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

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

PREFACE

In the United States, opportunistic infections reduce the quality and duration of life for approximately 1 million persons who have HIV infection (*1*), especially for the estimated 250,000 persons who are severely immunosuppressed, as measured by a CD4+ T-lymphocyte count below 200 cells/μL (*2*; CDC, unpublished data). In the late 1980s and early 1990s, efforts to prevent opportunistic infections focused first on chemoprophylaxis against *Pneumocystis carinii* pneumonia (PCP) (*3,4*), and then on chemoprophylaxis against disseminated *Mycobacterium avium* complex (MAC) disease (*5*).

During the past decade, clinicians and researchers have learned that, in addition to *P. carinii* and MAC, other pathogens can cause disease in patients with HIV infection. Knowledge regarding the reduction of risk of exposure to, and thus acquisition of, opportunistic pathogens also has increased. During this decade, the number of chemoprophylactic regimens available for preventing disease also has increased. Information about preventing exposure and preventing disease is often published in journals that are not regularly reviewed by health-care providers; some of it has not yet been published.

In 1994, the U.S Public Health Service (USPHS)—-primarily through the efforts of CDC and the National Institutes of Health (NIH) and the Infectious Diseases Society of America (IDSA)—-recognized the importance of preventing oportunistic infections and the need to consolidate information for health-care providers. In response, these organizations initiated an effort to develop comprehensive recommendations for the prevention of opportunistic infections in HIV-infected persons. Draft recommendations were reviewed by consultants from CDC, NIH, and IDSA, as well as by members of other Federal and non-Federal agencies, community organizations, physicians caring for HIV-infected persons, and HIV-infected persons themselves. These recommendations were discussed at a 2-day meeting convened by CDC, NIH, and IDSA in Atlanta in September 1994. Comments were solicited from the public, and final recommendations were approved by USPHS and IDSA. These recommendations were also endorsed by the American Academy of Pediatrics, the Infectious Diseases Society of Obstetrics and Gynecology, and the Society of Healthcare Epidemiologists of America. The recommendations are designed for the use of health-care providers, but they also can provide useful information for HIV-infected patients.

The full text of the USPHS/IDSA Guidelines for the Prevention of Opportunistic Infections in Persons Infected with Human Immunodeficiency Virus is being published in a supplement to *Clinical Infectious Diseases* (*6–8*). This report excerpts the disease-specific recommendations that form the basis for the guidelines. These recommendations address 17 opportunistic infections or groups of opportunistic infections by providing guidelines on a) preventing exposure to the opportunistic pathogens, b) preventing the first episode of disease (by chemoprophylaxis or vaccination), and c) preventing disease recurrence (by long-term maintenance drug therapy). This

report also includes the drug regimens used to prevent opportunistic infections in HIV-infected adults and adolescents and infants and children.

Several factors were considered in developing these recommendations, including a) the level of immunosuppression at which opportunistic disease is most likely to occur; b) the incidence of disease; c) the severity of disease in terms of morbidity, cost of care (including hospitalization), and mortality; d) the feasibility, efficacy, and cost of the prevention measure; e) the impact of the prevention measure on the quality of life; and f) (for chemoprophylaxis recommendations) drug toxicities, drug interactions, and the potential for the development of drug resistance.

Recommendations are rated according to the strength of the recommendation for or against use (letters A–E) and the quality of the evidence supporting the recommendation (Roman numerals I–III) (*6*) (Tables 1,2). When applying the letter ratings A–E to recommendations involving chemoprophylaxis, the strength of evidence and magnitude of clinical benefit were balanced against the toxicity, drug interactions, and cost of the chemoprophylactic regimen and the feasibility of alternative approaches such as early diagnosis and treatment of the opportunistic infection. Recommendations designated "A" are supported by evidence that is both statistically and clinically persuasive, are strongly recommended, should always be offered, and are considered standard care. Those designated "B" are recommended for consideration; such measures should generally be offered but should involve some discussion of the pros and cons between the provider and the patient. Measures designated "C" are considered optional, either because evidence of benefit is insufficient or because any proven benefit is minimal from the clinical standpoint and may not outweigh either the toxicity, drug interactions, or cost of the chemoprophylaxis or the feasibility of alternative approaches. Measures designated "D" should generally not be offered; those designated "E" are contraindicated. The Roman numeral ratings I–III refer to the quality of evidence that forms the basis for the recommendations regarding the use of a product or measure for preventing opportunistic infections in HIV-infected persons.

Applying this rating system to recommendations regarding prevention of exposure was complicated by the lack of information regarding the effectiveness of various counseling messages. Therefore, few "prevention of exposure" recommendations are rated "A"; many are considered optional (rating "C"). However, use of the rating system should facilitate understanding of the relative importance of the various prevention recommendations.

The prevention recommendations presented here differ from those previously published because they include strategies for preventing many opportunistic infections not previously discussed, particularly those associated with prevention of exposure. They also modify earlier recommendations. For example, for PCP prophylaxis for sulfa-intolerant patients, either dapsone or dapsone plus pyrimethamine are now recommended in preference to aerosolized pentamidine. For prophylaxis against initial episodes of disseminated MAC disease, the threshold of treatment has been lowered from 100 to 75 CD4+ T-lymphocytes/μL. Chemoprophylaxis against toxoplasmic encephalitis is now recommended.

In this report, the disease-specific recommendations are not listed in priority order. Health-care providers who manage and treat HIV-infected patients should consult the overview of the USPHS/IDSA guidelines, which addresses both the initial and follow-up evaluations of the HIV-infected patient (*7*). In addition to opportunistic infections

addressed in the disease-specific recommendations, the overview of the guidelines briefly addresses other infections that occur with increased frequency in HIV-infected persons (e.g., syphilis, hepatitis B, and other sexually transmitted diseases). Sections on preventing opportunistic infections in children and in pregnant women are included. In this report, only the tables concerning drugs and doses in adults and children (Tables 3a, 3b and 4a, 4b) and the summary of prevention of exposure recommendations (Table 5) have been excerpted from the overview. The approach to preventing opportunistic infections and other infections commonly encountered in HIV-infected persons, as described in the overview, should be integrated with other aspects of HIV care, as described elsewhere (*9).*

Reprints of this article and of individual components of the USPHS/IDSA guidelines can be obtained from the CDC National AIDS Clearinghouse, P.O. Box 6003, Rockville, MD 20849-6003. Telephone: (800) 458-5231.

Categories Reflecting Strength and Quality of Evidence Supporting Recommendations

TABLE 1. Categories reflecting the strength of each recommendation for or against the use of a product or measure for the prevention of opportunistic infection in HIV-infected persons

Category	Definition
A	Both strong evidence and substantial clinical benefit support a recommendation for use.
B	Moderate evidence—or strong evidence for only limited benefit—supports a recommendation for use.
C	Poor evidence supports a recommendation for or against use.
D	Moderate evidence supports a recommendation against use.
E	Good evidence supports a recommendation against use.

NOTE: Modified from Gross et al. (*10*).

TABLE 2. Categories reflecting the quality of evidence forming the basis for recommendations regarding the use of a product or measure for the prevention of opportunistic infection in HIV-infected persons

Category	Definition
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

NOTE: Modified from Gross et al. (*10*).

Disease-Specific Recommendations*

PNEUMOCYSTIS CARINII PNEUMONIA

Prevention of Exposure

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

Prevention of Disease

(2) Adults and adolescents with HIV infection (including those who are pregnant) should receive chemoprophylaxis against PCP if they have a CD4+ lymphocyte count of <200/gmL (AI), unexplained fever (>100° F) for ≥2 weeks (AII), or a history of oropharyngeal candidiasis (AII).

Trimethoprim-sulfamethoxazole (TMP-SMZ) is the preferred prophylactic agent (AI). TMP-SMZ may confer cross-protection against toxoplasmosis (AII) and many bacterial infections (AII). For patients with 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, its reinstitution should be strongly considered (AII). Whether it is best to reintroduce the drug at the original dose or at a lower and gradually increasing dose or to try a desensitization regimen is unknown.

If TMP-SMZ cannot be tolerated, alternative prophylactic regimens include dapsone (AI), dapsone plus pyrimethamine plus leucovorin (AI), and aerosolized pentamidine administered by the Respirgard II nebulizer (Marquest, Englewood, CO) (AI). Regimens including dapsone plus pyrimethamine are also protective against toxoplasmosis (AI) but not against most bacterial infections. Because data on their efficacy for PCP prophylaxis are insufficient, the following regimens generally cannot be recommended for this purpose: aerosolized pentamidine administered by other nebulization devices currently available in the United States, intermittently administered parenteral pentamidine, oral pyrimethamine/sulfadoxine, oral clindamycin plus primaquine, oral atovaquone, and intravenous trimetrexate. However, the use of these agents may be considered in unusual situations in which the recommended agents cannot be administered (CIII).

Prevention of Recurrence

(3) Adults and adolescents with a history of PCP should receive chemoprophylaxis with the regimens indicated above to prevent recurrence (AI).

*These recommendations address 17 opportunistic infections or groups of opportunistic infections and cover prevention of exposure, prevention of the first episode of disease, and prevention of recurrence (including relapse and reinfection). The recommendations are not presented in order of priority; the priorities in preventing opportunistic infections in HIV-infected persons are presented in "USPHS/IDSA Guidelines for the Prevention of Opportunistic Infections in Persons Infected with Human Immunodeficiency Virus: An Overview" (*7*).

Notes

Pediatric Notes

(4) Children born to HIV-infected mothers should receive prophylaxis with TMP-SMZ beginning at 4–6 weeks of age (*11*) (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+ lymphocyte count thresholds (*11,12*) (AII).

(5) Children with a history of PCP should receive chemoprophylaxis as indicated above to prevent recurrence (AI).

Note Regarding Pregnancy

(6) Chemoprophylaxis for PCP should be administered to pregnant women as to other adults and adolescents (AIII), although some providers, because of a general concern about administering drugs during the first trimester of pregnancy, may choose not to initiate such therapy until after the first trimester. Because of the increase in blood plasma volume and the reduced concentrations of drugs during pregnancy, the double-strength (DS) dose of TMP-SMZ (one DS tablet daily) should be used.

TOXOPLASMIC ENCEPHALITIS

Prevention of Exposure

(1) HIV-infected persons should be tested for 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; meat cooked until no longer pink inside generally has an internal temperature of 165° F 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

(3) *Toxoplasma*-seropositive patients with a CD4+ lymphocyte count of <100/gmL should receive prophylaxis against toxoplasmic encephalitis (TE) (AII). The doses of TMP-SMZ recommended for PCP prophylaxis appear to be effective against TE as well (AII). If patients cannot tolerate TMP-SMZ, the regimens including dapsone plus pyrimethamine that are recommended for PCP prophylaxis provide protection against TE (AI). Prophylactic monotherapy with dapsone, pyrimethamine, azithromycin, clarithromycin, or atovaquone cannot be recommended on the basis of current data (DII). Aerosolized pentamidine does not afford protection against TE (EI).

(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+ lymphocyte count falls below 100/gmL to determine whether they have seroconverted and are therefore at risk for TE (CIII). Patients who have seroconverted should receive prophylaxis for TE as described above (AII).

Prevention of Recurrence

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

Notes

Pediatric Note

(6) Current data are insufficient for the formulation of specific guidelines for children. The provider should consider the recommendations for adults; children >12 months of age who are seropositive for IgG antibody to *Toxoplasma*, have a CD4+ lymphocyte count of <100/μL, and are not already taking medication effective against *Toxoplasma* may be considered as candidates for chemoprophylaxis (CIII). Some providers would consider opting for chemoprophylaxis for very young children with higher CD4+ lymphocyte counts consistent with severe immunosuppression (*12*) and with evidence of toxoplasmic infection.

Notes Regarding Pregnancy

(7) 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 for women who are seropositive for IgG antibody to *Toxoplasma* (CIII). TMP-SMZ can be administered as described for prophylaxis of PCP. For prophylaxis of recurrent TE, pyrimethamine should be used with caution (CIII).

(8) In rare cases, HIV-infected pregnant women with serological 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 during pregnancy in consultation with appropriate specialists (CIII). Infants born to women with serological evidence of infections with HIV and *Toxoplasma* should be evaluated for congenital toxoplasmosis (CIII).

CRYPTOSPORIDIOSIS

Prevention of Exposure

(1) HIV-infected persons should be educated and counseled about the many ways that *Cryptosporidium* can be transmitted. Modes of transmission include contact with infected adults and diaper-age children, contact with infected animals, consumption of contaminated drinking water, and contact with contaminated water during recreational activities (BIII).

(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., during diaper changing), after handling of pets, and after gardening or other contact with soil. HIV-infected persons should avoid sexual practices such as oral-anal intercourse that may result in oral exposure to feces (BIII).

(3) HIV-infected persons should be advised that newborn and very young pets may pose a small risk of 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 with diarrhea into their households, should avoid purchasing a dog or cat <6 months of age, and should not adopt stray pets. HIV-infected persons who wish to assume the small risk of acquiring a puppy or kitten <6 months of age 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. Because water can be accidentally ingested, patients should be advised that swimming in lakes, rivers, or public swimming pools may put them at increased risk for infection (BII).

(6) 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 of water for 1 minute will eliminate the risk of cryptosporidiosis (AI). Use of submicron personal-use water filters* (i.e., home/office types) and/or bottled water† (*2*) may reduce the risk (CIII). The magnitude of the risk of acquiring cryptosporidiosis from drinking water in a nonoutbreak setting is uncertain,

* Only filters capable of removing particles 1 μm in diameter and larger 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 may not be capable of removing ≥99% of oocysts.

† Sources of bottled water (wells, springs, municipal tap-water supplies, rivers, lakes) and methods for its disinfection vary; 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 may not result in the removal of ≥99% of oocysts.

and current data are inadequate to recommend that all HIV-infected persons boil or avoid drinking tap water in nonoutbreak settings. However, HIV-infected persons who wish to take independent action to reduce the risk of 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.

Prevention of Disease

(7) No effective chemoprophylactic agents are available for cryptosporidiosis.

Prevention of Recurrence

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

Note

Pediatric Note

(9) At present, no data indicate that formula-preparation practices for infants should be altered in an effort to prevent cryptosporidiosis (CIII).

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 may 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 take into account such factors 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 or not the patient continues with such activities may 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 be screened by the Mantoux method with intermediate-strength (5-TU) PPD (AI). Routine evaluation for anergy is controversial; some experts recommend anergy testing for persons in settings where there is an increased risk of infection with *Mycobacterium tuberculosis* (i.e., in areas where the prevalence of such infection is >10%) (CIII).

(3) All HIV-infected persons with a positive result in the tuberculin skin test (TST; ≥5 mm of induration) should undergo chest radiography and clinical evaluation for the exclusion of active tuberculosis. HIV-infected individuals who have symptoms suggestive of tuberculosis should undergo chest radiography and clinical evaluation regardless of their TST status (AII).

(4) All HIV-infected persons with a positive TST result who have no evidence of active tuberculosis and no history of treatment or prophylaxis for tuberculosis should receive 12 months of preventive chemotherapy with isoniazid (AI). Since HIV-infected persons are at risk for peripheral neuropathy, those receiving isoniazid should also receive pyridoxine (BIII). The decision to use alternative antimycobacterial agents for chemoprophylaxis should be based on the relative risk of exposure to resistant organisms and may require consultation with public health authorities (AII). The need for direct observation as a means of documenting compliance with chemoprophylaxis should be considered on an individual basis (BIII).

(5) HIV-infected individuals who are close contacts of persons with infectious tuberculosis (i.e., acid-fast bacillary smear-positive pulmonary disease) should receive preventive therapy—regardless of TST results or prior courses of chemoprophylaxis—after active tuberculosis has been excluded (AII). Such persons should be tested with 5-TU PPD. If the TST result is initially negative, the individual should be evaluated again 3 months after the discontinuation of contact with the infectious source, and the information obtained should be considered in the course of decisions about whether chemoprophylaxis should continue (BIII).

(6) TST-negative, HIV-infected persons from risk groups or geographic areas with a high prevalence of *M. tuberculosis* infection (>10%) may be at increased risk of tuberculosis. Some experts recommend preventive therapy for anergic individuals or perhaps for all persons in this category (CIII). However, the efficacy of preventive therapy in this group has not been demonstrated, and decisions concerning the use of chemoprophylaxis in these situations must be individualized.

(7) Although the reliability of the TST may diminish as the CD4+ lymphocyte count declines, testing should be repeated at least annually for HIV-infected persons who are TST-negative on initial evaluation (BIII). In addition to documenting tuberculous infection, TST conversion in an HIV-infected person should alert health care providers to

the possibility of an infectious case in the environment and lead to notification of public health officials for investigation to identify a possible source case.

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

Prevention of Recurrence

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

Notes

Pediatric Note

(10) All infants born to HIV-infected mothers should have a TST (5-TU PPD) at 9–12 months of age (CIII). All children living in households with *M. tuberculosis*-infected (TST-positive) persons should be evaluated for tuberculosis (*13*) (CIII); those exposed to a person with active tuberculosis should receive preventive therapy after active tuberculosis has been excluded (AII).

Note Regarding Pregnancy

(11) HIV-infected pregnant women who have a positive TST result without evidence of active tuberculosis should receive standard chemoprophylaxis (AII). When possible, chest radiography should be undertaken and chemoprophylaxis should be initiated after the first trimester in order to avoid the critical period of major organogenesis. Preventive therapy with isoniazid should be accompanied by treatment with pyridoxine so that peripheral neuropathy does not develop. Alternative regimens (e.g., rifampin, rifabutin) should be used with caution during pregnancy.

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

(2) Prophylaxis with rifabutin should be considered for HIV-infected adults and adolescents who have a CD4+ lymphocyte count of <75/μL, although some experts would wait until the count is <50/μL (BII). Disseminated MAC disease should be ruled out (by a negative blood culture) before prophylaxis is initiated. Because treatment with rifabutin may result in the development of resistance to rifampin in individuals with active tuberculosis, the latter condition should be excluded before rifabutin prophylaxis is begun. Drug interactions, partial efficacy, and cost are among the other issues that should be considered in decisions about whether to institute prophylaxis for MAC disease. Data on the safety and efficacy of clarithromycin, azithromycin, and

combinations of clarithromycin or azithromycin with rifabutin have not yet been reviewed sufficiently to warrant recommendations concerning these regimens.

(3) Although the detection of MAC organisms in the respiratory or gastrointestinal tract may be predictive of the development of disseminated MAC infection, no data are available on the efficacy of prophylaxis with 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 at this time (DIII).

Prevention of Recurrence

(4) Patients who are treated for disseminated MAC infection should continue to receive full therapeutic doses for life (BIII). The use of a macrolide, usually clarithromycin, is generally recommended in conjunction with at least one other drug, such as ethambutol, clofazimine, ciprofloxacin, or rifabutin.

Notes

Pediatric Note

(5) HIV-infected children <12 years of age also develop disseminated MAC infections. Prophylaxis should be considered similar to that recommended for adults and adolescents (BI). For children 6–12 years of age, a CD4+ lymphocyte count of <75/μL is a reasonable threshold for the initiation of chemoprophylaxis. Some adjustment for age is necessary in the interpretation of CD4+ lymphocyte counts of children <6 years of age (*12*). No pediatric formulation of rifabutin is currently available, but a dosage of 5 mg/kg has been used in pharmacokinetic studies.

Note Regarding Pregnancy

(6) Information is insufficient for recommendations concerning the use of rifabutin or clarithromycin during pregnancy.

BACTERIAL RESPIRATORY INFECTIONS

Prevention of Exposure

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

Prevention of Disease

(2) As soon as possible after HIV infection is diagnosed, adults should receive a single dose of 23-valent polysaccharide pneumococcal vaccine (BIII). This recommendation is especially pertinent in light of the increasing incidence of invasive infections with drug-resistant strains of *S. pneumoniae*. Although the administration of protein-polysaccharide conjugate *H. influenzae* type b vaccine may be considered, data are insufficient to recommend the use of this vaccine in HIV-infected adults at this time.

(3) TMP-SMZ, administered daily, may be effective in preventing serious bacterial respiratory infections (although not those caused by drug-resistant *S. pneumoniae*); this fact 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) may promote the development of resistant organisms.

(4) An absolute neutrophil count that is depressed because of HIV disease or drug therapy may be increased by granulocyte colony-stimulating factor (G-CSF) or granulocyte-macrophage colony-stimulating factor (GM-CSF). However, data are insufficient for recommendations concerning the use of G-CSF or GM-CSF to prevent bacterial infections in HIV-infected patients with neutropenia.

Prevention of Recurrence

(5) Some clinicians may choose to offer antibiotic chemoprophylaxis to HIV-infected patients with recurrent serious bacterial respiratory infections (BIII). TMP-SMZ, administered for PCP prophylaxis, is appropriate for drug-sensitive organisms.

(6) All invasive pneumococcal isolates from HIV-infected patients should be tested for susceptibility to β-lactam antibiotics, and local patterns of resistance should be considered in the choice of regimens for empirical treatment (AII). Invasive infections due to *H. influenzae* should be treated with regimens effective against β-lactamase-producing strains until drug susceptibilities are known (AII).

Notes

Pediatric Notes

(7) Children with HIV infection should receive *H. influenzae* type b vaccine in accordance with the guidelines of the Advisory Committee for Immunization Practices (*14*) and the American Academy of Pediatrics (*13*) (AII). Children >2 years of age should also receive 23-valent polysaccharide pneumococcal vaccine (BII).

(8) To prevent serious bacterial infections in HIV-infected children with documented antibody deficiency, clinicians should use intravenous immunoglobulin (IVIG) (AI). The administration of IVIG should also be considered for HIV-infected children with recurrent serious bacterial infections (AI), but such treatment may not provide additional benefit to children receiving daily TMP-SMZ.

Note Regarding Pregnancy

(9) Pneumococcal vaccine is not contraindicated during pregnancy.

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 may 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). Produce should be thoroughly washed before being eaten (BIII).

(2) Health care providers should advise HIV-infected persons to avoid cross-contamination of foods. For example, uncooked meats should not come into contact with other foods, and hands, cutting boards, counters, and 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 have also 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 of food-borne disease as much as possible may choose to re-heat such foods until they are steaming hot before eating them (CIII).

Pets

(4) When obtaining a new pet, HIV-infected persons should avoid young animals (<6 months of age), especially those with 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 (such as snakes, lizards, and turtles) because of the risk of salmonellosis (BIII).

Travel

(8) The risk of food- and waterborne infections among immunosuppressed, HIV-infected persons is magnified during travel to developing countries. Those who elect to travel to such countries should avoid foods and beverages that may 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 may 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 upon 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 upon the level of immunosuppression and the region and duration of travel (CIII).

The use of fluoroquinolones—such as ciprofloxacin (500 mg/d)—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 may 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 (e.g., 500 mg of ciprofloxacin b.i.d. for 3–7 days) should be given to patients before their departure, to be taken empirically should traveler's diarrhea develop (BIII). Alternative antibiotics for children and pregnant women should be discussed (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 such as diphenoxylate and loperamide can be used for the treatment of mild diarrhea. However, the use of these drugs should be discontinued if symptoms persist beyond 48 hours. Moreover, these agents should not be given to patients with high fever or with blood in the stool (AII).

(11) Some experts recommend that HIV-infected persons with salmonella gastroenteritis receive antimicrobial therapy to prevent extraintestinal spread. 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 b.i.d. for 14 days)—can be used when antimicrobial therapy is opted for (CIII).

Prevention of Recurrence

(12) HIV-infected persons with salmonella septicemia require long-term therapy for the prevention of recurrence. The fluoroquinolones, primarily ciprofloxacin, are usually the drugs of choice for susceptible organisms (BII).

(13) Household contacts of HIV-infected persons with salmonellosis or shigellosis should be evaluated for 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).

Notes

Pediatric Notes

(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 <3 months of age and all HIV-infected children with severe immunosuppression should receive treatment for salmonella gastroenteritis to prevent extraintestinal spread. Possible choices of antibiotics include TMP-SMZ, ampicillin, cefotaxime, ceftriaxone, or chloramphenicol; ciprofloxacin may be considered for the treatment of children >6 years of age (CIII).

(16) HIV-infected children with salmonella septicemia require long-term therapy for the prevention of recurrence. TMP-SMZ is the drug of choice; ampicillin or chloramphenicol can be used if the organism is susceptible. Ciprofloxacin may be considered for the treatment of children >6 years of age (CIII).

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

Notes Regarding Pregnancy

(18) Since both pregnancy and HIV infection confer a risk for listeriosis, pregnant HIV-infected women should pay particular attention to recommendations concerned with this disease (BII).

(19) Fluoroquinolones should not be used during pregnancy. TMP-SMZ may 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 of developing relatively severe disease due to *Bartonella* species. These individuals should consider the potential risks of cat ownership (CIII). Those who elect to acquire a cat should adopt or purchase an older animal (>1 year of age) 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). HIV-infected persons should not allow cats to lick open cuts or wounds (BIII).

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

(4) There is no evidence of benefit to cat or owner from routine culture or serological testing of the pet for *Bartonella* infection (DII).

Prevention of Disease

(5) No data currently 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).

Note

Pediatric Note

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

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) Although data from a prospective controlled trial indicate that fluconazole can reduce the risk of mucosal (oropharyngeal, esophageal, and vaginal) candidiasis in patients with advanced HIV disease, 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 (DII).

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, intermittent or chronic administration of topical nystatin, topical clotrimazole, or an oral azole (ketoconazole, fluconazole, or itraconazole) may be considered (BI). 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, and drug interactions.

(4) Adults or adolescents with a history of documented esophageal candidiasis, particularly multiple episodes, should be considered candidates for chronic suppressive therapy with fluconazole (BI).

Notes

Pediatric Notes

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

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

CRYPTOCOCCOSIS

Prevention of Exposure

(1) Although HIV-infected persons cannot avoid exposure to *Cryptococcus neoformans* completely, avoiding sites that are likely to be heavily contaminated with *C. neoformans* (e.g., areas heavily contaminated with pigeon droppings) may reduce the risk of infection.

Prevention of Disease

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

(3) Data from a prospective controlled trial indicate that fluconazole can reduce the frequency of cryptococcal disease among patients with advanced HIV disease; thus, physicians may wish to consider chemoprophylaxis for adult and adolescent patients with a CD4+ lymphocyte count of <50/μL (BI). However, such prophylaxis should not be offered routinely because of the relative infrequency of cryptococcal disease, the possibility of drug interactions, the potential for development of resistance, and the cost of prophylaxis (DII). The need for prophylaxis or suppressive therapy for other fungal infections (e.g., candidiasis) should be considered in the course of decisions about prophylaxis for cryptococcosis.

Prevention of Recurrence

(4) Patients who complete initial therapy for cryptococcosis should receive lifelong suppressive treatment with fluconazole (AI).

Notes

Pediatric Note

(5) There are no data on which to base specific recommendations for children, but lifelong suppressive therapy with fluconazole after an episode of cryptococcosis is appropriate (CIII).

Note Regarding Pregnancy

(6) Although treatment with fluconazole is indicated to prevent the recurrence of cryptococcosis, this drug should be used with caution in pregnant women (CIII). At high doses, fluconazole has been associated with both fetal death and increased rates of fetal abnormalities in rats.

HISTOPLASMOSIS

Prevention of Exposure

(1) Although HIV-infected persons living in or visiting histoplasmosis-endemic areas cannot completely avoid exposure to *Histoplasma capsulatum*, they should avoid activities known to be associated with increased risk (e.g., cleaning chicken coops, disturbing soil beneath bird-roosting sites, and exploring caves) (CIII).

Prevention of Disease

(2) Routine skin testing with histoplasmin in histoplasmosis-endemic areas is not predictive of disease and should not be performed (EII).

(3) No recommendation can be made regarding chemoprophylaxis for HIV-infected persons in histoplasmosis-endemic areas or for histoplasmin-positive persons in nonendemic areas.

Prevention of Recurrence

(4) Patients who complete initial therapy should receive lifelong suppressive treatment with itraconazole (AII).

Note

Pediatric Note

(5) Because primary histoplasmosis can lead to disseminated infection in children, HIV-infected children with histoplasmosis should receive suppressive therapy for life (CIII).

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 soil as occurs at building excavation sites, on farms, 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 (EII).

(3) No recommendation can be made regarding routine chemoprophylaxis for HIV-infected individuals who live in coccidioidomycosis-endemic areas or for skin test-positive persons in nonendemic areas.

Prevention of Recurrence

(4) Patients who complete initial therapy for coccidioidomycosis should receive lifelong systemic suppressive treatment (AII). Fluconazole is the preferred agent; alternative drugs include itraconazole, ketoconazole, and amphotericin B.

Note

Pediatric Note

(5) Although no specific data are available on coccidioidomycosis in HIV-infected children, it is reasonable to administer lifelong suppressive therapy after an acute episode of the disease (CIII).

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 anticipate possible exposure to CMV

(e.g., through blood transfusion or employment in a child-care facility) should be tested for antibody to CMV (BIII). These groups include patients who have not had male homosexual contact and those who are not injection drug users.

(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 of exposure to this virus 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—like all children at these facilities—are at increased risk of acquiring CMV infection (BI). Parents and other caretakers of HIV-infected children should be advised of the increased risk to children at these centers (BIII). The risk of 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 receive only CMV antibody-negative or leukocyte-reduced cellular blood products in nonemergency situations (*15*) (BIII).

Prevention of Disease

(5) Data on the efficacy and safety of oral ganciclovir have not yet been adequately reviewed; thus no recommendation concerning this drug can be made at this time. Acyclovir is not effective in preventing CMV disease (EII). Since no chemoprophylactic agent is currently available, 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 and undergoes regular funduscopic examinations performed by a health care provider (CIII). 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 simple techniques such as reading newsprint (BIII).

Prevention of Recurrence

(6) CMV disease is not cured with courses of the currently available antiviral agents ganciclovir and foscarnet. Chronic suppressive or maintenance therapy is indicated. The presently approved regimens include parenteral or oral ganciclovir or parenteral foscarnet (AI). In spite of maintenance therapy, recurrences develop routinely and require reinstitution of high-dose induction therapy.

Note

Pediatric Note

(7) The recommendations for the prevention of CMV disease and of its recurrence apply to children as well as to adolescents and adults. However, oral ganciclovir has not been studied in children.

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 of 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 with frequent or severe recurrences can be given daily suppressive therapy with oral acyclovir (AI). Intravenous foscarnet can be used for the treatment of infection due to acyclovir-resistant isolates of HSV, which are routinely resistant to ganciclovir as well (AI).

Notes

Pediatric Note

(4) The recommendations for the prevention of initial disease and recurrence apply to children as well as to adolescents and adults.

Note Regarding Pregnancy

(5) The effectiveness of suppressive treatment with acyclovir in reducing the risk of perinatal HSV transmission has not been studied. Therefore, no relevant recommendation can be made.

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 are seronegative for VZV—should avoid exposure to persons with chickenpox or shingles (AII).

Prevention of Disease

(2) For the prophylaxis of chickenpox, HIV-infected children and adults who are susceptible to VZV should be given zoster immune globulin within 96 hours after close contact with a patient with chickenpox or shingles (AI). Data are lacking on the effectiveness of acyclovir for preventing chickenpox in HIV-infected children or adults.

* Controversy exists over the possible association of acyclovir therapy with prolonged survival of HIV-infected persons. Current data suggest that chronic acyclovir therapy may be considered but should not be standard practice (CIII).

(3) No preventive measures are currently available for shingles.

Prevention of Recurrence

(4) Recurrence of shingles is unusual, and no drug has been proven to prevent recurrence.

Note

Note Regarding Pregnancy

(5) Zoster immune globulin is not contraindicated during pregnancy and should be given to VZV-susceptible pregnant women after exposure to VZV (AI).

HUMAN PAPILLOMAVIRUS INFECTION

Prevention of Exposure

(1) HIV-infected persons should use latex condoms during every act of sexual intercourse to reduce the risk of exposure to human papillomavirus (HPV) as well as to other sexually transmitted pathogens (AII).

Prevention of Disease

HPV-Associated Genital Epithelial Cancers in HIV-Infected Women

(2) HIV-infected women should have annual cervical Pap smears as part of their initial and routine gynecologic care. In accordance with the recommendation of the Agency for Health Care Policy and Research (*9*), a 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 an HIV-infected woman has a history of abnormal Pap smears, the caregiver may choose to monitor this individual with Pap smears every 6 months (BIII).

(4) If the initial or follow-up Pap smear indicates inflammation with reactive squamous cellular changes, further management should be guided by diagnosis of the cause of the inflammation, and another Pap smear should be collected within 3 months (BIII). HIV-infected women with Pap smears showing only atypical cells of undetermined significance can be monitored with annual Pap smears (BIII).

(5) Controversy exists concerning the management of HIV-infected women with low-grade squamous intraepithelial lesions (SIL) evident on the cervical Pap smear; the natural history of this finding in this population has not yet been well defined. Some experts would collect another Pap smear within 3 months. If subsequent Pap smears again showed low-grade SIL, some of these authorities would refer the patient for colposcopic evaluation and biopsy (if indicated); while others would monitor compliant patients with repeat Pap smears at frequent intervals (e.g., every 3–6 months) (BIII). Other experts would refer all HIV-infected patients with low-grade SIL for colposcopy (BIII).

(6) If a Pap smear indicates high-grade SIL or squamous cell carcinoma, the woman should be referred for colposcopic examination and, if indicated, colposcopically directed biopsy (AI).

HPV-Associated Anal Intraepithelial Neoplasia and Anal Cancer in HIV-Infected Men Who Have Sex with Men

(7) Although the risks for anal intraepithelial neoplasia (AIN) and anal cancer are increased among HIV-infected men who have sex with men, the role of anal cytological screening and treatment of AIN in preventing anal cancer in these men is not well defined. Therefore, no recommendations can be made for periodic anal cytological screening for the detection and treatment of AIN.

Prevention of Recurrence

(8) The risks for recurrence of SIL 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 cytological screening and, when indicated, with colposcopic examination for recurrent lesions (AI).

Note

Pediatric Note

(9) Newborns have been known to acquire laryngeal HPV from their mothers. No recommendations can currently be made to prevent such acquisition.

Drug Regimens for Adults and Adolescents

TABLE 3A. Prophylaxis for first episode of opportunistic disease in HIV-infected adults and adolescents

Pathogen	Indication	Preventive regimens: First choice	Preventive regimens: Alternatives
I. Strongly recommended as standard of care			
*Pneumocystis carinii**	$CD4^+$ count of <200/μL *or* unexplained fever for ≥2 w *or* oropharyngeal candidiasis	TMP-SMZ, 1 DS po q.d. (AI)	TMP-SMZ, 1 SS po q.d. (AI) or 1 DS po t.i.w. (AII); dapsone, 50 mg po b.i.d. or 100 mg po q.d., (AI); dapsone, 50 mg po q.d., *plus* pyrimethamine, 50 mg po q.w., *plus* leucovorin, 25 mg po q.w. (AI); dapsone, 200 mg po q.w., *plus* pyrimethamine, 75 mg po q.w., *plus* leucovorin, 25 mg po q.w. (AI); aerosolized pentamidine, 300 mg q.m. via Respirgard II nebulizer (AI)
Mycobacterium tuberculosis†			
Isoniazid-sensitive	TST reaction of ≥5 mm *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 12 mo (AI); *or* isoniazid, 900 mg po, *plus* pyridoxine, 50 mg po b.i.w. x 12 mo (BIII)	Rifampin, 600 mg po q.d. x 12 mo (BII)
Isoniazid-resistant	Same as above; high probability of exposure to isoniazid-resistant tuberculosis	Rifampin, 600 mg po q.d. x 12 mo (BII)	Rifabutin, 300 mg po q.d. x 12 mo (CIII)
Multidrug-resistant (isoniazid and rifampin)	Same as above; high probability of exposure to multidrug-resistant tuberculosis	Choice of drugs requires consultation with public health authorities	None
Toxoplasma gondii§	IgG antibody to Toxoplasma and $CD4^+$ count of <100/μL	TMP-SMZ, 1 DS po q.d. (AII)	TMP-SMZ, 1 SS po q.d. *or* 1 DS po t.i.w. (AII); dapsone, 50 mg po q.d., *plus* pyrimethamine, 50 mg po q.w., *plus* leucovorin, 25 mg po q.w. (AI)
II. Recommended for consideration in all patients			
Streptococcus pneumoniae¶	All patients	Pneumococcal vaccine, 0.5 mL im x 1 (BIII)	None
Mycobacterium avium complex**	$CD4^+$ count of <75/μL	Rifabutin, 300 mg po q.d. (BII)	Clarithromycin, 500 mg po b.i.d. (CIII); azithromycin, 500 mg po t.i.w. (CIII)
III. Not recommended for most patients; indicated for consideration *only* in selected populations or patients			
Bacteria	Neutropenia	Granulocyte colony-stimulating factor 5–10 μg/kg sc q.d. x 2–4 w; *or* granulocyte-macrophage colony-stimulating factor, 250 $\mu g/m^2$, i v over 2 h q.d. x 2–4 w (CIII)	None
Candida species	$CD4^+$ count of <50/μL	Fluconazole, 100–200 mg po q.d. (CI)	Ketoconazole, 200 mg po q.d. (CIII)

TABLE 3A. Prophylaxis for first episode of opportunistic disease in HIV-infected adults and adolescents — Continued

Pathogen	Indication	Preventive regimens: First choice	Preventive regimens: Alternatives
Cryptococcus neoformans††	CD4+ count of <50/μL	Fluconazole, 100–200 mg po q.d. (BI)	Itraconazole, 200 mg po q.d. (CIII)
Histoplasma capsulatum††	CD4+ count of <50/μL, endemic geographic area	Itraconazole, 200 mg po q.d. (CIII)	Fluconazole, 200 mg po q.d. (CIII)
Coccidioides immitis††	CD4+ count of <50/μL, endemic geographic region	Fluconazole, 200 mg po q.d. (CIII)	Itraconazole, 200 mg po q.d. (CIII)
CMV§§	CD4+ count of <50/μL and CMV antibody positivity	Oral ganciclovir, 1 g po t.i.d. (CIII; only preliminary data available)	None
Unknown (herpesviruses?)¶¶	CD4+ count of <200/μL	Acyclovir, 800 mg po q.i.d. (CIII)	Acyclovir, 200 mg po t.i.d./q.i.d. (CIII)
IV. Recommended for consideration***			
Hepatitis B virus¶	All susceptible (anti-HBc-negative) patients	Energix-B, 20 μg im x 3 (BII); *or* Recombivax HB, 10 μg im x 3 (BII)	None
Influenza virus¶	All patients (annually, before influenza season)	Whole or split virus, 0.5 mL im/y (BIII)	Rimantadine, 100 mg po b.i.d. (CIII); *or* amantadine, 100 mg po b.i.d. (CIII)†††

NOTE. Not all of the recommended regimens reflect current Food and Drug Administration-approved labeling. Anti-HBc = antibody to hepatitis B core antigen; b.i.w. = twice weekly; CMV = cytomegalovirus; DS = double-strength tablet; q.m. = monthly; q.w. = weekly; ss = single-strength tablet; t.i.w. = three times weekly; TMP-SMZ = trimethoprim-sulfamethoxazole; and TST = tuberculin skin test. The Respirgard II nebulizer is manufactured by Marquest, Englewood, CO; Energix-B by SmithKline Beecham, Rixensart, Belgium; and Recombivax HB by Merck & Co., West Point, PA. Letters and Roman numerals in parentheses after regimens indicate the strength of the recommendation and the quality of the evidence supporting it (see text).

* Patients receiving dapsone should be tested for glucose-6-phosphate dehydrogenase deficiency. A dosage of 50 mg q.d. is probably less effective than a dosage of 100 mg q.d. The efficacy of parenteral pentamidine (e.g., 4 mg/kg/q.m.) is uncertain. Inadequate data are available on the efficacy and safety of atovaquone or clindamycin/primaquine. Sulfadoxine/pyrimethamine (Fansidar, Roche Laboratories, Nutley, NJ) is rarely used because it can elicit severe hypersensitivity reactions. TMP-SMZ and dapsone/pyrimethamine (and possibly dapsone alone) appear to be protective against toxoplasmosis. TMP-SMZ may reduce the frequency of some bacterial infections. Patients receiving therapy for toxoplasmosis with sulfadiazine/pyrimethamine are protected against *P. carinii* pneumonia and do not need TMP-SMZ.

† Directly observed therapy is required for 900 mg of isonizid b.i.w.; isoniazid regimens should include pyridoxine to prevent peripheral neuropathy. Exposure to multidrug-resistant tuberculosis may require prophylaxis with two drugs; consult public health authorities. Possible regimens include pyrazinamide plus either ethambutol or a fluoroquinolone (*16*).

§ Protection against *T. gondii* is provided by the preferred antipneumocystis regimens. Pyrimethamine alone probably provides little, if any, protection. Dapsone alone cannot be recommended on the basis of currently available data.

¶ Data are inadequate concerning clinical benefit of vaccines against *S. pneumoniae*, influenza virus, and hepatitis B virus in HIV-infected persons, although it is logical to assume that those patients who develop antibody responses will derive some protection. Some authorities are concerned that immunizations may stimulate the replication of HIV. Prophylaxis with TMP-SMZ may provide some clinical benefit by reducing the frequency of bacterial infections, but the prevalence of *S. pneumoniae* resistant to TMP-SMX is increasing. Hepatitis B vaccine has been recommended for all children and adolescents and for all adults with risk factors for hepatitis B infection. For additional information regarding vaccination against hepatitis B and vaccination and antiviral therapy against influenza, (*17–19*).

** Data on 500 mg of clarithromycin po b.i.d. have been presented but have not yet been thoroughly analyzed. Data on the efficacy and safety of azithromycin prophylaxis are not yet available.

†† There may be a few unusual occupational or other circumstances under which prophylaxis should be considered; consult a specialist.

§§ Data on oral ganciclovir are still being evaluated; the durability of its effect is unclear. Acyclovir is not protective against CMV.

¶¶ Data regarding the efficacy of acyclovir for prolonging survival are controversial; if acyclovir is beneficial, the biologic basis for the effect and the optimal dose and timing of therapy are uncertain.

*** These immunizations or chemoprophylactic regimens are not targeted against pathogens traditionally classified as opportunistic but should be considered for use in HIV-infected patients. While the use of those products is logical, their clinical efficacy has not been validated in this population.

††† During outbreaks of influenza A.

TABLE 3B. Prophylaxis for recurrence of opportunistic disease (after chemotherapy for acute disease) in HIV-infected adults and adolescents

Pathogen	Indication	Preventive regimens: First choice	Preventive regimens: Alternatives
I. Recommended for life as standard of care			
Pneumocystis carinii	Prior *P. carinii* pneumonia	TMP-SMZ, 1 DS po q.d. (AI)	TMP-SMZ, 1 SS po q.d. (AI) *or* 1 DS po t.i.w. (AII); dapsone, 50 mg po b.i.d. *or* 100 mg po q.d. (AI); dapsone, 50 mg po q.d., *plus* pyrimethamine, 50 mg po q.w., *plus* leucovorin, 25 mg po q.w. (AI); dapsone, 200 mg po q.w., *plus* pyrimethamine, 75 mg po q.w., *plus* leucovorin, 25 mg po q.w. (AI); aerosolized pentamidine, 300 mg q.m. via Respirgard II nebulizer (AI)
*Toxoplasma gondii**	Prior toxoplasmic encephalitis	Sulfadiazine, 1.0–1.5 g po q6h, *plus* pyrimethamine, 25–75 mg po q.d., *plus* leucovorin, 10–25 mg po q.d.–q.i.d. (AII)	Clindamycin, 300–450 mg po q6–8h, *plus* pyrimethamine, 25–75 po q.d., *plus* leucovorin, 10–25 mg po q.d.–q.i.d. (AII)
Mycobacterium avium complex†	Documented disseminated disease	Clarithromycin, 500 mg po b.i.d., *plus* one or more of the following: ethambutol, 15 mg/kg po q.d.; clofazimine, 100 mg po q.d.; rifabutin, 300 mg po q.d.; ciprofloxacin, 500–750 mg po b.i.d. (BIII)	Azithromycin, 500 mg po q.d., *plus* one or more of the following: ethambutol, 15 mg/kg po q.d.; clofazimine, 100 mg po q.d.; rifabutin, 300 mg po q.d.; ciprofloxacin, 500-750 mg po b.i.d. (BIII)
Cytomegalovirus§	Prior end-organ disease	Ganciclovir, 5–6 mg/kg iv 5–7 d/w or 1,000 mg po t.i.d. (AI); *or* foscarnet, 90–120 mg/kg iv q.d. (AI)	Sustained-release implants used investigationally
Cryptococcus neoformans	Documented disease	Fluconazole, 200 mg po q.d. (AI)	Itraconazole, 200 mg po q.d. (BIII); amphotericin B, 0.6–1.0 mg/kg iv q.w.–t.i.w. (AI)
Histoplasma capsulatum	Documented disease	Itraconazole, 200 mg po b.i.d. (AII)	Amphotericin B, 1.0 mg/kg iv q.w. (AI); fluconazole, 200-400 mg po q.d. (BIII)
Coccidiodes immitis	Documented disease	Fluconazole, 200 mg po q.d. (AII)	Amphotericin B, 1.0 mg/kg iv q.w. (AI); itraconazole, 200 mg po b.i.d. (AII); ketoconazole, 400–800 mg po q.d. (BII)
Salmonella species (non-typhi)¶	Bacteremia	Ciprofloxacin 500 mg po b.i.d. for several months (BII)	None
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)	None
Candida species (oral, vaginal, or esophageal)	Frequent/severe recurrences	Fluconazole, 100–200 mg po q.d. (AI)	Ketoconazole, 200 mg po q.d. (BII); itraconazole, 100 mg po q.d. (BII); clotrimazole troche, 10 mg po 5X/d (BII); nystatin, $5X10^5$ U po 5X/d (CIII)

NOTE. Not all of the recommended regimens reflect current Food and Drug Administration-approved labeling. DS = double-strength tablet; q.m. = monthly; q.w. = weekly; SS = single-strength tablet; t.i.w. = three times weekly; and TMP-SMZ = trimethoprim-sulfamethoxazole. The Respirgard II nebulizer is manufactured by Marquest, Englewood, CO. Letters and Roman numerals in parentheses after regimens indicate the strength of the recommendation and the quality of the evidence supporting it (see text).

* Only pyrimethamine/sulfadiazine confers protection against *P. carinii* pneumonia.

† The long-term efficacy of any regimen is not well established. Many multiple-drug regimens are poorly tolerated. Drug interactions (e.g., those seen with clarithromycin/rifabutin) can be problematic. Rifabutin has been associated with uveitis, especially when given at daily doses of >300 mg or along with fluconazole or clarithromycin.

§ Gangiclovir and foscarnet delay relapses by only modest intervals (often only 4–8 weeks). Ocular implants with sustained-release gangiclovir appear promising.

¶ Efficacious eradication of *Salmonella* has been demonstrated only for ciprofloxacin.

Drug Regimens for Children

TABLE 4A. Prophylaxis for first episode of opportunistic disease in HIV-infected infants and children

Pathogen	Indication	Preventive regimens: First choice	Preventive regimens: Alternatives
I. Strongly recommended as standard of care			
*Pneumocystitis carinii**	All infants 1–4 mo old born to HIV-infected women; HIV-infected or HIV-indeterminate infants <12 mo old; HIV-infected children 1–5 y old with $CD4^+$ count of <500/μL or $CD4^+$ percentage of <15%; HIV-infected children 6–12 y old with $CD4^+$ count of <200/μL or $CD4^+$ percentage of <15%	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., or 2 divided doses po t.i.w. on alternate days	Aerosolized pentamidine (children ≥5 y old), 300 mg q.m. via Respirgard II nebulizer (CIII); dapsone (children ≥1 mo old), 2 mg/kg (not to exceed 100 mg) po q.d. (CIII); iv pentamidine, 4 mg/kg every 2–4 w (CIII)
Mycobacterium tuberculosis			
Isoniazid-sensitive	TST reaction of ≥5 mm *or* prior positive TST result without treatment *or* contact with case of active tuberculosis	Isoniazid, 10–15 mg/kg (maximum, 300 mg) po or im q.d. X 12 mo *or* 20–30 mg/kg (maximum, 900 mg) po b.i.w. X 12 mo (BIII)	Rifampin, 10–20 mg/kg (maximum, 600 mg) po or iv q.d. X 12 mo (BII)
Isoniazid-resistant	Same as above; high probability of exposure to isoniazid-resistant tuberculosis	Rifampin, 10–20 mg/kg (maximum, 600 mg) po or iv q.d. X 12 mo (BII)	Uncertain
Multidrug-resistant (isoniazid and rifampin)	Same as above; high probability of exposure to multidrug-resistant tuberculosis	Choice of drugs requires consultation with public health authorities	None
Varicella-zoster virus	Significant exposure to varicella with *no* history of varicella	VZIG, 1 vial (1.25 mL)/10 kg (maximum, 5 vials) im, given ≤96 h after exposure, ideally within 48 h (AI) (Children routinely receiving IVIG should receive VZIG if the last dose of IVIG was given >14 d before exposure.)	None
Various pathogens	HIV exposure/infection	Immunizations**	None
II. Recommended for consideration in all patients			
Toxoplasma gondii†	IgG antibody to *Toxoplasma* with severe immunosuppression ($CD4^+$ count of <100/μL) (Prophylaxis may be considered at higher $CD4^+$ counts in the youngest infants, but no relevant data are available.)	TMP-SMZ, 150/750 mg/m^2/d in 2 divided doses po t.i.w. on consecutive days (CIII); acceptable alternative schedules for same dosage (CIII): single dose po t.i.w. on consecutive days, 2 divided doses po q.d., or 2 divided doses po t.i.w. on alternate days	Dapsone (children ≥1 mo old), 2 mg/kg *or* 15 mg/m^2 (maximum, 25 mg) po q.d., *plus* pyrimethamine, 1 mg/kg po q.d., *plus* leucovorin, 5 mg po every 3 d (CIII)
Mycobacterium avium complex	$CD4^+$ count of <75/μL	Children 6–12 y old: rifabutin, 300 mg po q.d. (BI); children <6 y old: 5 mg/kg po q.d. when suspension is available (BI)	All ages: azithromycin, 7.5 mg/kg in 2 divided doses po q.d. (CIII); clarithromycin, 5–12 mg/kg po q.d. (CIII)
III. Not recommended for most patients; indicated for consideration *only* in selected patients			
Invasive bacterial infections	Hypogammaglobulinemia	IVIG, 400 mg/kg q.m. (AI)	None
Candida species§	Severe immunosuppression	Nystatin (100,000 U/mL), 4–6 mL po q6h; *or* topical clotrimazole, 10 mg po 5X/d (CII)	Ketoconazole, 5–10 mg/kg po q12–24h (CI); fluconazole, 2–8 mg/kg po q.d. (CI)

TABLE 4A. Prophylaxis for first episode of opportunistic disease in HIV-infected infants and children — Continued

Pathogen	Indication	Preventive regimens: First choice	Preventive regimens: Alternatives
Cryptococcus neoformans	Severe immunosuppression	Fluconazole, 2–8 mg/kg po q.d. (BI)	Itraconazole, 2–5 mg/kg po q12–24h (CIII)
Histoplasma capsulatum	Severe immunosuppression, endemic geographic area	Itraconazole, 2–5 mg/kg po q12–24h (CIII)	Fluconazole, 2–8 mg/kg po q.d. (CIII)
Coccidioides immitis	Severe immunosuppression, endemic geographic area	Fluconazole, 2–8 mg/kg po q.d. (CIII)	Itraconazole, 2–5 mg/kg po q12–24h (CIII)
CMV[¶]	$CD4^+$ count of <50/μL and CMV antibody positivity	Children 6–12 y old: oral ganciclovir under investigation	None
Influenza A virus	High risk of exposure (e.g., institutional outbreak)	Rimantadine or amantadine, 5 mg/kg q.d. (maximum, 150 mg) in 2 divided doses po for children <10 y old; for children ≥10 y old, 5 mg/kg up to 40 kg, then 200 mg in 2 divided doses po q.d.	None

NOTE. Not all of the recommended regimens reflect current Food and Drug Administration-approved labeling. b.i.w. = twice weekly; CMV = cytomegalovirus; IVIG = intravenous immune globulin; q.m. = monthly; t.i.w. = three times weekly; TMP-SMZ = trimethoprim-sulfamethoxazole; and VZIG = varicella-zoster immune globulin. The Respirgard II nebulizer is manufactured by Marquest, Englewood, CO. Letters and Roman numerals in parentheses after regimens indicate the strength of the recommendation and the quality of the evidence supporting it (see text).

* The efficacy of parenteral pentamidine (e.g., 4 mg/kg q.m.) is controversial. TMP-SMZ and dapsone/pyrimethamine (and possibly dapsone alone) appear to be protective against toxoplasmosis, although relevant data have not been prospectively collected. Daily treatment with TMP-SMZ reduces the frequency of some bacterial infections. Patients receiving sulfadiazine/pyrimethamine for toxoplasmosis are protected against P. carinii pneumonia and do not need TMP-SMZ.

† Protection against T. gondii is provided by the preferred antipneumocystitis regimens. Dapsone alone cannot be recommended on the basis of currently available data. Pyrimethamine alone probably provides little, if any, protection.

§ Ketoconazole and fluconazole are preferred for prophylaxis of esophagitis and severe mucocutaneous infection.

¶ Data on oral ganciclovir are still being evaluated; the durability of its effect is unclear. Acyclovir is not protective against CMV.

** The following immunization schedule for HIV-exposed/infected infants is strongly recommended as the standard of care:

Age (mo)	Immunization (dose)	Age (mo)	Immunization (dose)
Newborn	Hep B (1)a		
1	Hep B (2)	7	Influenza (1)[e]
2	DTP (1), Hib (1)[b]	8	Influenza (2)[e]
3	EIPV (1)[b]	12	Hib (3 or 4)[c], MMR[f]
4	DTP (2), hIB (2)[b]	15	EIPV (3), DTaP (4)[g]
5	EIPV (2)[b]	18	DTaP (4)[g]
6	DTP (3), Hib (3), Hep B (3)[b,c,d]	24	Pneumococcal, 23-valent[h]

NOTE. DTaP = diphtheria and tetanus toxoids with acellular pertussis; DTP = diphtheria-tetanus-pertussis; EIPV = enhanced inactivated polio vaccine; Hep B = hepatitis B; Hib = Haemophilus influenzae type b; and MMR = measles-mumps-rubella. This schedule differs from that recommended for immunization of immunocompetent children (*20,21*) in the following ways: (1) EIPV replaces oral polio vaccine, and the first two doses of EIPV may be given at 3 and 5 months instead of 2 and 4 months; (2) the second dose of Hep B vaccine is given at 1 month; and (3) pneumococcal vaccine is recommended. This schedule is designed to deliver vaccine to HIV-infected children as early as possible and to limit the number of injections to two per visit.

[a] Infants born to mothers positive for hepatitis B surface antigen should receive hepatitis B immune globulin within 12 hours of birth in addition to Hep B vaccine (*17*).

[b] DTP and Hib vaccines are available together or separately. With the combined DTP-Hib vaccine, a single injection on each occasion is sufficient and can be given at 2, 4, and 6 months. Administration of EIPV as a second injection at 2 and 4 months can replace separate immunizations at 3 and 5 months.

[c] The need for a third dose of Hib vaccine depends on which formulation was used previously. Regardless of whether the primary series requires two or three doses, a booster dose is required at 12–15 months.

[d] If DTP and Hib are given as separate injections at 6 months, the third dose of Hep B vaccine may be postponed until the next visit.

[e] Primary immunization against influenza for children <9 years of age requires two doses of vaccine, the first of which can be given as early as 6 months of age (*13,18*). Subsequent vaccination should be undertaken annually, before the influenza season.

[f] HIV-infected children should receive prophylactic immunoglobulin after exposure to measles, whether or not they have been vaccinated against measles.

[g] DTaP can be administered at either 15 or 18 months. Alternatively, a fourth dose of DTP can be given as early as 12 months.

[h] Some authorities recommend revaccination for HIV-infected children vaccinated ≥6 years previously (*13*).

TABLE 4B. Prophylaxis for recurrence of opportunistic disease (after chemotherapy for acute disease) in HIV-infected infants and children

Pathogen	Indication	Preventive regimens: First choice	Preventive regimens: Alternatives
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 (AI); acceptable alternative schedules for same dosage (AI); single dose po t.i.w. on consecutive days, 2 divided doses po q.d., or 2 divided doses po t.i.w. on alternate days	Aerosolized pentamidine (children ≥5 y old), 300 mg q.m. via Respirgard II nebulizer (AI); dapsone (children ≥1 mo old), 2 mg/kg (not to exceed 100 mg) po q.d. (CIII); iv pentamidine (4 mg/kg) every 2–4 w (CIII)
Toxoplasma gondii[*]	Prior toxoplasmic encephalitis	Sulfadiazine, 85–120 mg/kg in 2–4 divided doses po q.d. *plus* pyrimethamine, 1 mg/kg or 15 mg/m^2 (maximum, 25 mg) po q.d., *plus* leucovorin, 5 mg po every 3 d (AII)	Clindamycin, 20–30 mg/kg in 4 divided doses po q.d., *plus* pyrimethamine, 1 mg/kg po q.d., *plus* leucovorin, 5 mg po every 3 d (AII)
Mycobacterium avium complex[†]	Prior disease	Clarithromycin, 30 mg/kg in 2 divided doses po q.d., *plus* at least one of the following: ethambutol, 15–25 mg/kg po q.d.; clofazimine, 50–100 mg po q.d.; rifabutin, 300 mg po q.d.; ciprofloxacin, 20–30 mg/kg in 2 divided doses po q.d. (CIII)	None
Cryptococcus neoformans	Documented disease	Fluconazole, 2–8 mg/kg po q.d. (CIII)	Itraconazole, 2–5 mg/kg po q12–24h (CIII); amphotericin B, 0.5–1.5 mg/kg iv q.w.–t.i.w. (AI)
Histoplasma capsulatum	Documented disease	Itraconazole, 2–5 mg/kg po q12–48 h (CIII)	Fluconazole, 2–8 mg/kg po q.d. (CIII); amphotericin B, 1.0 mg/kg iv q.w. (AI)
Coccidioides immitis	Documented disease	Fluconazole, 2–8 mg/kg po q.d. (CIII)	Amphotericin B, 1.0 mg/kg iv q.w. (AI)
Cytomegalovirus[§]	Prior end-organ disease	Ganciclovir, 10 mg/kg in 2 divided doses iv q.d. for 1 w, then 5 mg/kg iv q.d.; *or* foscarnet, 60–120 mg/kg iv q.d. (AI)	None
Salmonella species (non-typhi)[¶]	Bacteremia	TMP/SMZ, 150/750 mg/m^2 in 2 divided doses po q.d. for several months (CIII)	Ampicillin, 50–100 mg in 4 divided doses po q.d. (CIII); chloramphenicol, 50–75 mg/kg in 4 divided doses po q.d. (CIII) (For children >6 y old, consider ciprofloxacin, 30 mg in 2 divided doses po q.d. (CIII)
II. Recommended only if subsequent episodes are frequent or severe			
Invasive bacterial infections	More than 2 infections in 1-yr period	IVIG, 400 mg/kg q.m. (AI)	TMP-SMZ 150/750 mg/m^2 po q.d. (AI)
Herpes simplex virus	Frequent/severe recurrences	Acyclovir, 600–1,000 mg in 3–5 divided doses po q.d. (CIII)	
Candida species	Frequent/severe recurrences	Ketoconazole, 5–10 mg/kg po q12–24h; *or* fluconazole, 2–8 mg/kg po q.d. (BI)	

NOTE. Not all of the recommended regimens reflect current Food and Drug Administration-approved labeling. IVIG = intravenous immune globulin; q.m. = monthly; q.w. = weekly; t.i.w. = three times weekly; and TMP-SMZ = trimethoprim-sulfamethoxazole. The Respirgard II nebulizer is manufactured by Marquest, Englewood, CO. Letters and Roman numerals in parentheses after regimens indicate the strength of the recommendation and the quality of the evidence supporting it (see text).

[*] Only pyrimethamine/sulfadiazine confers protection against *P. carinii* pneumonia. Although the clindamycin/pyrimethamine regimen is an alternative for adults, it has not been tested in children. However, these drugs are safe and are used for other infections.

[†] Ciprofloxacin should not be given to children <6 years of age. Rifabutin (5 mg/kg po q.d.) may be given to children <6 years of age when a suspension becomes available.

[§] Oral ganciclovir has not been studied in children.

[¶] Choice of drug should be determined by susceptibilities of the organism isolated.

Prevention of Exposure Recommendations

TABLE 5. Advising patients about the avoidance of exposure to opportunistic pathogens

Sexual Exposures

(1) Patients should use male latex condoms during every act of sexual intercourse to reduce the risk of exposure to cytomegalovirus, herpes simplex virus, and human papillomavirus, as well as to other sexually transmitted pathogens (AII). Use of latex condoms will also prevent the transmission of HIV to others.
(2) Patients should avoid sexual practices that may result in oral exposure to feces (e.g., oral-anal contact) to reduce the risk of intestinal infections such as cryptosporidiosis, shigellosis, campylobacteriosis, amebiasis, giardiasis, and hepatitis A and B (BIII).

Environmental and Occupational Exposures

(1) Certain activities or types of employment may increase the risk 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 or not to continue with such activities should be made in conjunction with the health care provider and should take into account 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 facilities are at increased risk of acquiring CMV infection, cryptosporidiosis, and other infections (e.g., hepatitis A and giardiasis) from children. The risk of 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 are also at increased risk of 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) may pose a risk of 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 of cryptosporidiosis (BII).
(5) Hand washing after gardening or other contact with soil may reduce the risk of cryptosporidiosis and toxoplasmosis (BIII).
(6) In histoplasmosis-endemic areas, patients should avoid activities known to be associated with increased risk, including cleaning chicken coops, disturbing soil beneath bird-roosting sites, and exploring caves (CIII).
(7) In coccidioidomycosis-endemic areas, when possible, patients should avoid activities associated with increased risk, including those involving extensive exposure to disturbed soil, as occurs at building excavation sites, on farms, 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.

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 <6 months of age, 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 exercise caution when obtaining a pet from these sources. Stray animals should be avoided. Animals <6 months of age, 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 of cryptosporidiosis, salmonellosis, and campylobacteriosis (BIII). Hand washing by HIV-infected children should be supervised.

TABLE 5. Advising patients about the avoidance of exposure to opportunistic pathogens — Continued

Cats

(4) Patients should consider the potential risks of cat ownership because of the risks of toxoplasmosis and *Bartonella* infection, as well as enteric infection (CIII). Those who elect to obtain a cat should adopt or purchase an animal that is >1 year of age and in good health to reduce the risk of 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 the hands thoroughly afterward to reduce the risk of toxoplasmosis (BIII).
(6) Also to reduce the risk of toxoplasmosis, cats should be kept indoors, should not be allowed to hunt, and should not be fed raw or undercooked meat (BIII).
(7) Although declawing is not generally advised, patients should avoid activities that may result in cat scratches or bites to reduce the risk of *Bartonella* infection (BII). Patients should also wash sites of cat scratches or bites promptly (CIII); and should not allow cats to lick open cuts or wounds (BIII).
(8) Care of cats should include flea control, to reduce the risk of *Bartonella* infection (CIII).
(9) Testing of cats for toxoplasmosis (EII) or *Bartonella* infection (DII) is not recommended.

Birds

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

Other

(11) Contact with reptiles (such as snakes, lizards, and turtles) should be avoided to reduce the risk of salmonellosis (BIII).
(12) Gloves should be used during the cleaning of aquariums to reduce the risk of infection with *Mycobacterium marinum* (BIII).
(13) Contact with exotic pets, such as nonhuman primates, should be avoided (CIII).

Food- and Water-Related Exposures

(1) Raw or undercooked eggs (including foods that may contain raw eggs, such as some preparations of hollandaise sauce, Caesar and certain other salad dressings, and mayonnaise); raw or undercooked poultry, meat, seafood; and unpasteurized dairy products may contain enteric pathogens. Poultry and meat should be cooked until no longer pink in the middle (internal temperature, >165° F). 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 of food-borne disease can prevent listeriosis by reheating these foods until they are steaming hot before eating them (CIII).
(4) Patients should not drink water directly from lakes or rivers because of the risk of cryptosporidiosis and giardiasis. Even accidental ingestion of lake or river water while swimming or engaging in other types of recreational activities carries this risk (BII).
(5)

During outbreaks or in other situations in which a community "boil-water" advisory is issued, boiling of water for 1 minute will eliminate the risk of cryptosporidiosis (AI). Use of submicron, personal-use water filters (home/office types) and/or drinking bottled water* may reduce the risk (CIII). Current data are inadequate to recommend 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 the risk of waterborne cryptosporidiosis may choose to take precautions similar to those recommended during outbreaks. Such decisions are best made in conjunction with the 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 oocytes, the cost of the products, and the difficulty of using these products consistently.

* See section on cryptosporidiosis in disease-specific recommendations for information on personal-use filters and bottled water.

TABLE 5. Advising patients about the avoidance of exposure to opportunistic pathogens — Continued

Travel-Related Exposures

(1) Travel, particularly to developing countries, may carry 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 food- 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—may 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). Treatment of water with iodine or chlorine may not be as effective as boiling but can be used, perhaps in conjunction with filtration, when boiling is not practical (BIII).

(3) Waterborne infections may result from the swallowing of water during recreational activities. To reduce the risk of cryptosporidiosis and giardiasis, patients should avoid swallowing water during swimming and should not swim in water that may 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 of diarrhea among travelers. Under selected circumstances (e.g., those in which the risk of infection is very high and the period of travel brief), the provider and patient may may weigh the potential risks and benefits and decide that antibiotic prophylaxis is warranted (CIII). For those individuals to whom prophylaxis is offered, fluoroquinolones, such as ciprofloxacin (500 mg q.d.) can be considered (BIII). Trimethoprim-sulfamethoxazole (TMP-SMZ) (one double-strength tablet daily) has also 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) may gain some protection against traveler's diarrhea. For HIV-infected persons who are not already taking TMP-SMZ, the provider should use caution when 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 with them a sufficient supply of an antimicrobial agent to be taken as empirically should diarrhea develop (BIII). One appropriate regimen is 500 mg of ciprofloxacin b.i.d. 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 empiric therapy, if their stools contain blood, if fever is accompanied by shaking chills, or if dehydration develops. Antiperistaltic agents such as 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). These drugs are not recommended for children (DIII).

(6) Travelers should be advised about other preventive measures appropriate for anticipated exposures, such as chemoprophylaxis for malaria, protection against arthropod vectors, treatment with immune globulin, and vaccination (AII). They should avoid direct contact of the skin with soil and 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). An exception is measles vaccine, which is recommended for nonimmune persons. Inactivated (killed) poliovirus vaccine should be used instead of oral (live) poliovirus vaccine. Persons at risk for exposure to typhoid fever should be given inactivated parenteral typhoid vaccine instead of the live attenuated 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 immunization is not performed, patients should be advised of the risk, instructed in methods for avoiding the bites of vector mosquitoes, and provided with a vaccination waiver letter.

TABLE 5. Advising patients about the avoidance of exposure to opportunistic pathogens — Continued

8) In general, killed vaccines (e.g., diphtheria-tetanus, rabies, Japanese encephalitis vaccines) should be used for HIV-infected persons 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 the usual tourist itinerary, even if travel includes countries reporting cases of cholera (DII).

(9) Travelers should be told 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.

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

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