaginal 5-fluorouracil to prevent recurrent dysplasia is not recommended during pregnancy.

Hepatitis C Virus Infection

Prevention of Exposure

1. The chief route of hepatitis C virus (HCV) transmission in the United States is injection drug use. Because injection drug use is a complex behavior, clinicians should assess the individual'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 (*82–84*) —

- to stop using injection drugs (AIII); and

- to enter and complete a substance-abuse treatment program, including a relapse prevention program (AIII).

If they are continuing to inject drugs, patients should be advised (BIII) —

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

If they are continuing to use illegal drugs intranasally ("snorting"), patients should be advised (BIII) —

- to be aware that this practice has been associated with HCV transmission; and
- to not share equipment (e.g., straws) with other users.

2. Persons considering tattooing or body piercing should be informed of potential risks of 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) (*84*) (BIII).

3. To reduce risks for acquiring bloodborne infections, patients should be advised not to share dental appliances, razors, or other personal care articles (BIII).

4. Although the efficiency of sexual transmission of HCV remains controversial, safe-sexual practices should be encouraged, and barrier precautions (e.g., latex condoms) are recommended to reduce the risk for exposure to sexually transmitted pathogens (AII).

Prevention of Disease

5. HIV-infected patients should be screened for HCV infection 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 for HCV RNA). The presence of HCV RNA in blood might also be assessed in 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).

6. Persons coinfected with HIV and HCV should be advised not to drink excessive amounts of alcohol (AII). Avoiding alcohol altogether might be prudent because it is

unclear whether even occasional moderate alcohol use (e.g., <12 ounces of beer or <10 grams of alcohol per week) increases the incidence of cirrhosis among HCV-infected persons (CIII).

7. Patients with chronic hepatitis C should be vaccinated against hepatitis A because a) the risk for fulminant hepatitis associated with hepatitis A appears increased in HCV-coinfected persons; b) hepatitis A vaccine is safe for HIV-infected persons; and c) although immunogenicity is reduced in patients with advanced HIV infection, more than two thirds of patients develop protective antibody responses (BIII). Prevaccination screening for antibody to hepatitis A virus is cost-effective and therefore recommended when >30% prevalence of hepatitis A virus antibody is expected in the population being screened (e.g., persons >40 years of age) (*85*) (BIII).

8. HIV-HCV–coinfected patients have a higher incidence of chronic liver disease than patients infected with HIV alone (*86*) and should be evaluated for chronic liver disease and for the possible need for treatment (*83*). However, limited data exist regarding the safety and efficacy of antiviral treatment of patients coinfected with HIV and HCV. Moreover, because the optimal means of treating coinfected patients has not been established and many HIV-infected patients have conditions that complicate therapy (e.g., depression or illicit drug use), this care should occur in a clinical trial or be coordinated by providers with experience treating both HIV and HCV infections (BIII).

9. In some studies, the incidence of antiretroviral-associated liver enzyme elevations has been increased in patients coinfected with HIV and HCV (*87*); 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 antiretroviral therapy might have an inflammatory reaction that mimics an exacerbation of underlying liver disease. In this situation, careful monitoring of liver function is required.

Prevention of Recurrence

10. If the serum HCV RNA level becomes undetectable during HCV therapy and remains undetectable for 6 months after HCV therapy is stopped (sustained virologic response), >90% of HIV-uninfected patients with hepatitis C will remain HCV RNA negative for >5 years and have improved liver histology (*88*). For HIV-HCV–coinfected patients, the durability of treatment response and requirement for maintenance therapy are unknown.

Special Considerations

Children

11. Children born to women coinfected with HIV and HCV should be tested for HCV infection (*82*) (BI). In children with perinatal HCV infection, maternal HCV antibody can persist for up to 18 months, and HCV RNA can be intermittently undetectable. Thus, testing should be performed at or after 2 years of age. If earlier diagnosis is needed, HCV RNA should be assessed in more than one infant blood specimen obtained after 1 month of age. The average rate of HCV infection among infants born to coinfected women is approximately 15% (range, 5–36%) (*89*). Data are limited on the natural history and treatment of HCV infection in children.

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TABLE 1. Prophylaxis to prevent first episode of opportunistic disease in adults and adolescents infected with human immunodeficiency virus

Pathogen	Preventive Regimens		
	Indication	First Choice	Alternatives
I. Strongly recommended as standard of care			
*Pneumocystis carinii**	CD4+ count <200/μL or oropharyngeal candidiasis	Trimethoprim-sulfamethoxazole (TMP-SMZ), 1 DS po q.d. (AI) TMP-SMZ, 1 SS po q.d. (AI)	Dapsone, 50 mg po b.i.d. *or* 100 mg po q.d. (BI); dapsone, 50 mg po q.d. *plus* pyrimethamine, 50 mg po q.w. *plus* leucovorin, 25 mg po q.w. (BI); dapsone, 200 mg po *plus* pyrimethamine, 75 mg po *plus* leucovorin, 25 mg po q.w. (BI); aerosolized pentamidine, 300 mg q.m. via Respirgard II™ nebulizer (BI); atovaquone, 1500 mg po q.d. (BI); TMP-SMZ, 1 DS po t.i.w. (BI)
Mycobacterium tuberculosis Isoniazid-sensitive†	TST reaction ≥5mm *or* prior positive TST result without treatment *or* contact with case of active tuberculosis	Isoniazid, 300 mg po *plus* pyridoxine, 50 mg po q.d. x 9 mo (AII) or isoniazid, 900 mg po *plus* pyridoxine, 100 mg po b.i.w. x 9 mo (BI); rifampin, 600 mg *plus* pyrazinamide, 20 mg/kg po q.d. x 2 mo (AI)	Rifabutin 300 mg po q.d. *plus* pyrazinamide, 20 mg/kg po q.d. x 2 mo (BIII); rifampin 600 mg po q.d. x 4 mo (BIII)
Isoniazid-resistant	Same; high probability of exposure to isoniazid-resistant tuberculosis	Rifampin 600 mg *plus* pyrazinamide, 20 mg/kg po q.d. x 2 mo (AI)	Rifabutin, 300 mg *plus* pyrazinamide 20 mg/kg po q.d. x 2 mo (BIII); rifampin, 600 mg po q.d. x 4 mo (BIII); Rifabutin, 300 mg po q.d. x 4 mo (CIII)
Multidrug-(isoniazid and rifampin) resistant	Same; high probability of exposure to multidrug-resistant tuberculosis	Choice of drugs requires consultation with public health authorities	None

TABLE 1. Prophylaxis to prevent first episode of opportunistic disease in adults and adolescents infected with human immunodeficiency virus — Continued

Pathogen	Preventive Regimens		
	Indication	First Choice	Alternatives
Toxoplasma gondii§	IgG antibody to *Toxoplasma* and CD4+ count <100/μL	TMP-SMZ, 1 DS po q.d. (AII)	TMP-SMZ, 1 SS po q.d. (BIII): dapsone, 50 mg po q.d. *plus* pyrimethamine, 50 mg po q.w. *plus* leukovorin, 25 mg po q.w. (BI); atovaquone, 1500 mg po q.d. with or without pyrimethamine, 25 mg po q.d. *plus* leukovorin, 10 mg po q.d. (CIII)
Mycobacterium avium complex¶	CD4+ count <50/μL	Azithromycin, 1,200 mg po q.w., (AI) or clarithromycin, 500 mg po b.i.d. (AI)	Rifabutin, 300 mg po q.d. (BI); azithromycin, 1,200 mg po q.w. *plus* rifabutin, 300 mg po q.d. (CI)
Varicella zoster virus (VZV)	Significant 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) im, administered ≤96 h after exposure, ideally within 48 h (AIII)	
II. Generally recommended			
*Streptococcus pneumoniae***	All patients	Pneumococcal vaccine, 0.5 mL im (CD4+ ≥200/μL [BII]; CD4+ <200/μL [CIII])–might reimmunize if initial immunization was given when CD4+ <200/μL and if CD4+ increases to >200/μL on HAART(CIII)	None
Hepatitis B virus††	All susceptible (anti-HBc–negative) patients	Hepatitis B vaccine: 3 doses (BII)	None

TABLE 1. Prophylaxis to prevent first episode of opportunistic disease in adults and adolescents infected with human immunodeficiency virus — Continued

Pathogen	Preventive Regimens		
	Indication	First Choice	Alternatives
Influenza virus††	All patients (annually, before influenza season)	Whole or split virus, 0.5 mL im/yr (BIII)	Rimantadine, 100 mg po b.i.d. (CIII), or amantadine, 100 mg po b.i.d. (CIII)
Hepatitis A virus††	All susceptible (anti-HAV–negative) patients with chronic hepatitis C	Hepatitis A vaccine: two doses (BIII)	None
III. Not routinely indicated			
Bacteria	Neutropenia	Granulocyte-colony–stimulating factor (G-CSF), 5–10 μg/kg sc q.d. x 2–4 w or granulocyte-macrophage colony–stimulating factor (GM-CSF), 250 μg/m^2 iv over 2 h q.d. x 2–4 w (CII)	None
Cryptococcus neoformans§§	CD4+ count <50/μL	Fluconazole, 100–200 mg po q.d. (CI)	Itraconazole, 200 mg po q.d. (CIII)
Histoplasma capsulatum§§	CD4+ count <100/μL, endemic geographic area	Itraconazole capsule, 200 mg po q.d.(CI)	None
Cytomegalovirus (CMV)¶¶	CD4+ count <50/μL and CMV antibody positivity	Oral ganciclovir, 1 g po t.i.d. (CI)	None

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ABBREVIATIONS: Anti-HBc = antibody to hepatitis B core antigen; b.i.w.= twice a week; DS = double-strength tablet; HAART = highly active antiretroviral therapy; HAV = hepatitis A virus; HIV = human immunodeficiency virus; im = intramuscular; iv = intravenous; po = by mouth; q.d. = daily; q.m. = monthly; q.w. = weekly; SS= single-strength tablet; t.i.w. = three times a week; TMP-SMZ = trimethoprim-sulfamethoxazole; sc = subcutaneous; and TST = tuberculin skin test.

* 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 >200 but <250 cells/μL. 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 q.d. is probably less effective than that of 100 mg q.d. The efficacy of parenteral pentamidine (e.g., 4 mg/kg/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 and do not need additional prophylaxis against PCP.

† Directly observed therapy is recommended for isoniazid, 900 mg b.i.w.; isoniazid regimens should include pyridoxine to prevent peripheral neuropathy. Rifampin should not be administered concurrently with protease inhibitors or nonnucleoside reverse transcriptase inhibitors. Rifabutin should not be given with hard-gel saquinavir or delavirdine; caution is also advised when the drug is coadministered with soft-gel saquinavir. Rifabutin may be administered at a reduced dose (150 mg q.d.) with indinavir, nelfinavir, or amprenavir; at a reduced dose of 150 mg q.o.d. (or 150 mg three times weekly) with ritonavir; or at an increased dose (450 mg q.d.) with efavirenz; information is lacking regarding coadministration of rifabutin with nevirapine. 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 by atovaquone. Atovaquone may be used with or without pyrimethamine. Pyrimethamine alone probably provides little, if any, protection.

¶ See footnote † regarding use of rifabutin with protease inhibitors or nonnucleoside reverse transcriptase inhibitors.

** Vaccination should be offered to persons who have a CD4+ T-lymphocyte count <200 cells/μL, although the efficacy might be diminished. Revaccination 5 years after the first dose or sooner if the initial immunization was given when the CD4+ count was <200 cells/μL and the CD4+ count has increased to >200 cells/μL on HAART is considered optional. Some authorities are concerned that immunizations might stimulate the replication of HIV. However, one study showed no adverse effect of pneumococcal vaccination on patient survival (McNaghten AD, Hanson DL, Jones JL, Dworkin MS, Ward JW, and the Adult/Adolescent Spectrum of Disease Group. Effects of antiretroviral therapy and opportunistic illness primary chemoprophylaxis on survival after AIDS diagnosis. AIDS 1999 [in press]).

†† These immunizations or chemoprophylactic regimens do not target pathogens traditionally classified as opportunistic but should be considered for use in HIV-infected patients as indicated. Data are inadequate concerning clinical benefit of these vaccines in this population, although it is logical to assume that those patients who develop antibody responses will derive some protection. Some authorities are concerned that immunizations might stimulate HIV replication, although for influenza vaccination, a large observational study of HIV-infected persons in clinical care showed no adverse effect of this vaccine, including multiple doses, on patient survival (J. Ward, CDC, personal communication). Hepatitis B vaccine has been recommended for all children and adolescents and for all adults with risk factors for hepatitis B virus (HBV). Rimantadine and amantadine are appropriate during outbreaks of influenza A. Because of the theoretical concern that increases in HIV plasma RNA following vaccination during pregnancy might increase the risk of perinatal transmission of HIV, providers may wish to defer vaccination until after antiretroviral therapy is initiated. For additional information regarding vaccination against hepatitis A and B and vaccination and antiviral therapy against influenza see CDC. Prevention of hepatitis A through active or passive immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1996;45(No. RR-15); 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); and CDC. Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1999;48(No. RR-4).

§§ In a few unusual occupational or other circumstances, prophylaxis should be considered; consult a specialist.

¶¶ Acyclovir is not protective against CMV. Valacyclovir is not recommended because of an unexplained trend toward increased mortality observed in 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) in adults and adolescents infected with human immunodeficiency virus

		Preventive Regimens	
Pathogen	**Indication**	**First Choice**	**Alternatives**
I. Recommended for life as standard of care			
Pneumocystis carinii	Prior *P. carinii* pneumonia	Trimethoprim-sulfamethoxazole (TMP-SMZ), 1 DS po q.d. (AI); TMP-SMZ 1 SS po q.d. (AI)	Dapsone, 50 mg po b.i.d. *or* 100 mg po q.d. (BI); dapsone, 50 mg po q.d. *plus* pyrimethamine, 50 mg po q.w. *plus* leucovorin, 25 mg po q.w. (BI); dapsone, 200 mg po *plus* pyrimethamine, 75 mg po *plus* leucovorin, 25 mg po q.w. (BI); aerosolized pentamidine, 300 mg q.m. via Respirgard II™ nebulizer (BI); atovaquone, 1500 mg po q.d. (BI); TMP-SMZ, 1 DS po t.i.w. (CI)
*Toxoplasma gondii**	Prior toxoplasmic encephalitis	Sulfadiazine, 500–1,000 mg po q.i.d. *plus* pyrimethamine, 25–75 mg po q.d. *plus* leucovorin, 10–25 mg po q.d. (AI)	Clindamycin, 300–450 mg po q 6–8 h *plus* pyrimethamine, 25–75 mg po q.d. *plus* leucovorin, 10–25 mg po q.d. (BI); atovaquone, 750 mg po q. 6-12 h with or without pyrimethamine, 25 mg po q.d. *plus* leucovorin, 10 mg po q.d. (CIII)
Mycobacterium avium complex †	Documented disseminated disease	Clarithromycin, 500 mg po b.i.d. (AI) *plus* ethambutol, 15 mg/kg po q.d.(AII); with or without rifabutin, 300 mg po q.d. (CI)	Azithromycin, 500 mg po q.d. (AII) *plus* ethambutol, 15 mg/kg po q.d.(AII); with or without rifabutin, 300 mg po q.d.(CI)
Cytomegalovirus	Prior end-organ disease	Ganciclovir, 5–6 mg/kg iv 5–7 days/wk or 1,000 mg po t.i.d. (AI); or foscarnet, 90–120 mg/kg iv q.d. (AI); or (for retinitis) ganciclovir sustained-release implant q 6–9 months *plus* ganciclovir, 1.0–1.5 g po t.i.d. (AI)	Cidofovir, 5 mg/kg iv q.o.w. with probenecid 2 grams po 3 hours before the dose followed by 1 gram po given 2 hours after the dose, and 1 gram po 8 hours after the dose (total of 4 grams) (AI). Fomivirsen 1 vial (330 μg) injected into the vitreous, then repeated every 2–4 wks (AI)

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

	Preventive Regimens		
Pathogen	**Indication**	**First Choice**	**Alternatives**
Cryptococcus neoformans	Documented disease	Fluconazole, 200 mg po q.d. (AI)	Amphotericin B, 0.6–1.0 mg/kg iv q.w.–t.i.w. (AI); itraconazole, 200 mg po q.d. (BI)
Histoplasma capsulatum	Documented disease	Itraconazole capsule, 200 mg po b.i.d. (AI)	Amphotericin B, 1.0 mg/kg iv q.w. (AI)
Coccidioides immitis	Documented disease	Fluconazole, 400 mg po q.d. (AII)	Amphotericin B, 1.0 mg/kg iv q.w. (AI); itraconazole, 200 mg po b.i.d. (AII)
Salmonella species, (non-*typhi*)[§]	Bacteremia	Ciprofloxacin, 500 mg po b.i.d. for several 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 po t.i.d. or 400 mg po b.i.d.(AI) Famciclovir 500 mg po b.i.d. (AI)	Valacyclovir, 500 mg po b.i.d. (CIII)
Candida (oropharyngeal or vaginal)	Frequent/severe recurrences	Fluconazole 100–200 mg po q.d. (CI)	Itraconazole solution, 200 mg po q.d. (CI); ketoconazole, 200 mg po q.d. (CIII)
Candida (esophageal)	Frequent/severe recurrences	Fluconazole 100–200 mg po q.d. (BI)	Itraconazole solution, 200 mg po q.d. (BI); ketoconazole, 200 mg po q.d. (CIII)

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ABBREVIATIONS: b.i.d. = twice a day; DS = double-strength tablet; po = by mouth; q.d. = daily; q.m. = monthly; q.w. = weekly; q.o.w. = every other week; SS = single-strength tablet; t.i.d. = three times a day; t.i.w. = three times a week; and TMP-SMZ = trimethoprim-sulfamethoxazole.

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

† Many multiple-drug regimens are poorly tolerated. Drug interactions (e.g., those seen with clarithromycin and rifabutin) can be problematic; rifabutin has been associated with uveitis, especially when administered at daily doses of >300 mg or concurrently with fluconazole or clarithromycin. Rifabutin should not be administered concurrently with hard-gel saquinavir or delavirdine; caution is also advised when the drug is coadministered with soft-gel saquinavir. Rifabutin may be administered at reduced dose (150 mg q.d. with indinavir, nelfinavir, or amprenavir; or 150 mg q.o.d. with ritonavir) or at increased dose (450 mg q.d.) with efavirenz (CDC. Prevention and treatment of tuberculosis among patients infected with human immunodeficiency virus: principles of therapy and revised recommendations. MMWR 1998;47[RR-20]). Information is lacking regarding coadministration of rifabutin with nevirapine.

§ Efficacy of 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 up to threefold with high-fat meal.	Administer with food.
Ganciclovir (capsules)	High-fat meal results in 22% increase in the area under the curve (AUC).	Administer with food.
Itraconazole (capsules)	Significant increase in bioavailability when taken with a full meal. Grapefruit juice results in 30% decrease in itraconazole AUC.	Administer with food; avoid grapefruit juice or increased itraconazole dose might be necessary.
Itraconazole (solution)	31% increase in AUC 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.
Clarithromycin	Ritonavir	Inhibition of metabolism — increased drug levels by 77%	No adjustment needed in normal renal function; adjust if creatinine clearance is <30.
Clarithromycin	Nevirapine	Induction of metabolism — decrease in clarithromycin area under the curve (AUC) by 35%, increase in AUC of 14-OH clarithromycin by 27%	Effect on *Mycobacterium avium* prophylaxis might be decreased; monitor closely.
Ketoconazole	Antacids, didanosine, H2-blockers, proton pump inhibitors	Increase in gastric pH that impairs absorption of ketoconazole	Avoid use of ketoconazole with pH-raising agents or use alternative antifungal drug.
Quinolone antibiotics (ciprofloxacin, levofloxacin, ofloxacin)	Didanosine, antacids, iron products, calcium products, sucralfate	Chelation that results in marked decrease in quinolone drug levels	Administer interacting drug at least 2 hours after quinolone.
Rifabutin	Fluconazole	Inhibition of metabolism — marked increase in rifabutin drug levels	Monitor for rifabutin toxicity such as uveitis, nausea, neutropenia.
Rifabutin	Efavirenz	Induction of metabolism — significant decrease in rifabutin AUC	Increase rifabutin dose to 450 mg daily.
Rifabutin	Ritonavir, saquinavir, indinavir, nelfinavir, amprenavir, delavirdine	Inhibition of metabolism — marked increase in rifabutin drug levels	Contraindicated with hard-gel saquinavir (caution also advised with soft-gel saquinavir) and delavirdine; use ½ dose (150 mg daily), with indinavir, nelfinavir, amprenavir; ¼ dose (150 mg every other day) with ritonavir.

TABLE 5. Effects of opportunistic infection medications on drugs commonly administered to persons infected with human immunodeficiency virus

Affected drug	Interacting drug(s)	Mechanism/Effect	Recommendation
Indinavir, saquinavir, ritonavir, nelfinavir, amprenavir	Rifampin	Induction of metabolism — marked decrease in protease inhibitor drug levels	Avoid concomitant use.
Delavirdine, nevirapine, efavirenz	Rifampin	Induction of metabolism — marked decrease in drug levels	Avoid concomitant use.
Saquinavir (hard-gel), delavirdine	Rifabutin	Induction of metabolism — marked decrease in drug levels	Avoid concomitant use.
Terfenadine, astemizole, cisapride	Ketoconazole Itraconazole Fluconazole Clarithromycin	Inhibition of metabolism	Cardiotoxic life-threatening effects possible; avoid concomitant use.
Didanosine (ddI)	Ganciclovir	Increases ddI area under the curve (AUC) by approximately 100%	Clinical significance unknown; monitor for ddI-related adverse effects.

TABLE 6. Adverse effects of opportunistic infection medications used in the management of human immunodeficiency virus infection

Bone marrow suppression	Cidofovir, dapsone, ganciclovir, pyrimethamine, rifabutin, sulfadiazine, trimethoprim-sulfamethoxazole, trimetrexate
Diarrhea	Atovaquone, clindamycin
Hepatotoxicity	Clarithromycin, fluconazole, isoniazid, itraconazole, ketoconazole, pyrazinamide, rifabutin, rifampin
Nephrotoxicity	Amphotericin B, cidofovir, foscarnet, pentamidine
Ocular effects	Cidofovir, ethambutol, rifabutin
Pancreatitis	Pentamidine, trimethoprim-sulfamethoxazole
Peripheral neuropathy	Isoniazid
Skin rash	Atovaquone, dapsone, sulfadiazine, trimethoprim-sulfamethoxazole

TABLE 7. Dosages of drugs for primary prevention or maintenance therapy for persons with opportunistic infections and renal insufficiency

Drug	Normal Dosage	CrCl (ml/min/1.73m^2)	Adjusted dose	
Acyclovir	200 mg po t.i.d.	<10	200 mg q. 12 h	
	400 mg po q. 12 h	<10	200 mg q. 12 h	
	800 mg po q. 4 h	10–25	800 mg q. 8 h	
	800 mg po q. 4 h	<10	800 mg q. 12 h	
Cidofovir	5 mg/kg iv q.o.w. (with probenecid)	Increase in serum creatinine of 0.3–0.4 above baseline	3 mg/kg	
		Increase in serum creatinine of 0.5 above baseline or 3+ proteinuria	Discontinue.	
Ciprofloxacin	500 mg po q. 12 h	30–50	250–500 mg q. 12 h	
		<30	250–500 mg q. 18 h	
Clarithromycin	500 mg b.i.d.	<30	½ dose (or double interval)	
Famciclovir	500 mg po q. 12 h	20–39	250 mg q. 12 h	
		<20	250 mg q. 24 h	
Fluconazole	50–400mg po q.d.	10–50	½ dose	
		<10	¼ dose	
		Dialysis	Full dose after dialysis	
Foscarnet	90–120 mg/kg iv q.d.	CrCl*	Low dose	High dose
		>1.4	90 mg q. 24 h	120 mg q. 24 h
		1.0–1.4	70 mg q. 24 h	90 mg q. 24h
		0.8–1.0	50 mg q. 24 h	65 mg q. 24 h
		0.6–0.8	80 mg q. 48 h	105 mg q. 48 h
		0.5–0.6	60 mg q. 48 h	80 mg q. 48 h
		0.4–0.5	50 mg q. 48h	65 mg q. 48 h
		<0.4	Not recommended	Not recommended
Ganciclovir	Oral:			
	1 gram po t.i.d.	50–69	1,500 mg q.d. or 500 mg t.i.d.	
		25–49	1,000 mg q.d. or 500 mg b.i.d.	
		10–24	500 mg q.d.	
		<10	500 mg t.i.w. after dialysis	
	IV:			
	5 mg/kg q.d. or	50–69	2.5 mg/kg q. 24 h	
	6 mg/kg q.d. x	25–49	1.25 mg/kg q. 24 h	
	5 days/week	10–24	0.625 mg/kg q. 48 h	
		<10	0.625 mg/kg t.i.w.	
Trimethoprim-sulfamethoxazole	1 DS q.d.	<30	½ dose	
	1 DS t.i.w.			
	1 SS q.d.			

ABBREVIATIONS: b.i.d. = twice daily; CrCl = creatinine clearance; DS = double-strength tablet; iv = intravenous; l.d. = loading dose; q.d. = daily; q.o.w. = every other week; SS = single-strength tablet; t.i.d. = three times daily; t.i.w. = three times a week.

*Creatinine clearance for foscarnet is expressed as ml/min/kg.

TABLE 8. Wholesale acquisition costs of agents recommended for the prevention of opportunistic infections in adults infected with human immunodeficiency virus

Opportunistic pathogen	Drug/vaccine	Dose	Annual cost per patient
Pneumocystis carinii	Trimethoprim-sulfamethoxazole	160/800 mg q.d.	$60
	Dapsone	100 mg q.d.	$*72*
	Aerosolized pentamidine	300 mg q.m.	$1,185
	Atovaquone	1500 mg q.d.	$10,647
Mycobacterium avium complex	Clarithromycin	500 mg b.i.d.	$2,347
	Azithromycin	1,200 mg q.w.	$1,635
	Rifabutin	300 mg q.d.	$3,352
Cytomegalovirus	Ganciclovir (po)	1,000 mg t.i.d.	$17,269
	Ganciclovir implant*		$5,000
	Ganciclovir (iv)	5mg/kg q.d.	$9,113
	Foscarnet (iv)	90–120 mg/kg q.d.	$27,960–36,770
	Cidofovir (iv)	375 mg q.o.w.	$19,812
	Fomivirsen (intravitreal)	1 vial every 4 wks	$12,000
Mycobacterium tuberculosis	Isoniazid†	300 mg q.d.	$23
	Rifampin	600 mg q.d.	$1,540
	Pyrazinamide	1,500 mg q.d.	$1,005
	Ethambutol	900 mg q.d.	$1,527
Fungi	Fluconazole	200 mg q.d.	$4,267
	Itraconazole capsules	200 mg q.d.	$4,893
	Itraconazole solution	200 mg q.d.	$5,129
	Ketoconazole	200 mg q.d.	$1,230
Herpes simplex virus	Acyclovir	400 mg b.i.d.	$1,300
	Famciclovir	500 mg b.i.d.	$4,826
	Valacyclovir	500 mg b.i.d.	$1,435
Toxoplasma gondii	Pyrimethamine	50 mg q.w.	$45
	Leucovorin	25 mg q.w.	$1,248
	Sulfadiazine	500 mg q.i.d.	$1,421
Streptococcus pneumoniae	23-valent pneumococcal vaccine	0.5 ml im x 1	$13
Influenza virus	Influenza vaccine	0.5 ml im x 1	$5
Hepatitis B virus	Recombinant hepatitis B	10–20μg im x 3	$195
Hepatitis A virus	Hepatitis A vaccine	1.0 ml im x 2	$120
Bacterial infections	G-CSF	300 μg t.i.w.	$25,780
Varicella zoster virus	VZIG	5 vials (6.25 ml)	$560

ABBREVIATIONS: b.i.d. = twice daily; G-CSF = granulocyte-colony-stimulating factor; iv = intravenous; im = intramuscular; po = by mouth; q.d. = daily; q.o.w. = every other week; q.w. = once a week; ; t.i.d. = three times daily; t.i.w. = three times a week; VZIG = varicella zoster immune globulin.
* Implant generally lasts 6–9 months.
† Cost for 9 months of therapy.

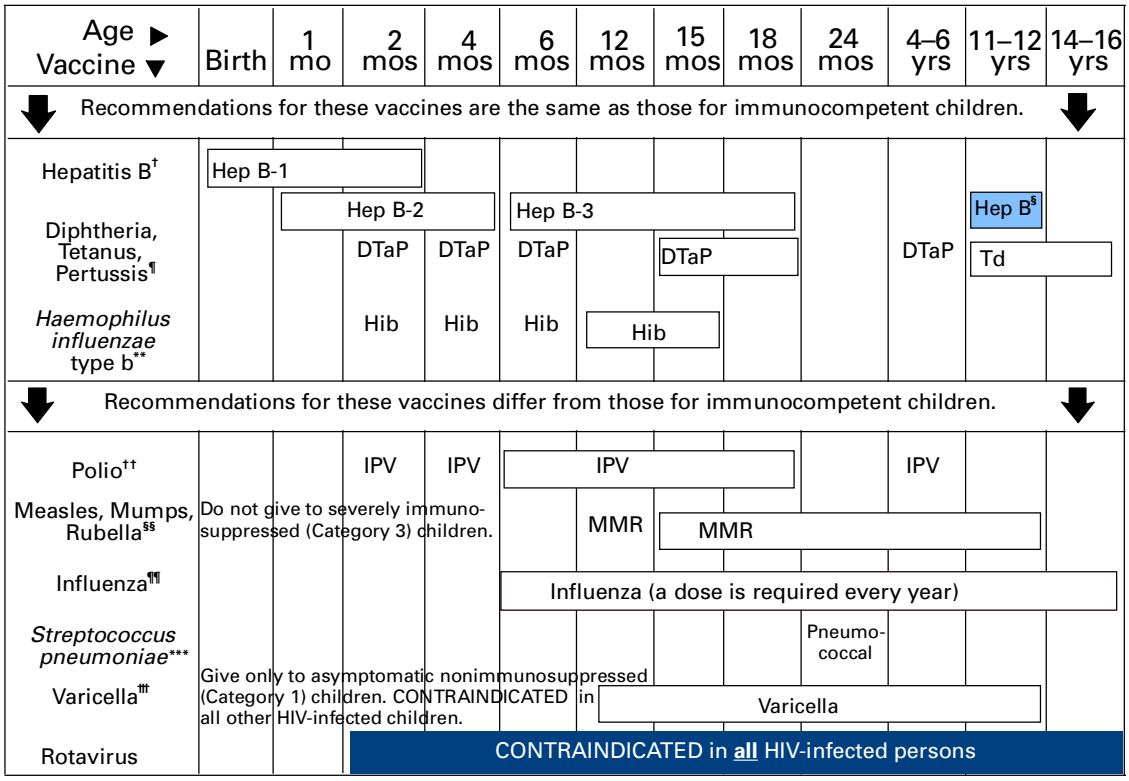
Source: Medical Economics. Drug topics red book. Montvale, New Jersey: Medical Economics Inc., 1999.

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

	Age		
	≤12 months	1–5 years	6–12 years
Immunologic category	**cells/μL (%)**	**cells/μL (%)**	**cells/μL (%)**
1. No evidence of suppression	≥1,500 (≥25)	≥1,000 (≥25)	≥500 (≥25)
2. Evidence of moderate suppression	750–1,499 (15–24)	500–999 (15–24)	200–499 (15–24)
3. 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).

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



NOTES: Modified from the immunization schedule for immunocompetent children. This schedule also applies to children born to HIV-infected mothers whose HIV infection status has not been determined. Once a child is known not to be HIV-infected, the schedule for immunocompetent children applies. This schedule indicates the recommended age for routine administration of currently licensed childhood vaccines. Some combination vaccines are available and may be used whenever administration of all components of the vaccine is indicated. Providers should consult the manufacturers' package inserts for detailed recommendations.

*Vaccines are listed under the routinely recommended ages. Bars indicate range of acceptable ages for vaccination. Shaded bar indicates catch-up vaccination: at 11–12 years of age, hepatitis B vaccine should be administered to children not previously vaccinated.

† ***Infants born to HBsAg-negative mothers*** should receive 2.5 µg of Merck vaccine (Recombivax HB®) or 10 µg of SmithKline Beecham (SB) vaccine (Engerix-B®). The 2nd dose should be administered ≥1 month after the 1st dose.

Infants born to HBsAg-positive mothers should receive 0.5 mL of hepatitis B immune globulin (HBIG) within 12 hours of birth and either 5µg of Merck vaccine (Recombivax HB®) or 10 µg of SB vaccine (Engerix-B®) at a separate site. The 2nd dose is recommended at 1–2 months of age and the 3rd dose at 6 months of age.

Infants born to mothers whose HBsAg status is unknown should receive either 5 µg of Merck vaccine (Recombivax HB®) or 10 µg of SB vaccine (Engerix-B®) within 12 hours of birth. The 2nd dose of vaccine is recommended at 1 month of age and the 3rd dose at 6 months of age. Blood should be drawn at the time of delivery to determine the mother's HBsAg status; if it is positive, the infant should receive HBIG as soon as possible (no later than 1 week of age). The dosage and timing of subsequent vaccine doses should be based upon the mother's HBsAg status.

§ Children and adolescents who have not been vaccinated against hepatitis B in infancy can begin the series during any childhood visit. Those who have not previously received 3 doses of hepatitis B vaccine should initiate or complete the series during the 11 to 12-year-old visit. The 2nd dose should be administered at least 1 month after the 1st dose, and the 3rd dose should be administered at least 4 months after the 1st dose and at least 2 months after the 2nd dose.

¶ DTaP (diphtheria and tetanus toxoids and acellular pertussis vaccine) is the preferred vaccine for all doses in the vaccination series, including completion of the series in children who have received >1 dose of whole-cell DTP vaccine. The 4th dose of DTaP may be administered as early as 12 months of age, provided 6 months have elapsed since the 3rd dose, and if the child is considered unlikely to return at 15–18 months of age. Td (tetanus and diphtheria toxoids, adsorbed, for adult use) is recommended at 11–12 years of age if at least 5 years have elapsed since the last dose of DTaP or DT. Subsequent routine Td boosters are recommended every 10 years.

** Three *H. influenzae* type b (Hib) conjugate vaccines are licensed for infant use. If PRP-OMP (PedvaxHib®) (Merck) is administered at 2 and 4 months of age, a dose at 6 months is not required. After the primary series has been completed any Hib conjugate vaccine may be used as a booster.

†† Inactivated poliovirus vaccine (IPV) is the only polio vaccine recommended for HIV-infected persons and their household contacts. Although the third dose of IPV is generally administered at 12–18 months, the third dose of IPV has been approved to be administered as early as 6 months of age. Oral poliovirus vaccine (OPV) should not be administerd to HIV-infected persons or their household contacts.

§§ MMR should not be administered to severely immunocompromised children. HIV-infected children without severe immunosupression should routinely receive their first dose of MMR as soon as possible upon reaching the first birthday. Consideration should be given to administering the second dose of MMR vaccine as soon as 1 month (i.e., minimum 28 days) after the first dose, rather than waiting until school entry.

¶¶ Influenza virus vaccine should be administered to all HIV-infected children >6 months of age each year. Children aged 6 months–8 years years who are receiving influenza vaccine for the first time should receive two doses of split virus vaccine separated by at least 1 month. In subsequent years, a single dose of vaccine (split virus for persons ≤12 years of age, whole or split virus for persons >12 years of age) should be administered each year. The dose of vaccine for children aged 6–35 months is 0.25 mL: the dose for children aged ≥3 years is 0.5 mL.

*** The 23-valent pneumococcal vaccine should be administered to HIV-infected children at 24 months of age. Revaccination should generally be offered to HIV-infected children vaccinated 3–5 years (children aged ≤10 years) or >5 years (children aged >10 years) earlier.

††† Varicella zoster virus vaccine, 0.5 mL, is given as a subcutaneous dose between 12 months and 12 years of age; a second dose should be given 3 months later. The vaccine should be given only to asymptomatic, nonimmunosuppressed children.

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

Pathogen	Preventive Regimens		
	Indication	**First Choice**	**Alternatives**
I. Strongly recommended as standard of care			
*Pneumocystis carinii**	HIV-infected or HIV-indeterminate, infants aged 1–12 mo; HIV-infected children aged 1–5 yr with CD4+ count <500/μL or CD4+ percentage <15%; HIV-infected children aged 6–12 yr with CD4+ count <200/μL or CD4+percentage <15%	Trimethoprim-sulfamethoxazole (TMP-SMZ), 150/750 mg/m^2/d in 2 divided doses po t.i.w. on consecutive days (AII) Acceptable alternative dosage schedules: (AII) • Single dose po t.i.w. on consecutive days; • 2 divided doses po q.d.; 2 divided doses po t.i.w. on alternate days	Dapsone (children aged ≥1 mo), 2 mg/kg (max 100 mg) po q.d. or 4 mg/kg (max 200 mg) po q.w. (CII); aerosolized pentamidine (children aged ≥5 yr), 300 mg q.m. via Respirgard II™ nebulizer (CIII); atovaquone (children aged 1–3 mo. and >24 mo., 30 mg/kg po q.d.; children aged 4–24 mo., 45 mg/kg po q.d.) (CII)
Mycobacterium tuberculosis†			
Isoniazid-sensitive	TST reaction, ≥5mm *or* prior positive TST result without treatment *or* contact with case of active tuberculosis	Isoniazid 10–15 mg/kg (max 300 mg) po q.d. x 9 mo (AII) or 20–30 mg/kg (max 900 mg) po b.i.w. x 9 mo (BIII)	Rifampin, 10–20 mg/kg (max 600 mg) po q.d. x 4–6 mo (BIII)
Isoniazid-resistant	Same as above; high probability of exposure to isoniazid-resistant tuberculosis	Rifampin, 10–20 mg/kg (max 600 mg) po q.d. x 4–6 mo (BIII)	Uncertain
Multidrug-(isoniazid and rifampin) resistant	Same as above; high probability of exposure to multidrug-resistant tuberculosis	Choice of drugs requires consultation with public health authorities	None
Mycobacterium avium complex†	For children aged ≥6 yrs, CD4+ count <50/μL; aged 2–6 yrs, CD4+ count <75/μL; aged 1–2 yrs, CD4+ count <500/μL; aged <1 yr, CD4+ count <750/μL	Clarithromycin, 7.5 mg/kg (max 500 mg) po b.i.d. (AII), or azithromycin, 20 mg/kg (max 1,200 mg) po q.w. (AII)	Azithromycin, 5 mg/kg (max 250 mg) po q.d. (AII); children aged ≥6 yrs, rifabutin, 300 mg po q.d. (BI)
Varicella zoster virus§	Significant exposure to varicella or shingles with no history of chickenpox or shingles	Varicella zoster immune globulin (VZIG), 1 vial (1.25 mL)/10 kg (max 5 vials) im, administered ≤96 hrs after exposure, ideally within 48 hrs (AII)	None

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

Pathogen	Preventive Regimens		
	Indication	First Choice	Alternatives
Vaccine-preventable pathogens¶	HIV exposure/infection	Routine immunizations (see Table 10)	None
II. Generally recommended			
*Toxoplasma gondii***	IgG antibody to *Toxoplasma* and severe immunosuppression	TMP-SMZ, 150/750 mg/m^2/d in 2 divided doses po q.d. (BIII)	Dapsone (children aged ≥1 mo), 2 mg/kg or 15 mg/m^2 (max 25 mg) po q.d. *plus* pyrimethamine, 1 mg/kg po q.d. *plus* leucovorin, 5 mg po every 3 days (BIII) Atovaquone, (aged 1–3 mo. and >24 mo., 30 mg/kg po q.d.; aged 14–24 mo. 45 mg/kg po q.d.) (CIII)
Varicella zoster virus¶	HIV-infected children who are asymptomatic and not immunosuppressed	Varicella zoster vaccine (see vaccine-preventable pathogens section of this table) (BII)	None
Influenza virus¶	All patients (annually, before influenza season)	Influenza vaccine (see vaccine-preventable pathogens section of this table) (BIII)	Rimantadine or amantadine (during outbreaks of influenza A); aged 1–9 yr, 5 mg/kg in 2 divided doses po q.d.; aged ≥10 yr, use adult doses (CIII)
III. Not recommended for most children; indicated for use only in unusual circumstances			
Invasive bacterial infections††	Hypogammaglobulinemia (i.e., IgG <400 mg/dL)	IVIG (400mg/kg every 2–4 wks) (AI)	None
Cryptococcus neoformans	Severe immunosuppression	Fluconazole, 3–6 mg/kg po q.d. (CII)	Itraconazole, 2–5 mg/kg po every 12–24 h (CII)
Histoplasma capsulatum	Severe immunosuppression, endemic geographic area	Itraconazole, 2–5 mg/kg po every 12–24 h (CIII)	None
Cytomegalovirus (CMV)§§	CMV antibody positivity and severe immunosuppression	Oral ganciclovir 30 mg/kg po t.i.d. (CII)	None

NOTES: Information included in these guidelines might not represent Food and Drug Administration (FDA) approval or approved labeling for the particular products or indications in question. Specifically, the terms "safe" and "effective" might not be synonymous with the FDA-defined legal standards for product approval. The Respirgard II™ nebulizer is manufactured by Marquest, Englewood, Colorado. Letters and Roman numerals in parentheses after regimens indicate the strength of the recommendation and the quality of the evidence supporting it (see Box, page 3).

ABBREVIATIONS: b.i.w. = twice a week; IVIG = intravenous immune globulin; q.d. = daily; q.m. = monthly; t.i.d. = three times a day; t.i.w. = three times a week.

* Daily TMP-SMZ reduces the frequency of some bacterial infections. TMP-SMZ, dapsone-pyrimethamine, and possibly atovaquone (with or without pyrimethamine) appear to 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 (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 HIV. Ped Infect Dis J 1999;18:432–9). The efficacy of parenteral pentamidine (e.g., 4 mg/kg q 2–4 wks) is controversial. Patients receiving therapy for toxoplasmosis with sulfadiazine-pyrimethamine are protected against PCP and do not need TMP-SMZ.

† Significant drug interactions might occur between rifamycins (rifampin and rifabutin) and protease inhibitors and nonnucleoside reverse transcriptase inhibitors. Consult a specialist.

§ 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 HIV-exposed children should be immunized according to the childhood immunization schedule in this report (Table 10), which has been adapted from the January–December 1999 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 inactivated poliovirus vaccine (IPV) replaces oral poliovirus vaccine (OPV), and vaccination against influenza (BIII) and *Streptococcus pneumoniae* (BII) should be offered. MMR should not be administered to severely immunocompromised children (DIII). Vaccination against varicella is indicated only for asymptomatic nonimmunosuppressed children (BII), and rotavirus vaccine is contraindicated in all HIV-infected children (EIII). Once 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 may be used with or without pyrimethamine. Pyrimethamine alone probably provides little, if any, protection (for definition of severe immunosuppression, see Table 9).

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

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

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

Pathogen	Preventive Regimens		
	Indication	First Choice	Alternative
I. Recommended for life as standard of care			
Pneumocystis carinii	Prior *P. carinii* pneumonia	TMP-SMZ, 150/750 mg/m^2 /d in 2 divided doses po t.i.w. on consecutive days (AII) Acceptable alternative schedules for same dosage: (AII) Single dose po t.i.w. on consecutive days; 2 divided doses po q.d; 2 divided doses po t.i.w. on alternate days	Dapsone (children aged ≥1 mo), 2 mg/kg (max 100 mg) po q.d. or 4 mg/kg (max 200 mg) po q.w. (CII); aerosolized pentamidine (children aged ≥5 yrs), 300 mg q.m. via Respirgard II™ nebulizer (CIII); atovaquone (aged 1–3 mo. and >24 mo., 30 mg/kg po q.d.; aged 4–24 mo., 45 mg/kg po q.d.) (CII)
*Toxoplasma gondii**	Prior toxoplasmic encephalitis	Sulfadiazine, 85–120 mg/kg/d in 2–4 divided doses po q.d. *plus* pyrimethamine, 1 mg/kg or 15 mg/m^2 (max 25 mg) po q.d. *plus* leucovorin, 5 mg po every 3 days (AI)	Clindamycin, 20–30 mg/kg/d in 4 divided doses po q.d. *plus* pyrimethamine, 1 mg/kg po q.d. *plus* leucovorin, 5 mg po every 3 days (BI)
Mycobacterium avium complex†	Prior disease	Clarithromycin, 7.5 mg/kg (max 500 mg) po b.i.d. (AII) *plus* ethambutol, 15 mg/kg (max 900 mg) po q.d. (AII); with or without rifabutin, 5 mg/kg (max 300 mg) po q.d. (CII)	Azithromycin, 5 mg/kg (max 250 mg) po q.d. (AII) *plus* ethambutol, 15 mg/kg (max 900 mg) po q.d. (AII); with or without rifabutin, 5 mg/kg (max 300 mg) po q.d. (CII)
Cryptococcus neoformans	Documented disease	Fluconazole, 3–6 mg/kg po q.d. (AII)	Amphotericin B, 0.5–1.0 mg/kg iv 1–3x/week (AI); itraconazole, 2–5 mg/kg po every 12–24h (BII).
Histoplasma capsulatum	Documented disease	Itraconazole, 2–5 mg/kg po every 12–48 h (AIII)	Amphotericin B, 1.0 mg/kg iv q.w. (AIII)
Coccidioides immitis	Documented disease	Fluconazole, 6 mg/kg po q.d. (AIII)	Amphotericin B, 1.0 mg/kg iv q.w. (AIII); itraconazole, 2–5 mg/kg po every 12–48 h (AIII)

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

Pathogen	Preventive Regimens		
	Indication	First Choice	Alternative
Cytomegalovirus	Prior end-organ disease	Ganciclovir, 5 mg/kg iv q.d.; or foscarnet, 90–120 mg/kg iv q.d. (AI)	(For retinitis) Ganciclovir sustained-release implant every 6–9 mo. *plus* ganciclovir, 30 mg/kg po t.i.d. (BIII)
Salmonella species (non-*typhi*)§	Bacteremia	TMP-SMZ, 150/750 mg/m^2 in 2 divided doses po q.d. for several months (CIII)	Antibiotic chemoprophylaxis with another active agent (CIII)
II. Recommended only if subsequent episodes are frequent or severe			
Invasive bacterial infections¶	>2 infections in 1-year period	TMP-SMZ, 150/750 mg/m^2, in 2 divided doses po q.d. (BI); *or* IVIG, 400 mg/kg every 2–4 wks. (BI)	Antibiotic chemoprophylaxis with another active agent (BIII)
Herpes simplex virus	Frequent/severe recurrences	Acyclovir, 80 mg/kg/d in 3–4 divided doses po q.d. (AII)	
Candida (oropharyngeal)	Frequent/severe recurrences	Fluconazole, 3–6 mg/kg po q.d. (CIII)	
Candida (esophageal)	Frequent/severe recurrences	Fluconazole, 3–6 mg/kg po q.d. (BIII)	Itraconazole solution, 5 mg/kg po q.d. (CIII); ketoconazole, 5–10 mg/kg po every 24–12h (CIII)

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ABBREVIATIONS: IVIG = intravenous immune globulin; po = by mouth; q.d. = daily; q.m. = monthly; q.w. = weekly; t.i.d. = three times a day; t.i.w. = three times a week; and TMP-SMZ = trimethoprim-sulfamethoxazole.

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

† Significant drug interactions might occur between rifabutin and protease inhibitors and nonnucleoside reverse transcriptase inhibitors. Consult an expert.

§ Drug 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 in persons aged <18 years; therefore, it should be used in children with caution and only if no alternatives exist.

¶ Antimicrobial prophylaxis should be chosen based on the microorganism and antibiotic sensitivities. TMP-SMZ, if used, should be administered daily. Providers should be cautious about 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 may be considered for children who have recurrent bacterial infections despite TMP-SMZ prophylaxis. Choice of antibiotic prophylaxis vs. 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), not monoclonal RSV antibody, may be substituted for IVIG during the RSV season to provide broad antiinfective protection, if this product is available.

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

Opportunistic Illness	Criteria for Discontinuing Prophylaxis		Criteria for Restarting Prophylaxis
	Primary	Secondary	
Pneumocystis carinii pneumonia	CD4+ >200 cells/μL for >3–6 months (CII)	No criteria recommended for stopping	Same as criteria for initiating (CIII)
Disseminated *Mycobacterium avium* complex	CD4+ >100 cells/μL for >3–6 months; sustained suppression of HIV plasma RNA (CII)	No criteria recommended for stopping	Same as criteria for initiating (CIII)
Toxoplasmosis	No criteria recommended for stopping	No criteria recommended for stopping	Not applicable
Cryptococcosis	Not applicable	No criteria recommended for stopping	Not applicable
Histoplasmosis	Not applicable	No criteria recommended for stopping	Not applicable
Coccidioidomycosis	Not applicable	No criteria recommended for stopping	Not applicable
Cytomegalovirus retinitis	Not applicable	• CD4+ >100–150 cells/μL for >3–6 months • Durable suppression of HIV plasma RNA • Nonsight–threatening lesion • Adequate vision in contralaterial eye • Regular ophthalmic examination (CIII)	Restart maintenance when CD4+ <50–100 cells/μL (CIII).

*The safety of discontinuing prophylaxis in children whose CD4+ counts have increased in response to highly active antiretroviral therapy has not been studied.

APPENDIX. Recommendations to Help Patients Avoid Exposure to Opportunistic Pathogens*

SEXUAL EXPOSURES

1. 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 an HIV strain 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 as a risk-reduction strategy (BIII).

2. 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 and B) (BIII).

INJECTION DRUG USE EXPOSURES

1. Injection drug use is a complex behavior that puts HIV-infected persons at risk for hepatitis C virus infection, additional, possibly drug-resistant strains of HIV, and other blood-borne pathogens. Providers should assess the individual'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).

2. If they are continuing to inject drugs, patients should be advised (BIII)

- to never reuse or share syringes, needles, water, or drug preparation equipment; if, nonetheless, injection equipment that has been used by other persons is shared, to first clean the equipment with bleach and water (U.S. Public Health Service. HIV prevention bulletin: medical advice for persons who inject illicit drugs. May 8, 1997. Rockville, Maryland: CDC, 1997);
- to use only sterile syringes obtained from a reliable source (e.g., pharmacies or syringe exchange programs);
- to use sterile (e.g., boiled) water to prepare drugs; if not possible, to use clean water from a reliable source (e.g., fresh tap water); to use a new or disinfected container ("cooker") and a new filter ("cotton") to prepare drugs;
- to clean the injection site with a new alcohol swab before injection;
- to safely dispose of syringes after one use.

*Letters and Roman numerals in parentheses indicate the strength of the recommendation and the quality of evidence supporting it (see Box, page 3).

ENVIRONMENTAL AND OCCUPATIONAL EXPOSURES

1. 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 about 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.

2. Child-care providers and parents of children in child care are at increased risk for acquiring CMV infection, cryptosporidiosis, and other infections (e.g., hepatitis A and giardiasis) from children. The risk for acquiring infection can be diminished by good hygienic practices, such as 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).

3. 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, the available data are insufficient to justify a recommendation against work in such settings.

4. Contact with young farm animals, especially animals with diarrhea, should be avoided to reduce the risk for cryptosporidiosis (BII).

5. Hand washing after gardening or other contact with soil might reduce the risk for cryptosporidiosis and toxoplasmosis (BIII).

6. 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).

7. 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.

General

1. 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*.

2. When obtaining a new pet, HIV-infected patients should avoid animals aged <6 months (or < 1 year for cats; see Cats section, which follows), especially 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, especially those with diarrhea, should be examined by a veterinarian for *Cryptosporidium*, *Salmonella*, and *Campylobacter* (BIII).

3. Patients should wash their hands after handling pets (especially 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

4. 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).

5. Litter boxes should be cleaned daily, preferably by an HIV-negative, nonpregnant person; if the HIV-infected patient performs this task, he or she should wash hands thoroughly afterward to reduce the risk for toxoplasmosis (BIII).

6. To 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).

7. Although declawing is not generally 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).

8. Care of cats should include flea control to reduce the risk for *Bartonella* infection (CIII).

9. Testing cats for toxoplasmosis (EII) or *Bartonella* infection (DII) is not recommended.

Birds

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

Other

11. Contact with reptiles (e.g., snakes, lizards, iguanas, and turtles) should be avoided to reduce the risk for salmonellosis (BIII).

12. Gloves should be used during the cleaning of aquariums to reduce the risk for infection with *Mycobacterium marinum* (BIII).

13. Contact with exotic pets (e.g., nonhuman primates) should be avoided (CIII).

FOOD- AND WATER-RELATED EXPOSURES

1. Raw or undercooked eggs (including foods that might contain raw eggs [e.g., some preparations of hollandaise sauce, Caesar and certain other salad dressings, and mayonnaise]); raw or undercooked poultry, meat, seafood; and unpasteurized dairy products might contain enteric pathogens. Poultry and meat should be cooked until no longer pink in the middle (internal temperature, >165 F° [73.8 C°]). Produce should be washed thoroughly before being eaten (BIII).

2. 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).

3. Although the incidence of listeriosis is low, it is a serious disease that occurs unusually frequently among HIV-infected persons who are severely immunosuppressed. Some soft cheeses and some ready-to-eat foods (e.g., hot dogs and cold cuts from delicatessen counters) have been known to cause listeriosis. An HIV-infected person who is severely immunosuppressed and who wishes to reduce the risk for foodborne disease can prevent listeriosis by reheating these foods until they are steaming before eating them (CIII).

4. 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 likely to be contaminated with human or animal waste and should avoid swallowing water during swimming (BII).

5. During outbreaks or in other situations in which a community "boil water advisory" is issued, boiling water for 1 minute will eliminate the risk for acquiring cryptosporidiosis (AI). Using submicron, personal-use water filters (home/office types) and/or drinking bottled water might also reduce the risk (see Cryptosporidiosis section in Disease-Specific Recommendations for information on personal-use filters and bottled water) (CIII). Current 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 may 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, the cost of the products, 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 (unpasteurized) or heat-treated (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

1. Travel, particularly to developing countries, might result in significant risks for the exposure of HIV-infected persons to opportunistic pathogens, especially for patients who are severely immunosuppressed. Consultation with health-care providers and/or with experts in travel medicine will help patients plan itineraries (BIII).

2. During travel to developing countries, HIV-infected persons are at even higher risk for foodborne and waterborne infections than they are in the United States. Foods and beverages — in particular, 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 generally safe include steaming-hot foods, fruits that are peeled by the traveler, bottled (especially carbonated) beverages, hot coffee or tea, beer, wine, and water brought to a rolling boil for 1 minute (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).

3. 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).

4. 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, several studies (none involving an HIV-infected population) have shown that prophylaxis can reduce the risk for diarrhea among travelers (CDC. Health information for international travel, 1999–2000. Atlanta, Georgia: U.S. Department of Health and Human Services, 1999:202). Under selected circumstances (e.g., those in which the risk for infection is very high and the period of travel brief), the provider and patient may 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 (BIII), although fluoroquinolones should not be given to children or pregnant women. Trimethoprim-sulfamethoxazole (TMP-SMZ) (one double-strength tablet daily) also has been shown to be effective, but resistance to this drug is now common in tropical areas. Persons already taking TMP-SMZ for prophylaxis against *Pneumocystis carinii* pneumonia (PCP) might gain some 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 the high rates of adverse reactions and the possible need for the agent for other purposes (e.g., PCP prophylaxis) in the future.

5. All HIV-infected travelers to developing countries should carry a sufficient supply of an antimicrobial agent to be taken empirically should diarrhea develop (BIII). One appropriate regimen is 500 mg of ciprofloxacin twice a day 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 develops. Antiperistaltic agents (e.g., diphenoxylate and loperamide) are used for the treatment of 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 beyond 48 hours (AII). Antiperistaltic agents are not recommended for children (DIII).

6. Travelers should be advised about 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 using towels on beaches) in areas where fecal contamination of soil is likely (BIII).

7. In general, 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 may 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 in 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.

8. In general, killed vaccines (e.g., diphtheria-tetanus, rabies, hepatitis A, 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 currently available cholera vaccine is not recommended for persons following a usual tourist itinerary, even if travel includes countries reporting cases of cholera (DII).

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

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