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

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PREFACE

In 1994, the U.S. Public Health Service (USPHS) and the Infectious Diseases Society of America (IDSA) developed guidelines for health-care providers and patients for prevention of opportunistic infections (OIs) in persons infected with human immunodeficiency virus (HIV) (1-3). These guidelines were revised in 1997 and published in *MMWR* (4), *Clinical Infectious Diseases* (5), the *Annals of Internal Medicine* (6), the *American Family Physician* (7), and *Pediatrics* (8); an accompanying editorial appeared in *JAMA* (9). Response to these guidelines (e.g., the many requests for reprints and observations from health-care providers) suggests they have served as a valuable reference for HIV care providers. Because recommendations were rated on the basis of the strength of the evidence supporting them, readers were able to assess for themselves the relative importance of each guideline.

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

The second decade of the epidemic has witnessed extraordinary progress in developing highly active antiretroviral therapies (HAART), as well as modest continuing progress in preventing and treating individual OIs. HAART has reduced the incidence of opportunistic infections and extended life substantially (10). HAART is the most effective approach to preventing opportunistic infections and should be considered for all HIV-infected persons who qualify for such therapy. However, in the United States some patients are not ready or able to take HAART, and others have failed all available HAART regimens. Such patients will benefit from opportunistic infection prophylaxis. In addition, prophylaxis against specific OIs continues to provide survival benefits even among those who have access to HAART.

Because important new data concerning the prevention of opportunistic diseases have emerged since 1997, the USPHS and the IDSA reconvened a working group on March 4-5, 1999 to determine which recommendations warranted revision. Participants included representatives from federal agencies, universities, and professional societies, as well as community health-care providers and patient advocates. Much attention was focused on recent data related to the advisability of discontinuing OI prophylaxis (primary prophylaxis and prophylaxis against recurrence) in persons whose CD4+ T-lymphocyte counts have increased to above

prophylaxis thresholds due to HAART. The meeting also addressed two additional pathogens not previously considered--human herpes virus type 8 (HHV-8) and hepatitis C virus (HCV). However, data concerning the prevention of all common HIV-associated OIs were reviewed. As in earlier editions of the guidelines, factors considered in revising guidelines included incidence of disease; severity of disease in terms of morbidity and mortality; level of immunosuppression at which disease is most likely to occur; feasibility, efficacy, and cost of preventive measures; impact of intervention on quality of life; and toxicities, drug interactions, and the potential for drug resistance to develop.

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

Primary Changes in the Recommendations:

The primary changes in the disease-specific recommendations that follow include 1) statements concerning discontinuation of prophylaxis against specific OIs when the CD4+ T-lymphocyte count increases in response to HAART, 2) recommendations regarding HHV-8 and HCV, 3) recommendations concerning injection drug users (as requested by some respondents to the 1997 guidelines), 4) recommendations concerning short-course chemoprophylaxis against tuberculosis in HIV-infected persons with positive tuberculin skin tests, 5) changes in secondary prophylaxis (chronic maintenance therapy) recommended to prevent recurrence of *Mycobacterium avium* complex and cytomegalovirus disease, 6) caution against using fluconazole in the first trimester of pregnancy, and 7) statements concerning use of varicella and rotavirus vaccine in HIV-infected infants.

The guidelines developed by the USPHS/IDSA working group have been made available for public comment by an announcement in the Federal Register and in the MMWR. Pending input and approval, the final document is expected to be endorsed by the USPHS and the IDSA, as well as by numerous other organizations.

How to Use the Information in This Report:

This report presents disease-specific recommendations for prevention of a) exposure to the opportunistic pathogen, b) first episode of disease, and c) disease recurrence. Recommendations are accompanied by a description of the rating system (see Box), drugs and doses for prevention of first episode of disease and disease recurrence in adults (Tables 1A and 1B), drug interactions, toxicities, and dose adjustments required in patients with renal impairment (Tables 2-4), costs of

commonly used prophylactic drugs and vaccines (Table 5), categories of immunosuppression in HIV-infected children (Table 6), drugs and doses for prevention of first episode of disease and disease recurrence in children (Tables 7A and 7B), recommendations for prevention of exposure to opportunistic pathogens (Table 8), and a summary of recommendations concerning discontinuation of chemoprophylaxis in persons whose CD4+ T-lymphocyte counts have increased in response to HAART (Table 9). Because of their length and complexity, the tables and figure have been placed at the end of the text, preceding the references.

Recommendations are rated by a revised version of the IDSA rating system (see Box) (11). In this system, a letter rating (letters A through E) signifies the strength of the recommendation for or against this preventive modality; and a Roman numeral (Roman numerals I through III) indicates the quality of the evidence supporting that recommendation.

This report is oriented toward prevention of specific opportunistic infections in HIV-infected persons in the United States and other industrialized countries. Recommendations for use of antiretroviral therapy, which is designed to prevent immunologic deterioration and delay the need for many of the chemoprophylactic strategies described in this document, are published elsewhere (10). Also, integrated approaches to the care of HIV-infected persons are addressed separately (12).

It is recognized that new data on prevention of OIs in HIV-infected persons are emerging, and that randomized controlled trials addressing some unresolved issues in OI prophylaxis are ongoing. The OI Working Group has therefore developed a mechanism for routine periodic review of emerging data, and for updating these guidelines on a regular basis. The most recent information is available from the AIDS Treatment Information Service world-wide web site (www.hivatis.org).

Copies of this report can be obtained from ATIS, telephone 1-800-448-0440 or 301-217-0023 (international) or 1-800-243-7012 (TTY). In addition, pamphlets containing material appropriate for patients can be obtained from ATIS, and also on the CDC's Division of HIV/AIDS Prevention internet homepage (www.cdc.gov/hiv).

CATEGORIES REFLECTING STRENGTH AND QUALITY OF EVIDENCE

Rating system for strength of recommendation and quality of evidence supporting the recommendation*

Category	Definition
	Categories Reflecting the Strength of Each Recommendation
A	Both strong evidence for efficacy and substantial clinical benefit support recommendation for use. ***Should always be offered***.
B	Moderate evidence for efficacy --or strong evidence for efficacy, but only limited clinical benefit--supports recommendation for use. ***Should generally be offered***.
C	Evidence for efficacy is insufficient to support a recommendation for or against use, or evidence for efficacy may not outweigh adverse consequences (e.g., toxicity, drug interactions) or cost of the chemoprophylaxis or alternative approaches. ***Optional***.
D	Moderate evidence for lack of efficacy or for adverse outcome supports a recommendation against use. ***Should generally not be offered***.
E	Good evidence for lack of efficacy or for adverse outcome supports a recommendation against use. ***Should never be offered***.
	Categories Reflecting Quality of Evidence Supporting the Recommendation
I	Evidence from at least one properly randomized, controlled trial.
II	Evidence from at least one well-designed clinical trial without randomization, from cohort or case-controlled analytic studies (preferably from more than one center), or from multiple time-series studies or dramatic results from uncontrolled experiments.
III	Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees.

*Modified from Gross, et al. Clin Infect Dis (11).

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 who has PCP, data are insufficient to support this recommendation as standard practice (CIII).

Prevention of Disease

Initiation of Primary Prophylaxis

(2) Adults and adolescents who have HIV infection (including pregnant women and those on HAART) should receive chemoprophylaxis against PCP if they have a CD4+T- lymphocyte count of <200/uL (AI), or a history of oropharyngeal candidiasis (AII) (13). Persons who have a CD4+ T-lymphocyte percentage < 14% or history of an AIDS-defining illness but do not otherwise qualify should be considered for prophylaxis (BII) (14, 15). When CD4+ T-lymphocyte count monitoring at least every 3 months is not possible, initiation of chemoprophylaxis at a CD4+ T-lymphocyte count of > 200 but <250 cells/uL should also be considered (BII) (14).

(3) Trimethoprim-sulfamethoxazole (TMP-SMZ) is the preferred prophylactic agent (AI) (15-17). One double-strength tablet/day is the preferred regimen (AI) (16). However, one single-strength tablet/day (19) is also effective and may be better tolerated (AI). One double strength tablet three times per week is also effective (BI) (18). TMP-SMZ at a dose of 1 double-strength tablet/day confers cross-protection against toxoplasmosis (20) and some common respiratory bacterial infections (16, 21). Lower doses of TMP-SMZ may also confer such protection. For patients who have an adverse reaction that is not life-threatening, treatment with TMP-SMZ should be continued if clinically feasible; for those who have discontinued such therapy due to an adverse reaction, its reinstitution should be strongly considered after the adverse event has resolved (AII). Patients who have experienced adverse events, primarily fever and rash, may tolerate reintroduction of the drug using a gradual increase in dose (desensitization) as per published regimens (BI) (22, 23) or reintroduction of TMP-SMZ at a reduced dose or frequency (CIII): up to 70% of patients can tolerate such reinstitution of therapy.

(4) If TMP-SMZ cannot be tolerated, prophylactic regimens that can be recommended as alternatives include dapsone (BI) (16), dapsone plus pyrimethamine plus leucovorin (BI) (24, 25), aerosolized pentamidine administered by the Respirgard II™ nebulizer (Marquest, Englewood, CO) (BI) (17) and atovaquone (BI) (26, 27). Atovaquone appears to be as effective as aerosolized pentamidine (27) or dapsone (AI) (26) but is substantially more expensive than the other regimens. For patients seropositive for *Toxoplasma gondii* who cannot tolerate TMP-SMZ, the following regimens can be recommended as alternatives

include dapsone plus pyrimethamine (AI) (24, 25) or atovaquone with or without pyrimethamine (CIII) should be used if an alternative to TMP-SMZ for prophylaxis against both PCP and TE is needed. Because data regarding their efficacy for PCP prophylaxis are insufficient for a firm recommendation, the following regimens generally cannot be recommended for this purpose: aerosolized pentamidine administered by other nebulization devices, intermittently administered parenteral pentamidine, oral pyrimethamine plus sulfadoxine, oral clindamycin plus primaquine, and intravenous trimetrexate. However, the use of these agents may be considered in unusual situations in which the recommended agents cannot be administered (CIII).

Discontinuation of Primary Prophylaxis

(5) Initial reports from three prospective observational studies (28-30), one retrospective review (31), and one randomized trial (32) all have suggested that PCP prophylaxis can be safely discontinued in patients responding to HAART with a sustained increase in CD4+ T-lymphocyte counts from <200 cells/uL to >200 cells/uL. Such reports have mostly included patients receiving primary prophylaxis (no prior episode of PCP) and protease inhibitor containing regimens. In these studies, median follow-up ranged from 6 to 12 months and the median CD4+ T-lymphocyte count at the time of discontinuation of prophylaxis was over 300 cell/uL. At the time PCP prophylaxis was discontinued, many patients had sustained suppression of HIV plasma RNA levels below detection limits of the available assays. While the optimal criteria for discontinuation remain to be defined, providers may wish to discontinue prophylaxis when patients have sustained a CD4+ T-lymphocyte count of >200 cells/uL for at least 3-6 months (CII). Additional criteria might include sustained reduction in viral load sustained for a comparable period (CIII).

Restarting Primary Prophylaxis

(6) There are no data to guide recommendations for reinstitution of primary prophylaxis. Pending the availability of such data, a reasonable approach would be to utilize the criteria for initiation of prophylaxis described above (CIII).

Prevention of Recurrence

(7) Adults and adolescents who have a history of PCP should be administered chemoprophylaxis (i.e., secondary prophylaxis or chronic maintenance therapy) with the regimens indicated above to prevent recurrence (AI) (15).

Discontinuation of Secondary Prophylaxis (chronic maintenance therapy)

(8) Although patients receiving secondary prophylaxis (prior episode of PCP) may also be at low risk for PCP when their CD4+ T-lymphocyte counts increase to > 200 cells/uL, inadequate numbers of patients have been evaluated at this time to

warrant a recommendation to discontinue of prophylaxis in such patients.

Notes

Pediatric Notes

(9) Children born to HIV-infected mothers should be administered prophylaxis with TMP-SMZ beginning at 4-6 weeks of age (33) (AII). Prophylaxis should be discontinued for children who are subsequently found not to be infected with HIV. HIV-infected children and children whose infection status remains unknown should continue to receive prophylaxis for the first year of life. The need for subsequent prophylaxis should be determined on the basis of age-specific CD4+ T-lymphocyte count thresholds (Table 7a) (AII). **The safety of discontinuing prophylaxis in HIV-infected children receiving HAART has not been studied.**

(10) Children who have a history of PCP should be administered lifelong chemoprophylaxis to prevent recurrence (AI) (33).

Note Regarding Pregnancy

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

Toxoplasmic Encephalitis

Prevention of Exposure

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

(2) All HIV-infected persons, but particularly those who lack IgG antibody to ***Toxoplasma***, should be counseled about the various sources of toxoplasmic infection. They should be advised not to eat raw or undercooked meat, particularly undercooked pork, lamb, or venison (BIII). Specifically, meat should be cooked to an internal temperature of 150 F° (65.5 C°); meat cooked until it is no longer pink inside generally has an internal temperature of 165 F° (73.8 C°) and therefore satisfies this requirement. HIV-infected persons should wash their hands after contact with raw meat and after gardening or other contact with soil; in addition, they should wash fruits and vegetables well before eating them raw (BIII). If the patient owns a cat, the litter box should be changed daily, preferably by an HIV-negative, nonpregnant person; alternatively, the patient should wash the hands thoroughly after changing the litter box (BIII). Patients should be encouraged to keep their cats inside and not to adopt or handle stray cats (BIII). Cats should be fed only canned or dried commercial food or well-cooked table food, not raw or undercooked meats (BIII). Patients need not be advised to part with their cats or to have their cats tested for toxoplasmosis (EII).

Prevention of Disease

Initiation of Primary Prophylaxis

(3) ***Toxoplasma***-seropositive patients who have a CD4+ T-lymphocyte count of <100/uL should be administered prophylaxis against toxoplasmic encephalitis (TE) (AII) (20). **The daily doses of TMP-SMZ recommended as the preferred regimens for PCP prophylaxis appear to**

be effective against TE as well and are therefore recommended (AII) (20). If patients cannot tolerate TMP-SMZ, a regimen that can be recommended as an alternative which is also effective against PCP is dapsone-pyrimethamine (AI) (24, 25). Atovaquone with or without pyrimethamine may be considered (CIII). Prophylactic monotherapy with dapsone, pyrimethamine, azithromycin, or clarithromycin cannot be recommended on the basis of current data (DII). Aerosolized pentamidine does not afford protection against TE and is not recommended for this purpose (EI) (16, 20).

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

Discontinuation of Primary Prophylaxis

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

Prevention of Recurrence

(6) **Patients who have had TE should be administered lifelong suppressive therapy (i.e., secondary prophylaxis or chronic maintenance therapy) with drugs active against *Toxoplasma* to prevent relapse (AI) (34, 35).** The combination of pyrimethamine plus sulfadiazine and leucovorin is highly effective for this purpose (AI) (34, 35). A commonly used regimen for patients who cannot tolerate sulfa drugs is pyrimethamine plus clindamycin (BI); however, only the combination of pyrimethamine plus sulfadiazine appears to provide protection against PCP as well (AII).

Discontinuation of Secondary Prophylaxis (chronic maintenance therapy)

(7) The numbers of patients who have stopped maintenance therapy after responding to HAART is insufficient to warrant recommending discontinuation of maintenance therapy at this time.

Notes

Pediatric Note

(8) TMP-SMZ, when administered for PCP prophylaxis, also provides prophylaxis against toxoplasmosis. **Children aged >12 months who qualify for PCP prophylaxis and who are receiving an agent other than TMP-SMZ or atovaquone should have serologic testing for *Toxoplasma* antibody (BIII), because other drugs for PCP prophylaxis**

may not be effective against *Toxoplasma*. If seropositive for *Toxoplasma*, children should be administered prophylaxis for both PCP and toxoplasmosis (i.e., dapsone plus pyrimethamine) (BIII) or atovaquone (CIII).

Notes Regarding Pregnancy

(9) TMP-SMZ can be administered for prophylaxis against TE as described for PCP (AIII). However, because of the low incidence of TE during pregnancy and the possible risk associated with pyrimethamine treatment, chemoprophylaxis with pyrimethamine-containing regimens can reasonably be deferred until after pregnancy (CIII). For prophylaxis against recurrent TE, the health-care provider and clinician should be well informed about the benefit of lifelong therapy and the concerns about teratogenicity of pyrimethamine. Most clinicians favor lifelong therapy for the mother, given the high likelihood that disease will recur promptly if therapy is stopped (AIII).

(10) In rare cases, HIV-infected pregnant women who have serologic evidence of remote toxoplasmic infection have transmitted ***Toxoplasma*** to the fetus in utero. Pregnant HIV-infected women who have evidence of primary toxoplasmic infection or active toxoplasmosis (including TE) should be evaluated and managed during pregnancy in consultation with appropriate specialists (CIII). Infants born to women who have serologic 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 (BIII). Modes of transmission include direct contact with infected adults and diaper-aged children, contact with infected animals, drinking contaminated water, contact with contaminated water during recreational activities, and eating contaminated food.

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

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

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

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

(6) Waterborne infection may also result from swallowing water during recreational activities.

Patients should be aware that many lakes, rivers, salt-water beaches and some swimming pools, recreational water parks and ornamental water fountains may be contaminated with human or animal waste that contains *Cryptosporidia*. Patients should avoid swimming in water that is likely to be contaminated and should avoid swallowing water while swimming or playing in recreational waters (BIII).

(7) Several outbreaks of cryptosporidiosis have been linked to municipal water supplies. During outbreaks or in other situations in which a community "boil-water" advisory is issued, boiling water for 1 minute will eliminate the risk of cryptosporidiosis (AI). Use of submicron personal-use water filters* (home/office types) and/or bottled water† may also reduce the risk (CIII). The magnitude of the risk of acquiring cryptosporidiosis from drinking water in a nonoutbreak setting is uncertain, and current data are inadequate to recommend that all HIV-infected persons boil water or avoid drinking tap water in nonoutbreak settings. However, HIV-infected persons who wish to take independent action to reduce the risk 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.

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

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* Only filters capable of removing particles 1 um in diameter should be considered. Filters that provide the greatest assureance of oocysts removal include those that operate by reverse osmosis, those labeled as “absolute” 1-um filters, and those labeled as meeting NSF (National Sanitation Foundation) standard no. 53 for “cyst removal.” The “nominal” 1-um filter rating is not standardized, and many filters in this category may not be capable of removing 99% of oocysts.

† Sources of bottled water (e.g. wells, springs, municipal tap-water supplies, rivers, and lakes) and methods for its disinfection differ; therefore, all brands should not be presumed to be free of cryptosporidial oocysts. Water from wells and springs is much less likely to be contaminated by oocysts than water from rivers or lakes. Treatment of bottled water by distillation or reverse osmosis ensures oocyst removal. Water passed through an “absolute” 1-um 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-um filters by bottlers as the only barrier to ***Cryptosporidia*** may not result in the removal of 99% of oocysts.

(9) Most foodborne outbreaks of cryptosporidiosis are believed to have been caused by infected food handlers. Therefore, specific recommendations to avoid exposure to contaminated food cannot be made. However, cryptosporidial oocysts survive in oysters for more than two months and have been found in oysters taken from some commercial oyster beds, so HIV-infected persons should avoid eating raw oysters (BIII). Cryptosporidium-infected patients should not work as food handlers, especially if the food to be handled is intended to be eaten without cooking (BII).

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

Prevention of Disease

(11) No agents have been proven to be effective as chemoprophylaxis against cryptosporidiosis. Rifabutin or clarithromycin, when taken for MAC prophylaxis, were associated with reduced risk of cryptosporidiosis in one study (36), but data are insufficient to warrant a recommendation for use.

Prevention of Recurrence

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

Note

Pediatric Note

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

Microsporidiosis

Prevention of Exposure

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

Prevention of Disease

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

Prevention of Recurrence

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

Tuberculosis

Prevention of Exposure

(1) HIV-infected persons should be advised that certain activities and occupations 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 be based on factors such as the patient's specific duties in the workplace, the prevalence of tuberculosis in the community, and the degree to which precautions are taken to prevent the transmission of tuberculosis in the workplace (BIII). Whether the patient continues with such activities 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 receive a tuberculin skin test (TST) by administration of intermediate-strength (5-TU) purified protein derivative (PPD) by the Mantoux method (AI). Routine evaluation for anergy is not recommended. **However, there are selected situations in which anergy evaluation may assist in guiding individual decisions about preventive therapy (37).**

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

(4) **All HIV-infected persons regardless of age who have a positive TST result yet have no evidence of active tuberculosis and no history of treatment or prophylaxis for tuberculosis should be administered 9 months of preventive chemotherapy with isoniazid (INH) daily (AII) or twice weekly (BI) or two months of therapy with rifampin and pyrazinamide (AI) or rifabutin and pyrazinamide (BIII) (37).** Because HIV-infected persons are at risk for peripheral neuropathy, those receiving INH should also receive pyridoxine (BIII). **A decision to use a regimen containing either rifampin or rifabutin should be made after careful consideration of potential drug interactions, especially those related to protease inhibitors and non-nucleoside reverse transcriptase inhibitors (see Drug Interaction Note). Directly observed therapy should be used with the intermittent dosing regimens (AI) and when otherwise operationally feasible (BIII) (37).**

(5) **HIV-infected persons who are close contacts of persons who have infectious tuberculosis should be administered preventive therapy-regardless of TST results, age, or prior courses of chemoprophylaxis-after the diagnosis of active tuberculosis has been excluded (AII) (37).** In addition to household contacts, such persons

might also include contacts in the same drug treatment or health care facility, coworkers, and other contacts if transmission of TB is demonstrated.

(6) For persons exposed to INH- and/or rifampin-resistant TB, the decision to use chemoprophylactic anti-mycobacterial agents other than INH alone, rifampin plus PZA, or rifabutin plus PZA, should be based on the relative risk of exposure to resistant organisms and should be made in consultation with public health authorities (AII).

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

(8) Although the reliability of the TST may diminish as the CD4+ T-lymphocyte count declines, annual repeat testing should be considered for HIV-infected persons who are TST-negative on initial evaluation and who belong to populations in which there is a substantial risk of exposure to ***M. tuberculosis*** (BIII). **Repeat TST for those whose immune function has improved because of HAART (i.e. those whose CD4+ T-lymphocyte count has increased to > 200 cells/uL) may also be considered (CIII).** In addition to documenting tuberculous infection, TST conversion in an HIV-infected person should alert health-care providers to the possibility of recent ***M. tuberculosis*** transmission and should prompt notification of public health officials for investigation to identify a possible source case.

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

Prevention of Recurrence

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

Notes

Drug Interaction Note

(11) Rifampin should not be administered with protease inhibitors or non-nucleoside reverse transcriptase inhibitors (EI) (37). Rifabutin is an acceptable alternative but should not be used with the protease inhibitors ritonavir or hard-gel saquinavir; caution is also advised if the drug is co-administered with soft-gel saquinavir, but data are lacking. Rifabutin may be administered at one half the usual daily dose (i.e., reduce from 300 mg to 150 mg qd) with indinavir, nelfinavir, or amprenavir. Similarly, rifabutin should not be used with the non-nucleoside reverse transcriptase inhibitor delavirdine but may be administered at an

increased dose (450 mg qd) with efavirenz. Information is lacking regarding co-administration of rifabutin with nevirapine.

Pediatric Note

(12) Infants born to HIV-infected mothers should have a TST (5-TU PPD) at or before age 9-12 months and should be retested at least every 2-3 years (CIII). **HIV-infected children living in households with TST-positive persons should be evaluated for tuberculosis (AIII); children exposed to a person who has active tuberculosis should be administered preventive therapy after active tuberculosis has been excluded regardless of TST results (AII).**

Note Regarding Pregnancy

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

Disseminated Infection with ***Mycobacterium avium*** Complex

Prevention of Exposure

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

Prevention of Disease

Initiation of Primary Prophylaxis

(2) Adults and adolescents who have HIV infection should receive chemoprophylaxis against disseminated MAC disease if they have a CD4+ T-lymphocyte count of <50 cells/uL (AI) (38). Clarithromycin (39, 40) or azithromycin (41) are the preferred prophylactic agents (AI). The combination of clarithromycin and rifabutin is no more effective than clarithromycin alone for chemoprophylaxis and is associated with a higher rate of adverse effects than either drug alone; this combination should not be used (EI) (39). The combination of azithromycin with rifabutin is more

effective than azithromycin alone; however, the additional cost, increased occurrence of adverse effects, and absence of a difference in survival when compared with azithromycin alone do not warrant a routine recommendation for this regimen (CI) (41). In addition to their preventive activity for MAC disease, clarithromycin and azithromycin confer protection against respiratory bacterial infections (BII). If clarithromycin or azithromycin cannot be tolerated, rifabutin is an alternative prophylactic agent for MAC disease (BI) (38, 39, 41). Tolerance, cost, and drug interactions are among the issues that should be considered in decisions regarding the choice of prophylactic agents for MAC disease. **Particular attention to interactions with antiretroviral protease inhibitors and non-nucleoside reverse transcriptase inhibitors is warranted (see Drug Interaction Note).** Before prophylaxis is initiated, disseminated MAC disease should be ruled out by clinical assessment, which may include obtaining a blood culture for MAC if warranted. Because treatment with rifabutin could result in the development of resistance to rifampin in persons who have active tuberculosis, the latter condition should also be excluded before rifabutin is used for prophylaxis.

(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 clarithromycin, azithromycin, rifabutin, or other drugs in patients with MAC organisms at these sites and a negative blood culture. Therefore, routine screening of respiratory or gastrointestinal specimens for MAC cannot be recommended at this time (DIII).

Discontinuation of Primary Prophylaxis

(4) Information from one observational study suggested a low rate of disseminated infection with MAC among persons who responded to HAART with an increase in CD4+ T-lymphocyte count from < 50 cells/uL to > 100 cells/uL (31). While the optimal criteria for discontinuation of MAC prophylaxis remain to be defined, it is reasonable to consider discontinuing prophylaxis in patients with a sustained CD4+ T-lymphocyte count of > 100 cells/uL (e.g. > 3-6 months) and sustained suppression of HIV plasma RNA (CIII).

Restarting Primary Prophylaxis

(5) There are no data on which to base recommendations for reinstitution of prophylaxis. Pending the availability of such data, a reasonable approach would be to utilize the criteria for initiation of prophylaxis described above (CIII).

Prevention of Recurrence

(6) Patients who have been treated for disseminated MAC disease should continue to receive full therapeutic doses of antimycobacterial agents for life (i.e., secondary prophylaxis or chronic maintenance therapy) (AII) (38). Unless there is good clinical or laboratory evidence of macrolide resistance, the use of a macrolide (clarithromycin or, alternatively, azithromycin) is recommended in combination with ethambutol (AII) with or without rifabutin (CI). Treatment of MAC

disease with clarithromycin in a dose of 1,000 mg twice a day is associated with a higher mortality rate than observed with clarithromycin administered at 500 mg twice a day; thus, the higher dose should not be used (EI) (42, 43). Clofazimine has been associated with a worse clinical outcome in the treatment of MAC disease and should not be used (DII) (43).

Discontinuation of Secondary Prophylaxis (chronic maintenance therapy)

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

Notes

Drug Interaction Note

(8) **Rifabutin should not be administered with certain protease inhibitors or non-nucleoside reverse transcriptase inhibitors (see Drug Interaction Note in section on Tuberculosis).** Although protease inhibitors may also increase clarithromycin levels, no recommendation for dose adjustment of either clarithromycin or protease inhibitors can be made based on existing data.

Pediatric Note

(9) HIV-infected children aged <13 years who have advanced immunosuppression may also develop disseminated MAC infections, and prophylaxis should be offered to high-risk children according to the following CD4+ T-lymphocyte thresholds: children aged ≥6 years, <50 cells/uL; children aged 2-6 years, <75 cells/uL; children aged 1-2 years, <500 cells/uL; and children aged <12 months, <750 cells/uL (AII). For the same reasons that clarithromycin and azithromycin are the preferred prophylactic agents for adults, they should also be considered for children (AII); oral suspensions of both are commercially available in the United States. **No liquid formulation of rifabutin suitable for pediatric use is commercially available in the United States. The safety of discontinuing MAC prophylaxis in children whose CD4+ T-lymphocyte counts have increased in response to HAART has not be studied.**

Note Regarding Pregnancy

(10) Chemoprophylaxis for MAC disease should be administered to pregnant women as well as to other adults and adolescents (AIII). However, because of general concern about administering drugs during the first trimester of pregnancy, some providers may choose to withhold prophylaxis during the first trimester. Of the available agents, the safety profile in animal studies and anecdotal safety in humans suggest that azithromycin is the drug of choice (BIII). Experience with rifabutin is limited. Clarithromycin has been demonstrated to be a teratogen in animals and should be used with caution

during pregnancy. **For secondary prophylaxis (chronic maintenance therapy), azithromycin plus ethambutol are the preferred drugs.**

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 feasible after HIV infection is diagnosed, adults and adolescents who have a CD4+ T-lymphocyte count of ≥200 cells/uL should be administered a single dose of 23-valent polysaccharide pneumococcal vaccine if they have not had this vaccine during the previous 5 years (BII) (45, 46).** For persons who have a CD4+ T-lymphocyte count of <200 cells/uL, vaccination can be offered, although the humoral response and, therefore, clinical efficacy are likely to be diminished (CIII). **The recommendation to vaccinate is increasingly pertinent because of the increasing incidence of invasive infections with drug-resistant (including TMP-SMZ-resistant and macrolide-resistant) strains of *S. pneumoniae*. Limited data suggest that administration of certain bacterial vaccines may transiently increase HIV replication and plasma HIV-1 RNA levels in a minority of HIV-infected persons.** However, evidence that adverse clinical outcomes are associated with this transient increase is lacking. Most experts believe that the benefit of pneumococcal vaccination outweighs the potential risk.

(3) The duration of the protective effect afforded by primary pneumococcal vaccination is unknown. **Periodic revaccination may be considered; an interval of 5 years has been recommended for non-HIV-infected persons (47). In addition, revaccination one time should also be considered if the initial immunization was given when the CD4+ T-lymphocyte count was < 200 cells/uL and if the CD4+ T-lymphocyte count has increased to > 200 cells/uL on HAART. (CIII).**

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

(5) TMP-SMZ, administered daily, reduces the frequency of bacterial respiratory infections; this should be considered in the selection of an agent for PCP prophylaxis (AII). However, indiscriminate use of this drug (when not indicated for PCP prophylaxis or other specific reasons) may promote the development of TMP-SMZ-resistant organisms. Thus, TMP-SMZ should not be prescribed solely to prevent bacterial respiratory infection (DIII). **Similarly, clarithromycin administered daily and azithromycin administered weekly for MAC prophylaxis may be effective in preventing bacterial respiratory infections; this should be considered in the**

selection of an agent for prophylaxis of MAC disease (BII). However, these drugs should not be prescribed solely for preventing bacterial respiratory infection (DIII).

(6) An absolute neutrophil count that is depressed due to HIV disease or drug therapy is associated with an increased risk of bacterial infections, including pneumonia. Reversal of neutropenia, either by cessation of myelosuppressive drugs (CII) or use of granulocyte colony-stimulating factor (G-CSF) (CII) may be considered to reduce the risk of bacterial infections.

Prevention of Recurrence

(7) Some clinicians may administer antibiotic chemoprophylaxis to HIV-infected patients who have very frequent recurrences of serious bacterial respiratory infections (CIII). TMP-SMZ, administered for PCP prophylaxis, and clarithromycin or azithromycin, administered for MAC prophylaxis, are appropriate for drug-sensitive organisms. **However, providers should be cautious about use of antibiotics solely for this purpose because of the potential for development of drug-resistant microorganisms and drug toxicity.**

Notes

Pediatric Notes

(8) Children who have HIV infection should be administered ***H. influenzae*** type b vaccine in accordance with the guidelines of the Advisory Committee on Immunization Practices (18) and the American Academy of Pediatrics (17) (AII). **Children aged >2 years also should be administered 23-valent polysaccharide pneumococcal vaccine (BII). Revaccination with pneumococcal vaccine generally should be offered after 3-5 years to children aged ≤ 10 years and after 5 years to children aged >10 years (BIII).**

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

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

Note Regarding Pregnancy

(11) **Pneumococcal vaccination is recommended during pregnancy for patients who have not been vaccinated during the previous 5 years (BIII).** In nonpregnant adults, vaccination has been associated with a transient burst of HIV replication. It is unknown whether the transient viremia can increase the risk of perinatal HIV transmission. Because of this concern, when feasible, vaccination may be deferred until after antiretroviral therapy has been initiated for the prevention of perinatal HIV transmission (CIII).

Bacterial Enteric Infections

Prevention of Exposure

Food

(1) Health-care providers should advise HIV-infected persons not to eat raw or undercooked eggs (including foods that 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^0). Produce should be washed thoroughly 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 also have documented an association between ready-to-eat foods (e.g., hot dogs and cold cuts from delicatessen counters) and listeriosis. An immunosuppressed, HIV-infected person who wishes to reduce the risk of foodborne disease as much as possible may choose to reheat such foods until they are steaming hot before eating them (CIII).

Pets

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

(5) HIV-infected persons should avoid contact with animals that have diarrhea (BIII). HIV-infected pet owners should seek veterinary care for animals with diarrheal illness, and a fecal sample from such animals should be examined for ***Cryptosporidium, Salmonella***, and ***Campylobacter***.

(6) HIV-infected persons should wash their hands after handling pets (especially before eating) and

should avoid contact with pets' feces (BIII).

(7) HIV-infected persons should avoid contact with reptiles (e.g., snakes, lizards, iguanas, and turtles) because of the risk 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 on local antimicrobial-resistance patterns of gastrointestinal pathogens, which are seldom known. Moreover, these agents can elicit adverse reactions and can promote the emergence of resistant organisms. However, for HIV-infected travelers, antimicrobial prophylaxis may be considered, depending on the level of immunosuppression and the region and duration of travel (CIII). The use of fluoroquinolones such as ciprofloxacin (500 mg/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 should be given to patients before their departure, to be taken empirically (e.g., 500 mg of ciprofloxacin twice a day for 3-7 days) should traveler's diarrhea develop (BIII). **Fluoroquinolones should be avoided in children ≤ 18 years and pregnant women, and alternative antibiotics should be considered (BIII).** Travelers should consult a physician if their diarrhea is severe and does not respond to empirical therapy, if their stools contain blood, if fever is accompanied by shaking chills, or if dehydration develops. Antiperistaltic agents (e.g., diphenoxylate and loperamide) can be used 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 administered to patients who have a high fever or who have blood in the stool (AII).

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

Prevention of Recurrence

(12) **HIV-infected persons who have *Salmonella* septicemia require long-term therapy (i.e., secondary prophylaxis, chronic maintenance 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 who have salmonellosis or shigellosis should be evaluated for persistent asymptomatic carriage of ***Salmonella*** or ***Shigella*** so that strict hygienic measures and/or antimicrobial therapy can be instituted and recurrent transmission to the HIV-infected person can be prevented (CIII).

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 aged <3 months and all HIV-infected children who have severe immunosuppression should be administered treatment for ***Salmonella*** gastroenteritis to prevent extraintestinal spread (CIII). **Possible choices of antibiotics include TMP-SMZ, ampicillin, cefotaxime, ceftriaxone, or chloramphenicol; fluoroquinolones should be used with caution and only if no alternatives exist.**

(16) HIV-infected children who have ***Salmonella*** septicemia should be offered long-term therapy for the prevention of recurrence (CIII). TMP-SMZ is the drug of choice; ampicillin or chloramphenicol can be used if the organism is susceptible. **Fluoroquinolones should be used with caution and only if no alternative exists.**

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

Notes Regarding Pregnancy

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

(19) Since extra-intestinal spread of *Salmonella* during pregnancy may lead to infection of the placenta and amniotic fluid with pregnancy loss similar to that seen with *Listeria monocytogenes*, pregnant women with *Salmonella* gastroenteritis should receive treatment (BIII). Possible choices for treatment include ampicillin, cefotaxime, ceftriaxone, or TMP-SMZ. Fluoroquinolones should be avoided.

(20) 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 persons should consider the potential risks of cat ownership (CIII). Those who elect to acquire a cat should adopt or purchase an older animal (aged >1 year) that is in good health (BII).

(2) Although declawing is not generally advised, HIV-infected persons should avoid rough play with cats and situations in which scratches are likely (BII). Any cat-associated wound should be washed promptly (CIII). 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 serologic 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).

Notes

Pediatric Note

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

Note Regarding Pregnancy

(8) If long-term suppression of bartonella is required, erythromycin should be used. Tetracyclines should not be used in pregnancy.

Candidiasis

Prevention of Exposure

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

Prevention of Disease

(2) Data from a prospective controlled trial indicate that fluconazole can reduce the risk of mucosal (oropharyngeal, esophageal, and vaginal) candidiasis (and Cryptococcosis as well) in patients with advanced HIV disease (48) (48-50). **However, routine primary prophylaxis is not recommended because of the effectiveness of therapy for acute disease, the low mortality associated with mucosal candidiasis, the potential for resistant *Candida* organisms to develop, the possibility of drug interactions, and the cost of prophylaxis (DIII).**

Prevention of Recurrence

(3) Many experts do not recommend chronic prophylaxis of recurrent oropharyngeal or vulvovaginal candidiasis for the same reasons that they do not recommend primary prophylaxis. **However, if recurrences are frequent or severe, chronic administration of an oral azole (fluconazole [CI] [48], or itraconazole solution [CI]) may be considered. Other factors that influence choices about such therapy include the impact of the recurrences on the patient's well-being and quality of life, the need for prophylaxis for other fungal infections, cost, toxicities, drug interactions, and the potential to induce resistance among Candida and other fungi. Prolonged use of systemically absorbed azoles, particularly in patients with low CD4+ T-lymphocyte counts (i.e. ≤ 100 cells/uL), increases the risk for the development of azole resistance.**

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

Notes

Pediatric Notes

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

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

Note Regarding Pregnancy

(7) There is limited experience with the use of antifungal drugs during human pregnancy. In addition, itraconazole is embryotoxic and teratogenic (50). Four cases of infants born with craniofacial and skeletal abnormalities following prolonged in-utero exposure to fluconazole have been reported. In addition,

itraconaole is embryotoxic and teratogenic in animal systems. These same potential risks of teratogenicity are presumed to apply to other systemically-absorbed azole antifungals, such as ketoconazole. Therefore, chemoprophylaxis against oropharyngeal, esophageal, or vaginal candidiasis using systemically-absorbed azoles should not be initiated during pregnancy (DIII), and azoles should be discontinued in HIV-infected women who become pregnant (DIII). Effective birth control should be recommended to all HIV-infected women on azole therapy for candidiasis (AIII).

Cryptococcosis

Prevention of Exposure

(1) HIV-infected persons cannot completely avoid exposure to *Cryptococcus neoformans*. There is no evidence that exposure to pigeon droppings is associated with an increased risk of acquiring cryptococcosis.

Prevention of Disease

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

(3) Prospective controlled trials indicate that fluconazole and itraconazole can reduce the frequency of cryptococcal disease among patients who have advanced HIV disease. However, most experts recommend that antifungal prophylaxis not be used routinely to prevent cryptococcosis because of the relative infrequency of cryptococcal disease, the lack of survival benefit associated with prophylaxis, the possibility of drug interactions, the potential for development of antifungal drug resistance, and cost. The need for prophylaxis or suppressive therapy for other fungal infections (e.g., candidiasis, histoplasmosis or coccidioidomycosis) should be considered in making decisions about prophylaxis for cryptococcosis. If used, fluconazole at doses of 100-200 mg daily is reasonable for patients whose CD4+ T-lymphocyte counts are $\leq$ 50 cells/uL (CI) (48-50).

Prevention of Recurrence

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

Discontinuation of Secondary Prophylaxis (chronic maintenance therapy)

(5) Although patients receiving secondary prophylaxis (chronic maintenance therapy) may be at low risk for recurrence of systemic mycosis when their CD4+ T-lymphocyte counts increase to > 100 cells/uL on HAART, the numbers of patients who have been evaluated are insufficient to warrant a recommendation to discontinue prophylaxis in such patients.

Notes

Pediatric Note

(6) 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 (AII).

Note Regarding Pregnancy

(7) Prophylaxis with fluconazole or itraconazole should not be initiated during pregnancy because of the low incidence of cryptococcal disease, the lack of a recommendation for primary prophylaxis against cryptococcosis in nonpregnant adults, and the potential for teratogenic effects of these drugs during pregnancy (DIII) (51-53). For patients who conceive while being administered primary prophylaxis and who elect to continue their pregnancy, prophylaxis should be discontinued. The occurrence of craniofacial and skeletal abnormalities in infants following prolonged in-utero exposure to fluconazole should be considered when assessing the therapeutic options for HIV-infected women who become pregnant and are receiving secondary prophylaxis (maintenance therapy) for cryptococcosis (51). In such patients, therapy with amphotericin B may be preferred, especially during the first trimester. Effective birth control should be recommended to all HIV-infected women on azole therapy for cryptococcosis (AIII).

Histoplasmosis

Prevention of Exposure

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

Prevention of Disease

(2) Routine skin testing with histoplasmin and serologic testing for antibody or antigen in histoplasmosis-endemic areas are not predictive of disease and should not be performed (DII).

(3) Data from a prospective randomized controlled trial indicate that itraconazole can reduce the frequency of histoplasmosis among patients who have advanced HIV infection and who live in *H.capsulatum* endemic areas (55). However, no survival benefit was observed in those receiving itraconazole. Prophylaxis with itraconazole may be considered in patients with CD4+ T-lymphocyte counts ≤ 100 cells/uL who are at especially high risk because of occupational exposure or who live in a community with a hyperendemic rate of histoplasmosis (≥ 10 cases per 100 patient-years) (CI).

Prevention of Recurrence

(4) Patients who complete initial therapy for histoplasmosis should be administered lifelong suppressive treatment (i.e. secondary prophylaxis or chronic maintenance therapy) with itraconazole (200 mg bid) (AI) (54).

Discontinuation of Secondary Prophylaxis (chronic maintenance therapy)

(5) Although patients receiving secondary prophylaxis (chronic maintenance therapy) may be at low risk for recurrence of systemic mycosis when their CD4+ T-lymphocyte counts increase to > 100 cells/uL on HAART, the numbers of patients who have been evaluated are insufficient to warrant a recommendation to discontinue prophylaxis in such patients.

Notes

Pediatric Note

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

Note Regarding Pregnancy

(7) Because of the embryotoxicity and teratogenicity of itraconazole in animal systems, primary prophylaxis against histoplasmosis should not be offered during pregnancy (DIII). These data as well as the observation of craniofacial and skeletal abnormalities in infants following prolonged in-utero exposure to fluconazole should be considered when assessing the need for chronic maintenance therapy in HIV-infected pregnant women with histoplasmosis. In such patients, therapy with amphotericin B may be preferred, especially during the

first trimester. Effective birth control should be recommended to all HIV-infected women on azole therapy for histoplasmosis (AIII).

Coccidioidomycosis

Prevention of Exposure

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

Prevention of Disease

(2) Routine skin testing with coccidioidin (spherulin) in coccidioidomycosis-endemic areas is not predictive of disease and should not be performed (DII). Within the endemic area, a positive serologic test may indicate an increased risk for active infection; however, routine testing does not appear to be useful and should not be performed (DIII).

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

Prevention of Recurrence

(4) Patients who complete initial therapy for coccidioidomycosis should be administered lifelong suppressive therapy (i.e., secondary prophylaxis or chronic maintenance therapy) (AII) using either fluconazole 400 mg po qd or itraconazole 200 mg bid (56). Patients with meningeal disease require consultation with an expert.

Discontinuation of Secondary Prophylaxis (chronic maintenance therapy)

(5) Although patients receiving secondary prophylaxis (chronic maintenance therapy) may be at low risk for recurrence of systemic mycosis when their CD4+ T-lymphocyte counts increase to > 100 cells/uL on HAART, the numbers of patients who have been evaluated are insufficient to warrant a recommendation to discontinue prophylaxis in such patients.

Notes

Pediatric Note

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

Note Regarding Pregnancy

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

Cytomegalovirus Disease

Prevention of Exposure

(1) HIV-infected persons who belong to risk groups with relatively low rates of seropositivity for cytomegalovirus (CMV) and therefore cannot be presumed to be seropositive, should be tested for antibody to CMV (BIII). These groups include patients who have had neither male homosexual contact nor used injection drugs.

(2) HIV-infected adolescents and adults should be advised that CMV is shed in semen, cervical secretions, and saliva and that latex condoms must always be used during sexual contact to reduce the risk of exposure to CMV and to other sexually transmitted pathogens (AII).

(3) **HIV-infected adults and adolescents who are child-care providers or parents of children in child-care facilities should be informed that they are at increased risk of acquiring CMV infection (BI). Similarly, parents and other care-takers 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 be administered only CMV antibody-negative or leukocyte-reduced cellular blood products in non-emergency situations (BIII).

Prevention of Disease

(5) **Prophylaxis with oral ganciclovir may be considered for HIV-infected adults and adolescents who are CMV seropositive and who have a CD4+ T-lymphocyte count of <50 cells/uL (CI) (57, 58). Ganciclovir-induced neutropenia, anemia, conflicting reports of efficacy, lack of proven survival benefit, the risk of developing ganciclovir resistant CMV, and cost are among the issues that should be**

considered in decisions about whether to institute prophylaxis in individual patients. Acyclovir is not effective in preventing CMV disease, and valacyclovir is not recommended because of an unexplained trend toward increased mortality observed in persons who have AIDS and who were administered this drug for CMV prophylaxis. Therefore, neither acyclovir nor valaciclovir should be used for this purpose (EI). The most important method for preventing severe CMV disease is recognition of the early manifestations of the disease. Early recognition of CMV retinitis is most likely when the patient has been educated on this topic. Patients should be made aware of the significance of increased "floaters" in the eye and should be advised to assess their visual acuity regularly by simple techniques such as reading newsprint (BIII). **Regular funduscopic examinations performed by a health-care provider or specifically by an ophthalmologist are recommended by some experts for patients with low (e.g., <50 cells/uL) CD4+ T-lymphocyte counts (CIII).**

Prevention of Recurrence

(6) CMV disease is not cured with courses of the currently available antiviral agents (i.e., ganciclovir, foscarnet, or cidofovir). Following induction therapy, secondary prophylaxis (chronic maintenance therapy) is recommended for life (AI). Regimens that are effective for chronic suppression include parenteral or oral ganciclovir, parenteral foscarnet, combined parenteral ganciclovir and foscarnet, parenteral cidofovir, and (for retinitis only) ganciclovir administration via intraocular implant (AI) (59-63). The intraocular implant alone does not provide protection to the contralateral eye or to other organ systems. The choice of a chronic maintenance regimen for patients treated for CMV disease should be made in consultation with an expert. For patients with retinitis, this decision should be made in consultation with an ophthalmologist, and should take into consideration the anatomic location of the retinal lesion, vision in the contralateral eye, the immunologic and virologic status of the patient, and response to HAART (BIII).

Discontinuation of Secondary Prophylaxis (chronic maintenance therapy)

(7) Several studies have found results of discontinuing maintenance therapy in patients with CMV retinitis whose CD4+ T-lymphocyte counts have increased to over 100-150 cells/uL and whose HIV plasma RNA has been suppressed in response to HAART. These patients largely continue to remain disease free for > 30-90 weeks, whereas in the pre-HAART era, retinitis typically recurred in 6-8 weeks. Discontinuation of prophylaxis may be considered in patients with a sustained (e.g. > 3-6 month) increase in CD4 count to > 100-150 cells/uL on HAART (CIII). Such decisions should be made in consultation with an ophthalmologist and should take into account such factors as magnitude and duration of CD4+ T-

lymphocyte increase, magnitude and duration of viral load suppression, anatomic location of the retinal lesion, vision in the contralateral eye, and the feasibility of regular ophthalmic monitoring (CII) (64, 65). Prophylaxis should not be discontinued in patients with extraocular CMV disease (DIII).

Restarting Secondary Prophylaxis

(8) There are no data to guide recommendations for reinstitution of secondary prophylaxis. Pending the availability of such data, a reasonable approach would be to restart prophylaxis when the CD4 count has decreased to < 50-100 cells/uL (CIII).

Notes

Pediatric Note

(9) Some experts recommend obtaining a CMV urine culture on all HIV-infected (or exposed) infants at birth or at an early postnatal visit to identify those infants with congenital CMV infection (CIII). In addition, beginning at 1 year of age, CMV antibody testing on an annual basis may be considered for CMV-seronegative (and culture-negative) HIV-infected infants and children who are severely immunosuppressed (Table 7A and 7B) (CIII). Annual testing will allow identification of children who have acquired CMV infection and might benefit from screening for retinitis.

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

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

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

Note Regarding Pregnancy

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

Herpes Simplex Virus Disease

Prevention of Exposure

(1) HIV-infected persons should use latex condoms during every act of sexual intercourse to reduce the risk 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 who have frequent or severe recurrences may be administered daily suppressive therapy with oral acyclovir or famciclovir (AI) (66, 67).** Intravenous foscarnet or cidofovir can be used to treat infection due to acyclovir-resistant isolates of HSV, which are routinely resistant to ganciclovir as well (AII).

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) Oral acyclovir prophylaxis in late pregnancy is a controversial strategy recommended by some experts to prevent neonatal herpes transmission. However, such prophylaxis is not routinely recommended. For patients who have frequent, severe recurrences of genital HSV disease, acyclovir prophylaxis may be indicated (BIII). No pattern of adverse pregnancy outcomes has been reported after acyclovir exposures.

Varicella-Zoster Virus Infection

Prevention of Exposure

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

(BIII).

Prevention of Disease

(2) Very little data regarding safety and efficacy of varicella vaccine in HIV-infected adults are available; and no recommendation for its use can be made for this population. See Pediatric Note for use of varicella vaccine in children.

(3) For the prophylaxis of chickenpox, HIV-infected children and adults who are susceptible to VZV (i.e., those who have no history of chickenpox or shingles or who have no detectable antibody against VZV) should be administered varicella zoster immune globulin (VZIG) as soon as possible but within 96 hours after close contact with a patient who has chickenpox or shingles (AIII). **Data are lacking on the effectiveness of acyclovir for preventing chickenpox in susceptible HIV-infected children or adults, and no recommendation can be made.**

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

Prevention of Recurrence

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

Notes

Pediatric Note

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

Note Regarding Pregnancy

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

Human Herpesvirus 8 Infection

Prevention of Exposure

(1) The mechanism of transmission of human herpesvirus 8 (HHV-8; Kaposi's sarcoma [KS]-associated herpesvirus) is not known. Epidemiologic evidence suggests that sexual transmission is likely in men who have sex with men (MSM),

and may occur in heterosexuals as well. However, the virus has been detected more frequently in saliva than in semen from HHV-8-seropositive HIV-infected persons. Although the efficacy of condom use for preventing HHV-8 infection has not been established, HIV-infected persons should use latex condoms during every act of sexual intercourse to reduce the risk of exposure to sexually transmitted pathogens (AII).

Prevention of Disease

(2) Because clinical utility of routine serologic testing to identify HHV-8 infection has not been established, no recommendation for serologic testing can be made at this time.

(3) Lower rates of KS have been observed in AIDS patients treated with ganciclovir or foscarnet for CMV retinitis (59). HHV-8 replication in vitro is inhibited by ganciclovir, foscarnet, and cidofovir. However, because the efficacy and clinical utility of these drugs in preventing KS has not been established, no recommendation can be made concerning use of these or other drugs to prevent KS in individuals co-infected with HIV and HHV-8.

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

Prevention of Recurrence

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

Note

Pediatric Note

(6) In parts of the world where HHV-8 is endemic, horizontal transmission may occur among young children, possibly via saliva. However, no recommendations are currently available for prevention of HHV-8 transmission in childhood.

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 sexually transmitted pathogens, although there is little evidence to suggest that condoms reduce the risk of infection with human papillomavirus (HPV).

Prevention of Disease

HPV-associated genital epithelial cancers in HIV-infected women

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

(3) If the results of the Pap smear are abnormal, care should be provided according to the Interim Guidelines for Management of Abnormal Cervical Cytology published by a National Cancer Institute Consensus Panel and briefly summarized below (68).

(4) For patients whose Pap smears are interpreted as atypical squamous cells of undetermined significance (ASCUS), several management options are available; the choice depends in part on whether the interpretation of ASCUS is qualified by a statement indicating that a neoplastic process is favored. Follow-up by Pap tests without colposcopy is acceptable, particularly when the diagnosis of ASCUS is not qualified further or the cytopathologist favors a reactive process. In such situations, Pap tests should be repeated every 4-6 months for 2 years until three consecutive smears have been negative. If a second report of ASCUS occurs in the 2-year follow-up period, the patient should be considered for colposcopic evaluation (BIII).

(5) Women who have a diagnosis of unqualified ASCUS associated with severe inflammation should be evaluated for an infectious process. If specific infections are identified, reevaluation should be performed after appropriate treatment, preferably after 2-3 months (BIII).

(6) If the diagnosis of ASCUS is qualified by a statement indicating that a neoplastic process is favored, the patient should be managed as if a low-grade squamous intraepithelial lesion (LSIL) were present (see note [5]) (BIII). If a patient who has a diagnosis of ASCUS is at high risk (i.e., previous positive Pap tests or poor compliance with follow-up), the option of colposcopy should be considered (BIII).

(7) Several management options are available for patients who have LSIL. Follow-up with Pap tests every 4-6 months is used by many clinicians and is currently used in countries outside the United States as an established method of management. Patients managed in this fashion must be carefully selected and considered reliable for follow-up. If repeat smears show persistent abnormalities, colposcopy and directed biopsy are indicated (BIII). Colposcopy and directed biopsy of any abnormal area on the ectocervix constitute another appropriate option (BIII).

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

(9) There are no data to suggest that these guidelines to prevent cervical disease should be modified for women on HAART.

HPV-associated anal intraepithelial neoplasia and anal cancer in HIV-infected MSM

(10) Evidence from several studies shows that HPV-positive MSM are at increased risk of anal high-grade squamous intraepithelial lesions (HSIL) and may be at increased risk for anal cancer. Coupled with a recent cost-effectiveness analysis projecting that screening and treatment for anal HSIL provides clinical benefits comparable to other measures to prevent OIs in HIV-infected persons (69), anal cytology screening of HIV-infected MSM may become a useful preventive measure in the near future. However, further studies of screening and treatment programs for anal HSIL need to be carried out before recommendations for routine anal cytology screening can be made.

Prevention of Recurrence

(11) The risks for recurrence of squamous intraepithelial lesions and cervical cancer after conventional therapy are increased among HIV-infected women. The prevention of illness associated with recurrence depends on careful follow-up of patients after treatment. Patients should be monitored with frequent cytologic screening and, when indicated, with colposcopic examination for recurrent lesions (AI) (68, 69).

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

Note Regarding Pregnancy

(13) Use of intravaginal 5-fluorouracil for prevention of recurrent dysplasia is not recommended during pregnancy.

Hepatitis C Virus Infection

Prevention of Exposure

(1) The chief route of hepatitis C virus (HCV) transmission in the United States is injection drug use. Because injection drug use is a complex behavior, assessment of an individual's readiness to change this practice and efforts to provide education and support directed at recovery should be encouraged. Patients

should be counseled (70-72):

- **to stop using injection drugs (AIII),**
- **to enter and complete a substance-abuse treatment program, including a relapse prevention program (AIII).**
- **If continuing to inject, patients should be counseled (BIII):**
  - **To never reuse or "share" syringes, needles, water, or drug preparation equipment; if, nonetheless, injection equipment that has been used by other persons is shared, to first clean the equipment with bleach and water as for prevention of HIV;**
  - **To use only sterile syringes obtained from a reliable source (e.g., pharmacies or syringe exchange programs);**
  - **To use sterile (e.g., boiled) water to prepare drugs; if not possible, to use clean water from a reliable source (such as fresh tap water).**
  - **To use a new or disinfected container ("cooker") and a new filter ("cotton") to prepare drugs;**
  - **To clean the injection site before injection with a new alcohol swab; and**
  - **To safely dispose of syringes after one use.**

- **If continuing to use illegal drugs intranasally ("snorting"), patients should be counseled that this practice has been associated with HCV transmission and should be instructed not to share equipment (e.g. "straws") with other users (BIII).**

(2) Persons considering tattooing or body piercing should be informed of potential risks of acquiring bloodborne infections, which could be transmitted if equipment is not sterile or if proper infection control procedures are not followed (e.g., washing hands, using latex gloves, and cleaning and disinfecting surfaces (72) (BIII).

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

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

Prevention of Disease

(5) HIV-infected patients should be screened for HCV infection using enzyme immunoassays (EIA) licensed for detection of antibody to HCV (anti-HCV) in blood (BIII). Positive anti-HCV results should be verified with additional testing (i.e., RIBA™ or RT-PCR for HCV RNA). The presence of HCV RNA in blood might also be assessed in HIV-infected persons with undetectable antibody but other evidence of chronic liver disease (e.g., unexplained elevated liver-specific enzymes) or when acute HCV infection is suspected (CIII).

(6) HIV-HCV coinfected persons should be advised not to drink excessive amounts of alcohol (AII). It may be prudent to avoid alcohol altogether since it is unclear whether even occasional moderate alcohol use (e.g., less than 12 ounces of beer or 10 grams of alcohol per week) increases the incidence of cirrhosis in HIV-infected persons (see below) (CIII).

(7) Patients with chronic hepatitis C should be vaccinated against hepatitis A since: (1) the risk of fulminant hepatitis associated with hepatitis A appears increased in HCV-coinfected persons; (2) hepatitis A vaccine is safe in HIV-infected persons; and (3) although immunogenicity is reduced in patients with advanced HIV infection, more than two thirds develop protective antibody responses (BIII). Prevaccination screening for antibody to hepatitis A virus is cost-effective and therefore recommended when greater than thirty percent prevalence of HAV is expected in the population being screened (e.g., persons >40 years of age) (73) (BIII).

(8) HIV-HCV-coinfected patients should be evaluated for chronic liver disease and for possible need for treatment (71). However, there are limited data regarding the safety and efficacy of antiviral treatment of HIV-HCV-coinfected patients. Moreover, since the optimal means of treating HIV-HCV-coinfected patients has not been established and many HIV-infected patients have conditions which complicate therapy (e.g., depression or illicit drug use), this care should occur in a clinical trial or be coordinated by providers with experience treating both HIV and HCV infections (BIII).

(9) The incidence of antiretroviral-associated liver enzyme elevations is increased in HIV-HCV coinfected patients in some but not all studies; such increases may not require treatment modifications. Thus, while liver enzymes should be carefully monitored, HAART therapy should not be routinely withheld from HIV-HCV infected patients (DIII). However, HIV-HCV-coinfected patients receiving antiretroviral therapy may experience an inflammatory reaction that may mimic an exacerbation

of underlying liver disease. In this setting, careful monitoring of liver function is required.

Prevention of Recurrence

(10) If the serum HCV RNA level becomes undetectable on therapy and remains undetectable for 6 months after stopping HCV therapy (sustained virologic response), more than 90% of HIV-uninfected patients with hepatitis C will remain HCV RNA negative for >5 years and have improved liver histology. In HIV-HCV-coinfected patients, the durability of treatment response and requirement for maintenance therapy in sustained responders are unknown.

Note

Pediatric Note

(11) Children born to HIV/HCV-infected women should be tested for HCV infection (70) (BI). In children with perinatal HCV infection, maternal HCV antibody may persist for up to 18 months and HCV RNA can be intermittently undetectable. Thus, testing should be performed at or after two years of age. If earlier diagnosis is needed, HCV RNA should be assessed in more than one infant blood specimen obtained after one month of age. The average rate of HCV infection among infants born to HIV-HCV coinfected women is approximately 15 percent (range 5-36 percent). There are limited data regarding the natural history and treatment of HCV infection in children.

DRUG REGIMENS FOR ADULTS AND ADOLESCENTS

Table 1A. 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 <200/uL or oropharyngeal candidiasis or unexplained fever ≥ 2 weeks	Trimethoprim-sulfamethoxazole (TMP-SMZ), 1 DS po q.d. (AI) TMP-SMZ, 1 SS po q.d. (AI)	Dapsone, 50 mg po b.i.d. ***or*** 100 mg po q.d. (BI); dapsone, 50 mg po q.d. ***plus*** pyrimethamine, 50 mg po q.w. ***plus*** leucovorin, 25 mg po q.w. (BI); dapsone, 200 mg po ***plus*** pyrimethamine, 75 mg po ***plus*** leucovorin, 25 mg po q.w. (BI); aerosolized pentamidine, 300 mg q.m. via Respirgard II ™ nebulizer (BI); ***atovaquone 1500 mg po q.d. (BI); TMP-SMZ, 1 DS po t.i.w. (CI)***
Mycobacterium tuberculosis			
Isoniazid-sensitive[†]	TST reaction ≥5mm ***or*** prior positive TST result without treatment ***or*** contact with case of active tuberculosis	***Isoniazid, 300 mg po plus pyridoxine, 50 mg po q.d. x 9 mo (AII) or isoniazid, 900 mg po plus pyridoxine, 100 mg po b.i.w. x 9 mo (BI); Rifampin 600 mg plus pyrazinamide 20 mg/kg po q.d. x 2 mo (AI)***	***Rifabutin 300 mg po q.d. plus pyrazinamide 20 mg/kg po q.d. x 2 mo (BIII); rifampin 600 mg po q.d. x 4 mo (BIII)***
Isoniazid-resistant	Same; high probability of exposure to isoniazid-resistant tuberculosis	***Rifampin 600 mg plus pyrazinamide 20 mg/kg po q.d. x 2 mo (AI)***	***Rifabutin 300 mg plus pyrazinamide 20 mg/kg po q.d. x 2 mo (BIII); rifampin 600 mg po q.d. x 4 mo (BIII) plus Rifabutin, 300 mg po q.d. x 4 mo (CIII)***
Multidrug-(isoniazid and rifampin) resistant	Same; high probability of exposure to multidrug-resistant tuberculosis	Choice of drugs requires consultation with public health authorities	None
Toxoplasma gondii[§]	IgG antibody to ***Toxoplasma*** and $CD4^+$ count <100/uL	TMP-SMZ, 1 DS po q.d. (AII)	TMP-SMZ, 1 SS po q.d. (BIII): dapsone, 50 mg po q.d***. plus*** pyrimethamine, 50 mg po q.w. ***plus*** leucovorin, 25 mg po q.w. (BI); ***atovaquone 1500 mg po q.d. (CIII)***
Mycobacterium avium complex[¶]	$CD4^+$ count <50/uL	Azithromycin, 1,200 mg po q.w. (AI) or clarithromycin, 500 mg po b.i.d. (AI)	Rifabutin, 300 mg po q.d. (BI); azithromycin, 1,200 mg po q.w. ***plus*** rifabutin, 300 mg po q.d. (CI)
Varicella zoster virus (VZV)	Significant exposure to chickenpox or shingles for patients who have no history of either condition or, if available, negative antibody to VZV	Varicella zoster immune globulin (VZIG), 5 vials (1.25 mL each) im, administered ≤96 h after exposure, ideally within 48 h (AIII)	

Table 1A. Prophylaxis for first episode of opportunistic disease in HIV-infected adults a adolescents - Continued

		Preventive Regimens	
Pathogen	**Indication**	**First Choice**	**Alternatives**
II. Generally recommended			
Streptococcus pneumoniae **	All patients	***Pneumococcal vaccine, 0.5 m/L im (CD4$^+$ ≥200/uL [BII]; CD4$^+$ <200/uL (CIII) – may reimmunize if initial immunization was given when CD4+ < 250/uL and if CD4+ increases to > 200/uL on HAART(CIII)***	None
Hepatitis B virus ††	***All susceptible (anti-HBc- and anti-HBs -negative) patients***	***Hepatitis B vaccine: 3 doses (BII)***	None
Influenza virus ††	All patients (annually, before influenza season)	Whole or split virus, 0.5 uL im/yr (BIII)	Rimantadine, 100 mg po b.i.d. CIII) or amantadine, 100 mg po b.i.d. (CIII)
Hepatitis A virus†	***All susceptible (anti-HAV-negative) patients with chronic hepatitis C***	***Hepatitis A vaccine: two doses (BIII)***	***None***

Table 1A. Prophylaxis for first episode of opportunistic disease in HIV-infected adults and adolescents - Continued

		Preventive Regimens	
Pathogen	**Indication**	**First Choice**	**Alternatives**
III. Not routinely indicated			
Bacteria	Neutropenia	***Granulocyte-colony-stimulating factor (G-CSF), 5-10 ug/kg sc q.d. x 2-4w or granulocyte-macrophage colony-stimulating factor (GM-CSF), 250 ug/m^2 iv over 2 h q.d. x 2-4w (CII)***	***None***
Cryptococcus neoformans [§§]	$CD4^+$ count <50/uL	Fluconazole, 100-200 mg po q.d. (CI)	Itraconazole, 200 mg po q.d. (CIII)
Histoplasma capsulatum [§§]	$CD4^+$ count <100/uL, endemic geographic area	Itraconazole, 200 mg po q.d.(CI)	None
Cytomegalovirus(CMV)[¶¶]	$CD4^+$ count <50/uL and CMV antibody positivity	Oral ganciclovir, 1 g po t.i.d. (CI)	None

NOTE: Information included in these guidelines may not represent Food and Drug Administration (FDA) approval or approved labeling for the particular products or indications in question. Specifically, the terms "safe" and "effective" may not be synonymous with the FDA-defined legal standards for product approval. Anti-HBc = antibody to hepatitis B core antigen; b.i.w.= twice a week; CMV = cytomegalovirus; DS = double-strength tablet; q.m. = monthly; q.w. = weekly; SS= single-strength tablet; t.i.w. = three times a week; TMP-SMZ =trimethoprim-sulfamethoxazole; and TST = tuberculin skin test. 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 evidence supporting it (see text).

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

† ***Directly observed therapy recommended for isoniazid (INH), 900 mg b.i.w.; INH regimens should include pyridoxine to prevent peripheral neuropathy. Rifampin should not be administered concurrently with protease inhibitors or non-nucleoside reverse transcriptase inhibitors. Rifabutin should not be given with hard-gel saquinavir, ritonavir, or delavirdine; caution is also advised when the drug is co-administered with soft-gel saquinavir. Rifabutin may be administered at a reduced dose (150 mg qd) with indinavir, nelfinavir, or amprenavir, or at an increased dose (450 mg qd) with efavirenz; information is lacking regarding co-administration of rifabutin with nevaripine.*** 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.

§ ***Protection against Toxoplasma is provided by TMP-SMZ, dapsone plus pyrimethamine, and possibly by atovaquone. The latter may be used with or without pyrimethamine***. Pyrimethamine alone probably provides little, if any, protection.

¶ ***See footnote above (†) regarding use of rifabutin with protease inhibitors or non-nucleoside reverse transcriptase inhibitors.***

** Vaccination should be offered to persons who have a CD4+ T-lymphocyte count <200 cells/uL, although the efficacy may be diminished. ***Revaccination ≥5 years after the first dose or sooner if the initial immunization was given when the CD4+ count was < 200 cells/uL and if the CD4+ count has increased to > 200 cells/uL on HAART is considered optional.*** Some authorities are concerned that immunizations may stimulate the replication of HIV. However, one study showed no adverse effect of pneumococcal vaccination on patient survival (75).

†† ***These immunizations or chemoprophylactic regimens do not target pathogens traditionally classified as opportunistic but should be considered for use in HIV-infected patients as indicated***. Data are inadequate concerning clinical benefit of these vaccines in this population, although it is logical to assume that those patients who develop antibody responses will derive some protection. Some authorities are concerned that immunizations may stimulate HIV replication, although, for influenza vaccination, a large observational study of HIV-infected persons in clinical care showed no adverse effect of this vaccine, including multiple doses, on patient survival (J. Ward, CDC, personal communication). Hepatitis B vaccine has been recommended for all children and adolescents and for all adults with risk factors for HBV. Rimantadine/amantadine are appropriate during outbreaks of influenza A. Because of the theoretical concern that increases in HIV plasma RNA following vaccination during pregnancy might increase the risk of perinatal transmission of HIV, providers may wish to defer vaccination until after antiretroviral therapy is initiated. ***For additional information regarding vaccination against hepatitis A and B and vaccination and antiviral therapy against influenza, see references 73, 74, 75, and 76.***

§§ There may be a few unusual occupational or other circumstances under which to consider prophylaxis; consult a specialist.

¶¶ Acyclovir is not protective against CMV. Valaciclovir is not recommended because of an unexplained trend toward increased mortality observed in persons who have AIDS who were being administered this drug for prevention of CMV disease.

Table 1B. Prophylaxis for recurrence of opportunistic disease (after chemotherapy for acute disease) in HIV-infected adults and adolescents

		Preventive Regimens	
Pathogen	**Indication**	**First Choice**	**Alternatives**
I. Recommended for life as standard of care			
Pneumocystis carinii	Prior ***P. carinii*** pneumonia	Trimethoprim-sulfamethoxazole (TMP-SMZ), 1 DS po q.d. (AI); TMP-SMZ 1 SS po q.d. (AI)	Dapsone, 50 mg po b.i.d. ***or*** 100 mg po q.d. (BI); dapsone, 50 mg po q.d. ***plus*** pyrimethamine, 50 mg po q.w. plus leucovorin, 25 mg po q.w. (BI); dapsone, 200 mg po ***plus*** pyrimethamine, 75 mg po ***plus*** leucovorin, 25 mg po q.w. (BI); aerosolized pentamidine, 300 mg q.m. via Respirgard II™ nebulizer (BI); ***Atovaquone 1500 mg po q.d. (BI); TMP-SMZ, 1 DS po t.i.w. (CI)***
Toxoplasma gondii*	Prior toxoplasmic encephalitis	Sulfadiazine 500-1000 mg po q.i.d. ***plus*** pyrimethamine 25-75 mg po q.d. plus leucovorin 10 mg po q.d. (AI)	Clindamycin, 300-450 mg po q 6-8 h ***plus*** pyrimethamine, 25-75 mg po q.d. ***plus*** leucovorin, 10-25 mg po q.d. (BI)
Mycobacterium avium complex †	Documented disseminated disease	***Clarithromycin, 500 mg po b.i.d. (AI) plus ethambutol, 15 mg/kg po q.d.(AII); with or without rifabutin, 300 mg po q.d. (CI)***	***Azithromycin, 500 mg po q.d. (AII) plus ethambutol, 15 mg/kg po q.d.(AII); with or without rifabutin, 300 mg po q.d.(CI)***
Cytomegalovirus	Prior end-organ disease	***Ganciclovir, 5-6 mg/kg iv 5-7 days/wk or 1,000 mg po t.i.d. (AI); or foscarnet, 90-120 mg/kg iv q.d. (AI); or (for retinitis) ganciclovir sustained-release implant q 6-9 months plus ganciclovir, 1.0-1.5 g po t.i.d. (AI)***	***Cidofovir, 5 mg/kg iv q.o.w. AI); Fomivirsen 1 vial injected into the vitreous, then repeated q 2-4 wks (AI)***
Cryptococcus neoformans	Documented disease	Fluconazole, 200 mg po q.d. (AI)	Amphotericin B, 0.6-1.0 mg/kg iv q.w.-t.i.w. (AI); itraconazole, 200 mg po q.d. (BI)
Histoplasma capsulatum	Documented disease	***Itraconazole, 200 mg po b.i.d. (AI)***	***Amphotericin B, 1.0 mg/kg iv q.w.(AI)***
Coccidioides immitis	Documented disease	Fluconazole, 400 mg po q.d. (AII)	Amphotericin B, 1.0 mg/kg iv q.w.(AI); itraconazole, 200 mg po b.i.d.(AII)
Salmonella species (non-typhi)§	Bacteremia	Ciprofloxacin, 500 mg po b.i.d. for several months (BII)	None

Table 1B. Prophylaxis for recurrence of opportunistic disease (after chemotherapy for acute disease) in HIV-infected adults and adolescents - Continued

		Preventive Regimens	
Pathogen	**Indication**	**First Choice**	**Alternatives**
II. Recommended only if subsequent episodes are frequent or severe			
Herpes simplex virus	Frequent/severe recurrences	Acyclovir, 200 mg po t.i.d. or 400 mg po b.i.d.(AI) ***Famciclovir 500 mg po b.i.d. (AI)***	None
Candida (oropharyngeal or vaginal)	***Frequent/severe recurrences***	***Fluconazole 100-200 mg po q.d. (CI)***	***Itraconazole solution, 200 mg po q.d. (CI); ketoconazole, 200 mg po q.d. (CIII)***
Candida (esophageal)	***Frequent/severe recurrences***	***Fluconazole 100-200 mg po q.d. (BI)***	***Itraconazole solution, 200 mg po q.d. (BI); ketoconazole, 200 mg po q.d. (CIII)***

NOTE: Information included in these guidelines may not represent Food and Drug Administration (FDA) approval or approved labeling for the particular products or indications in question. Specifically, the terms "safe" and "effective" may not be synonymous with the FDA-defined legal standards for product approval. DS = double-strength tablet; q.m. = monthly; q.w. = weekly; SS = single-strength tablet; t.i.w. = three times a week; 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).

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

† Many multiple-drug regimens are poorly tolerated. Drug interactions (e.g., those seen with clarithromycin/ rifabutin) can be problematic; rifabutin has been associated with uveitis, especially when administered at daily doses of >300 mg or concurrently with fluconazole or clarithromycin. ***Rifabutin should not be administered concurrently with hard gel saquinavir, ritonavir, or delavirdine; caution is also advised when the drug is co-administered with soft-gel saquinavir. Rifabutin may be administered at reduced dose (150 mg q.d.) with indinavir, nelfinavir, or amprenavir, or at increased dose (450 mg q.d.) with efavirenz. Information is lacking regarding co-administration of rifabutin with nevirapine.***

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

Table 2. Clinically Relevant Drug-Food and Drug-Drug Interactions with Agents Used for the Prevention of Opportunistic Infections in HIV-Infected Patients

Food Interactions Affecting Drugs Used to Prevent Opportunistic Infections

Drug	Food Effect	Recommendation
Atovaquone	Bioavailability increased up to 3-fold with high fat meal	Administer with food
Ganciclovir (capsules)	High fat meal results in 22% ↑ in AUC	Administer with food
Itraconazole (capsules)	Significant increase in bioavailability when taken with a full meal. Grapefruit juice results in 30% decrease in itraconazole AUC	Administer with food; avoid grapefruit juice or increased itraconazole dose may be necessary
Itraconazole (solution)	31% increase in AUC when taken under fasting conditions	Recommended to be taken without food if possible

Drug Interactions Affecting Drugs Used to Prevent Opportunistic Infections

Affected drug	Interacting drug(s)	Mechanism / Effect	Recommendation
Atovaquone	Rifampin	Induction of metabolism – decreased drug levels	Concentrations may not be therapeutic – avoid combination or increase atovaquone dose
Clarithromycin	Ritonavir	Inhibition of metabolism – increased drug levels by 77%	No adjustment needed in normal renal function – adjust if CrCL < 30
Clarithromycin	Nevirapine	Induction of metabolism – decrease in clarithromycin AUC by 35%, increase in AUC of 14-OH clarithromycin by 27%	Effect on ***Mycobacterium avium intracellulare*** prophylaxis may be decreased, monitor closely
Ketoconazole	Antacids, didanosine, H2-blockers, proton pump inhibitors	Increase in gastric pH impairs absorption of ketoconazole	Avoid use of ketoconazole with pH-raising agents or use alternative antifungal drug
Quinolone antibiotics (ciprofloxacin, levofloxacin, ofloxacin, etc)	Didanosine, antacids, iron products, calcium products, sucralfate	Chelation resulting in marked decrease in quinolone drug levels	Administer cation preparation at least 2 hours after quinolone
Rifabutin	Fluconazole	Inhibition of metabolism - marked increase in rifabutin drug levels	Monitor for rifabutin toxicity such as uveitis, nausea, neutropenia
Rifabutin	Efavirenz	Induction of metabolism - Significant decrease in rifabutin AUC	Increase rifabutin dose to 450 mg q.d.
Rifabutin	Ritonavir, saquinavir, indinavir, nelfinavir, amprenavir, delavirdine	Inhibition of metabolism - marked increase in rifabutin drug levels	Contraindicated with ritonavir, hard-gel saquinavir (caution also advised with soft-gel saquinavir), and delavirdine – use 1/2 dose (150 mg qd) with indinavir, nelfinavir, amprenavir

Effects of Opportunistic Infection Medication on Drugs Commonly Used in HIV-infected Persons

Affected drug	Interacting drug(s)	Mechanism / Effect	Recommendation
Indinavir, Saquinavir, Ritonavir, Nelfinavir, Amprenavir	Rifampin	Induction of metabolism – marked decrease in protease inhibitor drug levels	Avoid concomitant use
Delavirdine, Nevirapine, Efavirenz	Rifampin	Induction of metabolism – marked decrease in drug levels	Avoid concomitant use
Ritonavir, Saquinavir (hard gel), Delavirdine	Rifabutin	Induction of metabolism – marked decrease in drug levels	Avoid concomitant use
Terfenadine, astemizole Cisapride	Ketoconazole Itraconazole Fluconazole Clarithromycin	Inhibition of metabolism	Cardiotoxic life-threatening effects possible- avoid concomitant use
Didanosine	Ganciclovir	Increases ddI AUC by approximately 100%	Clinical significance unknown; monitor for ddI-related adverse effects

Table 3. Adverse effects of Drugs Used in the Management of HIV Infection

Bone Marrow Suppression	Cidofovir, Cotrimoxazole, Cytotoxic chemotherapy, Dapsone, Flucytosine, Ganciclovir, Hydroxyurea, Interferon-α, Pyrimethamine, Ribavirin, Rifabutin, Sulfadiazine, Trimetrexate, Zidovudine
Diarrhea	Atovaquone, Didanosine, Clindamycin, Nelfinavir, Ritonavir
Hepatotoxicity	Clarithromycin, Delavirdine, Efavirenz, Fluconazole, Indinavir, Isoniazid, Itraconazole, Ketoconazole, Nelfinavir, Nevirapine, Rifabutin, Rifampin, Ritonavir
Nephrotoxicity	Adefovir, Aminoglycosides, Amphotericin B, Cidofovir, Foscarnet, Indinavir, Pentamidine
Ocular Effects	Cidofovir, Ethambutol, Rifabutin
Pancreatitis	Cotrimoxazole, Didanosine, Lamivudine (children), Pentamidine
Peripheral Neuropathy	Didanosine, Isoniazid, Stavudine, Zalcitabine, Thalidamide
Skin Rash	Abacavir, Atovaquone, Cotrimoxazole, Dapsone, Delavirdine, Efavirenz, Nevirapine, Atovaquone

Table 4. Dosing of Drugs for Primary Prevention or Maintenance Therapy for Opportunistic Infections in Renal Insufficiency

Drug	Normal Dose	Renal Dysfunction
Acyclovir	200 mg - 800 mg BID - 5ID	Regimen / CrCl (ml/min/1.73m^2) / Adjusted dose 200 mg PO TID / < 10 / 200 mg q12h 400 mg PO q12h / < 10 / 200 mg q12h 800 mg PO q4h / 10-25 / 800 mg q8h 800 mg PO q4h / 0-10 / 800 mg q12h
Cidofovir	5 mg/kg IV every other week (with probenecid)	Reduce from 5 mg/kg to 3 mg/kg for an increase in serum creatinine of 0.3-0.4 above baseline. Discontinue for an increase in creatinine ≥ 0.5 above baseline or development of 3+ proteinuria
Ciprofloxacin	500 mg PO q12 hr	**ıl/min) / Dose** 30 - 50 / 250 mg-500 mg q 12 hrs < 29 / 250 mg-500 mg q 18 hrs
Clarithromycin	500 mg BID	Reduce dose by one-half or double interval if creatinine clearance < 30 ml/min
Famciclovir	500 mg q12h	CrCl (ml/ m) / Dose 20-39 / 250 mg q12h < 20 / 250 mg q24h
Fluconazole	50 mg- 400mg QD	CrCl (ml/ m) / Dose 10-50 / 1/2 dose < 10 / 1/4dose dialysis / full dose after dialysis
Foscarnet	90-120 mg/kg/day	CrCl (ml/min/kg) / Maintenance low dose / high dose > 1.4 / 90mg q24h / 120mg q24h 1.0 - 1.4 / 70mg q24h / 90mg q24h 0.8 – 1.0 / 50mg q24h / 65 mg q24h 0.6 - 0.8 / 80mg q48h / 105mg q48h 0.5 - 0.6 / 60mg q48h / 80mg q48h 0.4 - 0.5 / 50mg q48h / 65mg q48h < 0.4 / not recc / not recc
Ganciclovir	Oral: 1 gram TID (capsules) IV: 5 mg/kg QD or 6	CrCl (ml/min) / IV Dose (mg/kg) / Capsules 50-69 / 2.5 q24h / 1500 mg qd or 500mg tid 25-49 / 1.25 q24h / 1000 mg qd or 500mg bid 10-24 / 0.625 q48h / 500 mg qd

	mg/kg QD x 5 days/week (IV)	< 10	0.625 TIW	500 mg TIW after dialysis
Levofloxacin	250 mg-500 mg QD	**ıl/min)**	**Dose**	
		50 - 80	500 mg LD, then 250 mg q 24 hrs	
		< 49	500 mg LD, then 250 mg q 48 hrs	
TMP/SMX	1 DS QD 1 DS TIW 1 SS QD	Recommended to reduce dose by 50% in patients with CrCl 15-30 m/min		

TABLE 5. Wholesale acquisition costs of agents recommended for prevention of opportunistic infections in patients who have HIV infection

Opportunistic Pathogen	Drug/Vaccine	Dose	Annual Cost *
Pneumocystis carinii	Trimethoprim-sulfamethoxazole	160/800 mg q.d.	$60
	Dapsone	100 mg q.d.	$***72***
	Aerosolized pentamidine	300 mg q.m.	$1,185
	Atovaquone	***1500 mg q.d.***	***$10,650***
Mycobacterium avium complex	Clarithromycin	500 mg b.i.d.	$***2,350***
	Azithromycin	1,200 mg q.w.	$***1,640***
	Rifabutin	300 mg q.d.	$***3,350***
Cytomegalovirus	Ganciclovir (po)	1,000 mg t.i.d.	$***17,270***
	Ganciclovir implant		$5,000
	Ganciclovir (iv)	5mg/kg q.d.	$9,110
	Foscarnet (iv)	90-120 mg/kg q.d.	$27,960-36,770
	Cidofovir (iv)	375 mg q.o.w.	$19,812
Mycobacterium tuberculosis	Isoniazid	300 mg q.d.	$***31***
	Rifampin	600 mg q.d.	$1,170
	Pyrazinamide	1,500 mg q.d.	$1,000
	Ethambutol	900 mg q.d.	$1,580
Fungi	Fluconazole	200 mg q.d.	$***4,270***
	Itraconazole	200 mg q.d.	$***4,890***
	Ketoconazole	200 mg q.d.	$1,220
Herpes simplex virus	Acyclovir	400 mg t.i.d.	$***1,960***
	Famciclovir	***500 mg b.i.d.***	***$4,830***
Toxoplasma gondii	Pyrimethamine	500 mg q.w.	$***450***
	Leucovorin	25 mg q.w.	$***980***
Streptococcus pneumoniae	23-valent pneumococcal vaccine	0.5 ml im x 1	$***13***
Influenza virus	Influenza vaccine	0.5 ml im x 1	$5
Hepatitis B virus	Recombinant hepatitis B	10-20ug im x 3	$***195***
Hepatitis A virus	***Hepatitis A vaccine***	***1.0 ml im x 2***	***$120***
Bacterial Infections	***GCSF***	***300 ug t.i.w.***	***$25,780***
Varicella zoster virus	***VZIG***	***625 u***	***$560***

* Rounded to the nearest $10.

Source: ***Drug Topics Red Book***, Medical Economics Inc., Montvale, NJ, 1999.

Table 6. Immunologic categories for HIV-infected children based on age-specific CD4+ T-lymphocyte counts and percentage of total lymphocytes*

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

* Adapted from 1994 revised classification system for human immunodeficiency virus infection in children aged <13 years (62).

† Percentage of total lymphocytes.

DRUG REGIMENS FOR CHILDREN

Table 7A. 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			
Pneumocystis carinii*	HIV-infected or HIV-indeterminate infants aged 1-12 mo; HIV-infected children aged 1-5 yr with $CD4^+$ count<500/uL or $CD4^+$ percentage <15%; HIV-infected children aged 6-12 yr with $CD4^+$ count <200/uL or $CD4^+$percentage <15%	Trimethoprim-sulfamethoxazole (TMP-SMZ),150/750 mg/m^2/d in 2 divided doses po t.i.w. on consecutive days (AII) Acceptable alternative dosage schedules: (AII) Single dose po t.i.w. on consecutive days; 2 divided doses po q.d.; 2 divided doses po t.i.w. on alternate days	***Dapsone (children aged ≥1 mo), 2 mg/kg (max 100 mg) po q.d. or 4 mg/kg (max. 200 mg) po q.w. (CII); Aerosolized pentamidine (children aged ≥5 yr), 300 mg q.m. via Respirgard II™ nebulizer (CIII); Atovaquone (age 1-3 mo. and > 24 mo., 30 mg/kg po q.d.; age 4-24 mo. 45 mg/kd po q.d.) (CII)***
Mycobacterium tuberculosis†			
Isoniazid-sensitive	TST reaction ≥5mm ***or*** prior positive TST result without treatment ***or*** contact with case of active tuberculosis	***Isoniazid 10-15 mg/kg (max 300 mg) po q.d. x 9 mo (AI) or 20-30 mg/kg (max 900 mg) po b.i.w. x 9 mo (BIII)***	***Rifampin, 10-20 mg/kg (max 600 mg) po q.d. x 4-6 mo (BIII)***
Isoniazid-resistant	Same as above; high probability of exposure to isoniazid-resistant tuberculosis	***Rifampin, 10-20 mg/kg (max 600 mg) po q.d. x 4-6 mo (BIII)***	Uncertain
Multidrug-(isoniazid and rifampin) resistant	Same as above; high probability of exposure to multidrug-resistant tuberculosis	Choice of drugs requires consultation with public health authorities	None
Mycobacterium avium complex†	For children aged ≥6 yrs, $CD4^+$ count <50/uL; aged 2-6 yrs, $CD4^+$ count <75/uL; aged 1-2 yrs, $CD4^+$ count <500/uL; aged <1 yr, $CD4^+$ count<750/uL	Clarithromycin, 7.5 mg/kg (max 500 mg) po b.i.d. (AII), ***o***r azithromycin, 20 mg/kg (max 1,200 mg) po q.w. (AII)	***Azithromycin, 5 mg/kg (max 250 mg) po q.d. (AII); children aged ≥6 yrs, rifabutin, 300 mg po q.d. (BI)***
Varicella zoster virus§	Significant exposure to varicella with no history of chickenpox or shingles	Varicella zoster immune globulin (VZIG), 1 vial (1.25 mL)/10 kg (max 5 vials) im, administered ≤96 hrs after exposure, ideally within 48 hrs (AII)	None
Vaccine-preventable pathogens¶	HIV exposure/infection	Routine immunizations (see Figure)	None

Table 7A. Prophylaxis for first episode of opportunistic disease in HIV-infected infants and children-Continued

		Preventive Regimens	
Pathogen	**Indication**	**First Choice**	**Alternatives**
II. Generally recommended			
Toxoplasma gondii **	IgG antibody to ***Toxoplasma*** and severe immunosuppression	TMP-SMZ, 150/750 mg/m^2 /d in 2 divided doses po q.d. (BIII)	Dapsone (children aged ≥1 mo), 2 mg/kg or 15 mg/m^2 (max 25 mg) po q.d. ***plus*** pyrimethamine, 1 mg/kg po q.d. ***plus*** leucovorin, 5 mg po every 3 days (BIII) ***Atovaquone, (age 1-3 mo. and > 24 mo., 30 mg/kg po q.d.; age 14-24 mo. 45 mg/kg po q.d.) (CIII)***
Varicella zoster virus¶	***HIV-infected children who are asymptomatic and not immunosuppressed***	***Varicella zoster vaccine (see vaccine-preventable pathogens) (BII)***	***None***
Influenza virus¶	***All patients (annually, before influenza season)***	***Influenza vaccine (see vaccine-preventable pathogens) (BIII)***	***Rimantadine or amantadine (during outbreaks of influenza A); age 1-9, 5 mg/kg in 2 divided doses po q.d.; age ≥ 10, use adult doses (CIII)***

Table 7A. Prophylaxis for first episode of opportunistic disease in HIV-infected infants and children-Continued

		Preventive Regimens	
Pathogen	**Indication**	**First Choice**	**Alternatives**
III. Not recommended for most children; indicated for use only in unusual circumstances			
Invasive bacterial infections[††]	Hypogammaglobulinemia	IVIG (400mg/kg/q.m.) (AI)	None
Cryptococcus neoformans	Severe immunosuppression)	Fluconazole, 3-6 mg/kg po q.d. (CII)	Itraconazole, 2-5 mg/kg po q 12-24 h (CIII)
Histoplasma capsulatum	Severe immunosuppression, endemic geographic area	Itraconazole, 2-5 mg/kg po q 12-24 h (CII)	None
Cytomegalovirus (CMV) [§§]	CMV antibody positivity and severe immunosuppression	***Oral ganciclovir 30 mg/kg po t.i.d. (CII)***	None

NOTE: Information included in these guidelines may not represent Food and Drug Administration (FDA) approval or approved labeling for the particular products or indications in question. Specifically, the terms "safe" and "effective" may not be synonymous with the FDA-defined legal standards for product approval. b.i.w.=twice a week; CMV= cytomegalovirus; IVIG = intravenous immune globulin; q.m. = monthly; t.i.w. = three times a week; 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).

* Daily TMP-SMZ reduces the frequency of some bacterial infections. ***TMP-SMZ, dapsone-pyrimethamine, and possibly atovaquone (with or without pyrimethamine) appear to protect against toxoplasmosis, although data have not been prospectively collected. When compared with weekly dapsone, a recent study suggested that daily dapsone is associated with lower incidence of PCP but higher hematologic toxicity and mortality ( ). The efficacy of parenteral pentamidine (e.g., 4 mg/kg/q 2-4 wks) is controversial.*** Patients receiving therapy for toxoplasmosis with sulfadiazine-pyrimethamine are protected against ***Pneumocystis carinii*** pneumonia (PCP) and do not need TMP-SMZ.

† ***Significant drug interactions may occur between rifamycins (rifampin and rifabutin) and protease inhibitors and non-nucleoside reverse transcriptase inhibitors. Consult a specialist.***

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

¶ HIV-infected and HIV-exposed children should be immunized according to the following childhood immunization schedule (Figure), which has been adapted from the January-December 1999 schedule recommended for immunocompetent children by the Advisory Committee on Immunization Practices, the American Academy of Pediatrics, and the American Academy of Family Physicians. ***This schedule differs from that for immunocompetent children in that IPV replaces OPV, and vaccination against influenza (BIII) and S. pneumoniae (BII) should be offered.*** MMR should not be administered to severely immunocompromised children (DIII). ***Vaccination against varicella is indicated only for asymptomatic non-immunosuppressed children (BII), and rotavirus vaccine is contraindicated in all HIV-infected children (EIII).*** Once an HIV-exposed child is determined not to be HIV infected, the schedule for immunocompetent children applies.

** ***Protection against Toxoplasma is provided by the preferred anti-pneumocystis regimens and possibly by atovaquone. The latter may be used wth or without pyrimethamine. Pyrimethamine alone probably provides little, if any, protection. For definition of severe immunosuppression, see Table 6.***

†† ***Respiratory syncytial virus (RSV) IVIG, not monclonal RSV antibody, may be substituted for IVIG during the RSV season to provide broad anti-infective protection, if this product is available***

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

Table 7B. Prophylaxis for recurrence of opportunistic disease (after chemotherapy for acute disease) in HIV-infected infants and children

		Preventive Regimens	
Pathogen	**Indication**	**First Choice**	**Alternative**
I. Recommended for life as standard of care			
Pneumocystis carinii	Prior ***P. carinii*** pneumonia	TMP-SMZ, 150/750 mg/m^2 /d in 2 divided doses po t.i.w. on consecutive days (AII) Acceptable alternative schedules for same dosage: (AII) Single dose po t.i.w. on consecutive days; 2 divided doses po q.d; 2 divided doses po t.i.w. on alternate days	***Dapsone (children aged ≥1mo), 2 mg/kg (max 100 mg) po q.d. or 4 mg/kg (max 200 mg po q.w. (CII); Aerosolized pentamidine (children aged ≥5 yrs), 300 mg q.m. via Respirgard II™ nebulizer (CIII); Atovaquone (age 1-3 mo. and > 24 mo., 30 mg/kg po q.d.; age 4-24 mo., 45 mg/kg po q.d.) (CII)***
Toxoplasma gondii *	Prior toxoplasmic encephalitis	Sulfadiazine, 85-120 mg/kg/d in 2-4 divided doses po q.d***. plus*** pyrimethamine, 1 mg/kg or 15 mg/m^2 (max 25 mg) po q.d. ***plus*** leucovorin, 5 mg po every 3 days (AI)	Clindamycin, 20-30 mg/kg/d in 4 divided doses po q.d. ***plus*** pyrimethamine, 1 mg/kg po q.d. ***plus*** leucovorin, 5 mg po every 3 days (BI)
Mycobacterium avium complex†	Prior disease	***Clarithromycin, 7.5 mg/kg (max 500 mg) po b.i.d. (AII) plus ethambutol, 15 mg/kg (max 900 mg) po q.d. (AII); with or without rifabutin, 5 mg/kg (max 300 mg) po q.d. (CII)***	
Cryptococcus neoformans	Documented disease	***Fluconazole, 3-6 mg/kg po q.d. (AII)***	***Amphotericin B, 0.5-1.0 mg/kg iv 1-3x/week (AI); itraconazole, 2-5 mg/kg po q 24-12h (BII).***
Histoplasma capsulatum	Documented disease	Itraconazole, 2-5 mg/kg po q 12-48h (AIII)	***Amphotericin B, 1.0 mg/kg iv q.w. (AIII)***
Coccidioides immitis	Documented disease	Fluconazole, 6 mg/kg po q.d. (AIII)	***Amphotericin B, 1.0 mg/kg iv q.w. (AIII); itraconazole 2-5 mg/kg po q12-48h (AIII)***
Cytomegalovirus	Prior end-organ disease	***Ganciclovir, 5 mg/kg iv q.d.; or foscarnet, 90-120 mg/kg iv q.d. (AI)***	***(For retinitis) - Ganciclovir sustained-release implant q 6-9 mo. plus ganciclovir 30 mg/kg po t.i.d. (BIII)***
Salmonella species (non-typhi) §	Bacteremia	TMP-SMZ, 150/750 mg/m^2 in 2 divided doses po q.d. for several months (CIII)	Antibiotic chemoprophylaxis with another active agent (CIII)

Table 7B. Prophylaxis for recurrence of opportunistic disease (after chemotherapy for acute disease) in HIV-infected infants and children - Continued

		Preventive Regimens	
Pathogen	**Indication**	**First Choice**	**Alternative**
II. Recommended only if subsequent episodes are frequent or severe			
Invasive bacterial infections ¶	>2 infections in 1-year period	TMP-SMZ, 150/750 mg/m^2 in 2 divided doses po q.d. (BI); ***or*** IVIG, 400 mg/kg q.m. (BI)	Antibiotic chemoprophylaxis with another active agent (BIII)
Herpes simplex virus	Frequent/severe recurrences	Acyclovir, 80 mg/kg/d in 3-4 divided doses po q.d. (AII)	
Candida (oropharyngeal)	Frequent/severe recurrences	***Fluconazole, 3-6 mg/kg po q.d. (CIII)***	
Candida (esophageal)	Frequent/severe recurrences	***Fluconazole, 3-6 mg/kg po q.d. (BIII)***	***Itraconazole pill, 5-10 mg/kg po q24h (CIII); ketoconazole, 5-10 mg/kg po q 24-12h (CIII)***

NOTE: Information included in these guidelines may not represent Food and DrugAdministration (FDA) approval or approved labeling for the particular products or indications in question. Specifically, the terms “safe” and “effective” may not be synonymous with the FDA-defined legal standards for product approval. IVIG = intravenous immune globulin; q.m.= monthly; q.w. = weekly; t.i.w. = three times a week; 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 recommendations and the quality of the evidence supporting it (see text).

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

† ***Significant drug interactions may occur between rifabutin and protease inhibitors and non-nucleoside reverse transcriptase inhibitors. Consult an expert.***

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

¶ Antimicrobial prophylaxis should be chosen based on the microorganism and antibiotic sensitivities. TMP-SMZ, if used, should be administered daily. Providers should be cautious about using antibiotics solely for this purpose because of the potential for development of drug-resistant microorganisms. ***IVIG may not provide additional benefit to children receiving daily TMP-SMZ, but may be considered for children who have recurrent bacterial infections despite TMP-SMZ prophylaxis. Choice of antibiotic prophylaxis vs. IVIG should also involve consideration of adherence, ease of intravenous access, and cost. If IVIG is used, RSV-IVIG, not monoclonal RSV antibody, may be substituted for IVIG during the RSV season to provide broad anti-infective protection, if this product is available.***

PREVENTION OF EXPOSURE RECOMMENDATIONS

Table 8. Advising patients concerning prevention of exposure to opportunistic pathogens

Sexual Exposures

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

(1) 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 (e.g., cryptosporidiosis, shigellosis, campylobacteriosis, amebiasis, giardiasis, and hepatitis A and B) (BIII).

Injection Drug Use Exposures

(1) Injection drug use is a complex behavior which puts HIV-infected persons at risk for hepatitis C virus infection, additional, possibly drug-resistant strains of HIV, and other blood-borne pathogens. Assessments of an individual's readiness to change this practice and efforts to provide education and support directed at recovery should be encouraged. Patients should be counseled to stop using injection drugs (AIII), to enter and complete substance-abuse treatment, including relapse prevention programs (AIII) (72).

(2) If continuing to inject, patients should be counseled (BIII):

- ***a) To never reuse or "share" syringes, needles, water, or drug preparation equipment; if, nonetheless, injection equipment that has been used by other persons is shared, to first clean the equipment with bleach and water (72);***
- ***b) To use only sterile syringes obtained from a reliable source (e.g. pharmacies or syringe exchange programs);***
- ***c) To use sterile (e.g., boiled) water to prepare drugs; if not possible to use clean water from a reliable source (such as fresh tap water);***
- ***d) To use a new or disinfected container ("cooker") and a new filter ("cotton") to prepare drugs;***
- ***e) To clean the injection site before injection with a new alcohol swab; and***
- ***f) To safely dispose of syringes after one use.***

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 other settings identified as high risk by local health authorities. Decisions about whether to continue with such activities should be made in conjunction with the health-care provider and should be based on such factors as the patient's specific duties in the workplace, the prevalence of tuberculosis in the community, and the degree to which precautions designed to prevent the transmission

of tuberculosis are taken in the workplace (BIII). These decisions will affect the frequency with which the patient should be screened for tuberculosis.

(1) Child care providers and parents of children in child care 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 also are at increased risk of acquiring these same infections; parents and other caretakers of HIV-infected children should be advised of this risk (BIII).

(1) 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.

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

(1) Hand washing after gardening or other contact with soil may reduce the risk of cryptosporidiosis and toxoplasmosis (BIII).

(1) In areas endemic for histoplasmosis, patients should avoid activities known to be associated with increased risk (e.g., creating dust when working with surface soil, cleaning chicken coops that are heavily contaminated with compost droppings, disturbing soil beneath bird-roosting sites, cleaning, remodeling or demolishing old buildings, and cave exploring) (CIII).

(1) In areas endemic for coccidioidomycosis, when possible, patients should avoid activities associated with increased risk, including those involving extensive exposure to disturbed native soil (e.g., at building excavation sites or during dust storms) (CIII).

Pet-Related Exposures

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

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***.

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

(1) 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 for HIV-infected children should be supervised.

Cats

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

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

(1) 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).

(1) 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).

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

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

Birds

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

Other

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

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

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

Food- and Water- Related Exposures

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

(1) 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).

(1) 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 foodborne disease can prevent listeriosis by reheating these foods until they are steaming before eating them (CIII).

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

(1) During outbreaks or in other situations in which a community "boil water advisory" is issued, boiling water for 1 minute will eliminate the risk of acquiring cryptosporidiosis (AI). Using submicron, personal-use

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

Travel-Related Exposures

(1) Travel, particularly to developing countries, 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).

(1) During travel to developing countries, HIV-infected persons are at even higher risk for foodborne and waterborne infections than they are in the United States. Foods and beverages-in particular, raw fruits and vegetables, raw or undercooked sea-food 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). Treating 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).

(1) Waterborne infections may result from swallowing 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).

(1) 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 weigh the potential risks and benefits and decide that antibiotic prophylaxis is warranted (CIII). ***For those persons to whom prophylaxis is offered, fluoroquinolones (e.g., ciprofloxacin [500 mg q.d.]) can be considered (BIII), although fluroquinolones should not be given to children or pregnant women.*** Trimethoprim-sulfamethoxazole (TMP-SMZ) (one double-strength tablet daily) also has been shown to be effective, but resistance to this drug is now common in

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

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, health-care providers should be cautious in prescribing this agent for prophylaxis of diarrhea because of the high rates of adverse reactions and the possible need for the agent for other purposes (e.g., PCP prophylaxis) in the future.

(1) All HIV-infected travelers to developing countries should carry a sufficient supply of an antimicrobial agent to be taken empirically should diarrhea develop (BIII). One appropriate regimen is 500 mg of ciprofloxacin 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 empirical therapy, if their stools contain blood, if fever is accompanied by shaking chills, or if dehydration develops. Antiperistaltic agents (e.g., diphenoxylate and loperamide) are used for the treatment of diarrhea; however, they should not be used by patients with high fever or with blood in the stool, and their use should be discontinued if symptoms persist beyond 48 hours (AII). These drugs are not recommended for children (DIII).

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

(1) In general, live-virus vaccines should be avoided (EII). ***One exception is measles vaccine, which is recommended for nonimmune persons.*** However, measles vaccine is not recommended for those who are severely immunosuppressed (DIII); immune globulin should be considered for measles-susceptible, severely immunosuppressed persons who are anticipating travel to measles-endemic countries (BIII). ***Another exception is varicella vaccine, which may be given to asymptomatic non-immunosuppressed children (BII).*** Inactivated (killed) poliovirus vaccine should be used instead of oral (live) poliovirus vaccine, which is contraindicated for HIV-infected persons. Persons at risk for exposure to typhoid fever should be administered an inactivated parenteral typhoid vaccine instead of the live attenuated oral preparation. Yellow fever vaccine is a live-virus vaccine with uncertain safety and efficacy in HIV-infected persons. Travelers with asymptomatic HIV infection who cannot avoid potential exposure to yellow fever should be offered the choice of vaccination. If travel to a zone with yellow fever is necessary and vaccination is not administered, patients should be advised of the risk, instructed in methods for avoiding the bites of vector mosquitoes, and provided with a vaccination waiver letter.

(1) In general, killed vaccines (e.g., diphtheria-tetanus, rabies, hepatitis A, Japanese encephalitis vaccines) should be used for HIV-infected persons just as they would be used for non-HIV-infected persons anticipating travel (BIII). Preparation for travel should include a review and updating of routine vaccinations, including diphtheria-tetanus for adults and all routine immunizations for children. The currently available cholera vaccine is not recommended for persons following a usual tourist itinerary, even if travel includes countries reporting cases of cholera (DII).

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

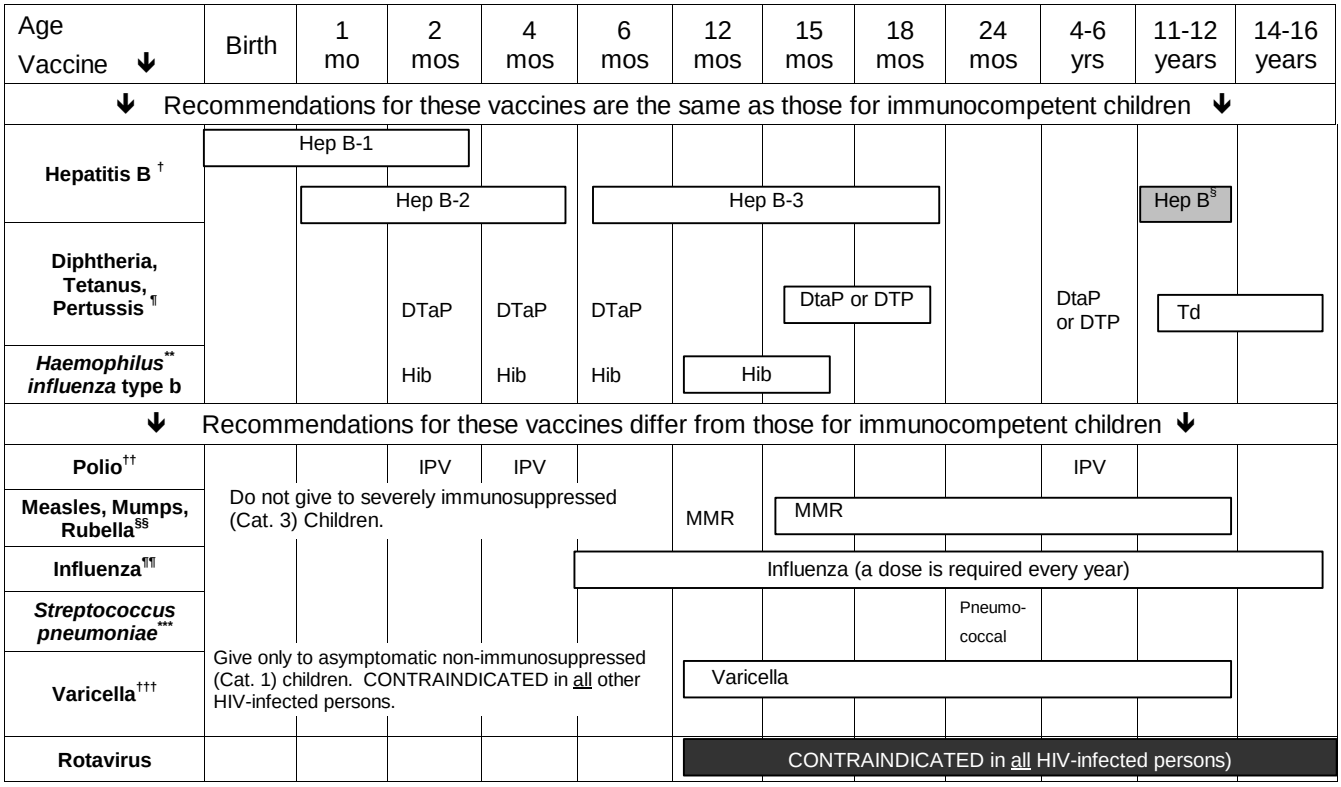
*Table 9. Criteria for Discontinuing and Restarting Opportunistic Infection Prophylaxis for Adult Patients with HIV Infection **

	Discontinuation Criteria for Prophylaxis		
Opportunistic Illness	***Primary***	***Secondary***	***Criteria for Restarting Prophylaxis***
Pneumocystis carinii pneumonia	***CD4+ > 200 cells/uL for > 3-6 months (CII)***	***No criteria recommended for stopping***	***Same as criteria for initiating (CIII)***
Disseminated Mycobacterium avium complex	***CD4+ > 100 cells/uL for > 3-6 months; sustained suppression of HIV plasma RNA (CIII)***	***No criteria recommended for stopping***	***Same as criteria for initiating (CIII)***
Toxoplasmosis	***No criteria recommended for stopping***	***No criteria recommended for stopping***	***N/A***
Cryptococcosis	***N/A***	***No criteria recommended for stopping***	***N/A***
Histoplasmosis	***N/A***	***No criteria recommended for stopping***	***N/A***
Coccidioidomycosis	***N/A***	***No criteria recommended for stopping***	***N/A***
Cytomegalovirus	***N/A***	***- CD4 > 100-150 cells/uL for > 3-6 months - Non-site threatening lesion - Adequate vision in contralaterial eye - Regular ophthalmic examination - No extraocular disease (CIII)***	***Restart maintenance when CD4 < 50-100 cells/uL (CIII)***

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

IMMUNIZATION SCHEDULE FOR HIV-INFECTED CHILDREN

FIGURE. Recommended immunization schedule for HIV-infected children*



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

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

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

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

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

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

¶ DTaP (diphtheria and tetanus toxoids and acellular pertussis vaccine) is the preferred vaccine for all doses in the vaccination series, including completion of the series in children who have received >1 dose of whole-cell DTP vaccine. Whole-cell DTP is an acceptable alternative to DTaP. The 4th dose of DTaP may be administered as early as 12 mos of age, provided 6 mos have elapsed since the 3rd dose, and if the child is considered unlikely to return at 15-18 mos of age. Td (tetanus and diphtheria toxoids, adsorbed, for adult use) is

recommended at 11-12 yrs of age if at least 5 yrs have elapsed since the last dose of DTP, DTaP, or DT. Subsequent routine Td boosters are recommended every 10 yrs.

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

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

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

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

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

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

References

1. USPHS/IDSA Prevention of Opportunistic Infections Working Group. USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus: a summary. MMWR 1995;44(No. RR-8).

2. USPHS/IDSA Prevention of Opportunistic Infections Working Group. USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus: disease specific recommendations. Clin Infect Dis 1995;21(suppl 1):S32-S43.

3. USPHS/IDSA Prevention of Opportunistic Infections Working Group. USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus: a summary. Ann Intern Med 1996;124:348-68.

4. USPHS/IDSA Prevention of Opportunistic Infections Working Group. USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus. MMWR 1997;46(No. RR-12).

5. Kaplan JE, Masur H, Holmes KK, et al. USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus: introduction. Clin Infect Dis 1995;21(suppl 1):S1-S11.

6. Kaplan JE, Masur H, Holmes KK, et al. USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus. Ann Intern Med 1997; 127:922-46.

7. Kaplan JE, Masur H, Holmes KK, et al. USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus. Am Fam Physician 1997; 56:823-34, 1131-46, 1387-92.

8. Kaplan JE, Masur H, Holmes KK, et al. USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus. Pediatrics 1998; 102:1064-85.

9. Kaplan JE, Masur H, Jaffe HW, Holmes KK. Preventing opportunistic infections in persons infected with HIV: 1997 guidelines (editorial). JAMA 278:337-338, 1997.

10. Report of the NIH panel to define principles of therapy of HIV infection and guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents. Ann Intern Med 1998; 128:1057-1100.

11. Gross PA, Barrett TL, Dellinger EP, et al. Purpose of quality standards for infectious diseases. Clin Infect Dis 1994; 18:421.

12. El-Sadr W, Oleske JM, Agins BD, et al. Evaluation and management of early HIV infection. Clinical practice guideline no. 7. Rockville, MD: US Department of Health and Human Services, Public Health Service, 1994; AHCPR publication no. 94-0572.

13. Phair J, Munoz A, Detels R, et al. and the Multicenter AIDS Cohort Study Group. The risk of ***Pneumocystis carinii*** pneumonia among men infected with HIV-1. N Engl J Med 1990; 322:1607.

14. Kaplan JE, Hanson DL, Navin TR, Jones JL. Risk factors for primary ***Pneumocystis carinii*** pneumonia in human immunodeficiency virus – infected adolescents and adults in the United States: reassessment of indications for chemoprophylaxis. J Infect Dis 1998; 178:1126-1132.

15. Masur H. (Chairman): Guidelines for prophylaxis against ***Pneumocystis carinii*** pneumonia for persons infected with HIV. MMWR 1989; 38(S5):1-9.

16. Bozzette SA, Finkelstein DM, Spector SA, et al. A randomized trial of three antipneumocystis agents in patients with advanced human immunodeficiiency virus infection. NIAID AIDS Clinical Trials Group. N Engl J Med 1995; 332:693.

17. Schneider MME, Hoepelman AIM, Eertlnck Schattenkerk JKM, et al., and the Dutch AIDS Treatment Group. A controlled trial of aerosolized pentamidine or trimethopirm-sulfamethoxazole as primary prophylaxis against ***Pneumocystis carinii*** pneumonias in patients with human immunodeficiency virus. N Engl J Med 1992; 327:1836.

18. El-Sadr W, Luskin-Hawk R, Yurik TM, et al. A randomized trial of daily and thrice weekly trimethoprim-sulfamethoxazole for the prevention of ***Pneumocystis carinii*** pneumonia in HIV infected individuals. Clin Infect Dis 1999; in press.

19. Schneider MME, Nielsen TL, Nelsing S, et al. Efficacy and toxicity of two doses of trimethoprim-sulfamethoxazole as primary prophylaxis against ***Pneumocystis carinii***

pneumonia in patients with human immunodeficiency virus. J Infect Dis 1995; 171:1632.

20. Carr A, Tindall B, Brew BJ, et al. Low-dose trimethoprim-sulfamethoxazole prohylaxis for toxoplasmic encephalitis in patients with AIDS. Ann Intern Med 1992; 117:106.

21. Hardy WD, Feinberg J, Finkelstein DM, et al., for the AIDS Clinical Trials Group. A controlled trial of trimethoprim-sulfamethoxazole or aerosolized pentamidine for secondary prophylaxis of ***Pneumocystis carinii*** pneumonia in patients with the acquired immunodeficiency syndrome: AIDS Clinical Trials group 021. N Engl J Med 1992; 327:1842.

22. Leoung G, Standford J, Giordano M, et al. A randomized, double-blind trial of TMP/SMX dose escalation vs. direct challenge in HIV+ persons at risk for PCP and with prior treatment-limiting rash or fever. In: Abstracts of the 37th Interscience Conference on Antimicrobial Agents and Chemotherapy, Toronto, September 28-October 1, 1997, Abstract No. LB10.

23. Para MF, Dohn M, Frame P, et al., for the ACTG 268 Study Team: ACTG 268 Trial – gradual initiation of trimethoprim/sulfamethoxazole (T/S) as primary prophylaxis for ***Pneumocystis carinii*** pneumonia (PCP). In: Abstracts of the 4th Conference on Retroviruses and Opportunistic Infections, Washington, DC. Alexandria, VA, Westover Management Group, 1997, Abstract No. 2.

24. Podzamczer D, Salazar A, Jiminez J, et al. Intermittent trimethoprim-sulfamethoxazole compared with dapsone-pyrimethamine for the simultaneous primary prophylaxis of Pneumocystis pneumonia and toxoplasmosis in patients infected with HIV. Ann Intern Med 1995; 122:755.

25. Opravil M, Hirschel B, Lazzarin A, et al. Once-weekly administration of dapsone/pyrimethamine vs. aerosolized pentamidine as combined prophylaxis for ***Pneumocystis carinii*** pneumonia and toxoplasmic encephalitis in human immunodeficiency virus-infected patients. Clin Infect Dis 1995; 20:531.

26. El Sadr W, Murphy RL, Yurik TM, et al. Atovaquone compared with dapsone for the prevention of ***Pneumocystis carinii*** pneumonia in patients with HIV infection who cannot tolerate trimethoprim, sulfonamides, or both. N Engl J Med 1998; 339:1889-95.

27. Caldwell P, Murphy R, Chan C. Atovaquone suspension for prophylaxis of

Pneumocystis carinii pneumonia; effects of baseline prophylaxis on safety and efficacy. In: Conference Records, 12th World AIDS Conference, Geneva, June 28-July 3, 1998, Abstract No. 22718.

28. Furrer H, Egger M, Opravil M, et al. Discontinuation of primary prophylaxis against ***Pneumocystis carinii*** pneumonia in HIV-1-infected adults treated with combination antiretroviral therapy. N Engl J Med 1999; 340:1301-6.

29. Weverling GJ, Mocroft A, Ledergerber B, et al. Discontinuation of ***Pneumocystis carinii*** pneumonia prophylaxis after start of highly active antiretroviral therapy in HIV-1 infection. EuroSIDA Study Group. Lancet 1999; 353:1293-8.

30. Schneider MME, Borleffs JCC, Stokl RP et al. Discontinuation of ***Pneumocystis carinii*** pneumonia prophylaxis in HIV-1 infected patients treated with highly active antiretroviral therapy. Lancet 1999; 353:201-3.

31. Dworkin M, Hanson D, Jones J, Kaplan J, and the Adult/Adolescent Spectrum of HIV Disease Project (ASD). The risk for ***Pneumocystis carinii*** pneumonia (PCP) and disseminated nontuberculous mycobacteriosis (dMb) after an antiretroviral therapy (ART) associated increase in the CD4+ T-lymphocyte count. In: Abstracts of the 5th Conference on Retroviruses and Opportunistic Infections, Chicago, IL. January 31 - February 4, 1999. Abstract No. 692.

32. Lopez JC, Pena JM, Miro JM, Podzamczer D, and the GESIDA 04/98 Study Group. Discontinuation of PCP prophylaxis (PRO) is safe in HIV-infected patients (PTS) with immunological recovery with HAART. Preliminary results of an open, randomized and multicenter clinical trial (GESIDA 04/98). In: Abstracts of the 6th Conference on Retroviruses and Opportunistic Infections, Chicago, IL January 31 - February 4, 1999; Abstract No. LB7.

33. CDC. 1995 revised guidelines for prophylaxis against ***Pneumocystis carinii*** pneumonia for children infected with or perinatally exposed to human immunodeficiency virus. MMWR 1995; 44(No. RR-4).

34. Dannemann B, McCutchan JA, Israelski K, et al. Treatment of toxoplasmic encephalitis in patients with AIDS: a randomized trial comparing pyrimethamine plus clindamycin to pyrimethamine plus sulfadiazine. Ann Intern Med 1992; 116:33.

35. Katlama C, De Wit S, O'Doherty E, et al. Pyrimethamine-clindamycin vs. pyrimethamine-sulfadiazine as acute and long-term therapy for toxoplasmic encephalitis in patients with AIDS. Clin Infect Dis 1996; 22:268.

36. Holmberg SD, Moorman AC, Von Bargen JC, et al. Possible effectiveness of clarithromycin and rifabutin for cryptosporidiosis chemoprophylaxis in HIV diseases. JAMA 1998; 279:384.

37. CDC Conference on HIV-Related Tuberculosis. Prevention and treatment of tuberculosis among patients infected with human immunodeficiency virus: principles of therapy and revised recommendations. MMWR 1998; 47 (RR-20).

38. Masur H, and the Public Health Service Task Force on Prophylaxis and Therapy for ***Mycobacterium avium*** complex. Recommendations on prophylaxis and therapy for disseminated ***Mycobacterium avium*** complex disease in patients infected with the human immunodeficiency virus. N Engl J Med 1993; 329:898.

39. Benson CA, Cohn DL, Williams P, and the ACTG 196/CPCRA 009 Study Team. A phase III prospective, randomized, double-blind study of the safety and efficacy of clarithromycin (CLA) vs. rifabutin (RBT) vs. CLA + RBT for prevention of ***Mycobacterium avium*** complex (MAC) disease in HIV+ patients with CD4 counts $\leq$ 100 cells/uL. In: Abstracts of the 3rd Conference on Retroviruses and Opportunistic Infections, Washington, DC. Alexandria, VA, Foundation for Retrovirology and Human Health, 1996, Abstract No. 205.

40. Pierce M, Crampton S, Henry D, et al. A randomized trial of clarithromycin as prophylaxis against disseminated ***Mycobacterium avium*** complex infection in patients with advanced acquired immunodeficiency syndrome. N Engl J Med 1996; 335:384-91.

41. Havlir DV, Dube MP, Sattler FR, et al. Prophylaxis against disseminated ***Mycobacterium avium*** complex with weekly azithromycin, daily rifabutin, or both. N Engl J Med 1996; 335:392.

42. Chaisson RE, Benson CA, Dube MP, et al. Clarithromycin therapy for bacteremic ***Mycobacterium avium*** complex disease in patients with AIDS. Ann Intern Med 1994; 121:905.

43. Cohn DL, Fisher E, Peng GT, et al. A prospective randomized trial of four three-drug regimens in the treatment of disseminated Mycobacterium avium complex disease in AIDS patients: excess mortality associated with high dose clarithromycin. Clin Infect Dis (in press).

44. Shafran SD, Singer J, Zarowney DP, et al. A comparison of two regimens for the treatment of ***Mycobacterium avium*** complex bacteremia in AIDS: rifabutin, ethambutol, and clarithromycin versus rifampin, ethambutol, clofazimine, and ciprofloxacin. N Engl. J Med 1996; 335:377,

45. Gebo KA, Moore RD, Keruly JC, Chaisson RE. Risk factors for pneumococcal disease in human immunodeficiency virus-infected patients. J Infect Dis 1996; 173:857-862.

46. Ward JW, Hanson DL, Jones J, Kaplan J. Pneumococcal vaccination and the incidence of pneumonia among HIV-infected persons. In: Program and abstracts of the 34th Annual Meeting of the Infectious Diseases Society of America. Alexandria, Virginia: Infectious Diseases Society of America, 1996, Abstract No. 245.

47. Centers for Disease Control and Prevention. Prevention of pneumococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1997; 46(No. RR-8):1-24.

48. Powderly WG, Finkelstein D, Feinberg J, et al. A randomized trial comparing fluconazole with clotrimazole troches for the prevention of fungal infections in patients with advanced human immunodeficiency virus infection. N Engl J Med 1995; 332:700.

49. Schuman P, Capps L, Peng G, et al. Weekly fluconazole for the prevention of mucosal candidiasis in women withHIV infection. Ann Intern Med 1997; 126:689.

50. Havlir DV, Dube MP, McCutchan A, et al. Prophylaxis with weekly versus daily fluconazole for fungal infections in patients with AIDS. Clin Infect Dis 1998; 27:1369-75.

51. Aleck KA, Bartley DL. Multiple malformation syndrome following fluconazole use in pregnancy: report of an additional patient. Am J Med Genet 1997; 72:253-6.

52. Pursley TJ, Blomquist IK, Abraham J, Andersen HF, Bartley JA. Fluconazole-induced congenital anomalies in three infants. Clin Infect Dis 1996; 22:336-40.

53. Janssen Pharmaceutical Company. Product information: Sporanox oral solution. Physicians Desk Reference, Medical Economics Company, 1999; 1441.

54. Wheat J, Hafner R, Wulfson M, et al., and the NIASID Clinical Trails & Mycoses Study Group Collaborators: Prevention of relapse histoplasmosis with itraconazole in patients with the acquired immunodeficiency syndrome. Ann Intern Med 1993; 118:610.

55. McKinsey DS, Wheat LJ, Cloud GA, et al. Itraconazole prophylaxis against fungal infections in patients with advanced human immunodeficiency virus infection: randomized placebo-controlled double-blind study. Clin Infect Dis 1999; 28:in press.

56. Galgiani JN, Cloud GA, Catanzaro A, et al. Fluconazole (FLU) vs. itraconazole (ITRA) for coccidioidomycosis. Randomized, multicenter, double-blinded trial in nonmeningeal progressive infections. In: Abstracts from 36th Annual Meeting of the Infectious Diseases Society of America. Alexandria, Virginia: Infectious Diseases Society of America, 1998, Abstract No. 100.

57. Spector SA, McKinley GF, Lalezari FP, et al. Oral ganciclovir for the prevention of cytomegalovirus retinitis in persons with AIDS. N Engl J Med 1996; 334:1491.

58. Brosgart CL, Torres RA, Thompson MA, et al. A randomized, placebo controlled trial of the safety and efficacy of oral ganciclovir for prophylaxis of cytomegalovirus disease in HIV-infected individuals. AIDS 1998; 12:269.

59. Martin DF, Kupperman BD, Wolitz RA. Oral ganciclovir for cytomegalovirus retinitis treated with a ganciclovir implant. N Engl J Med 1999; 340:1063-70.

60. Drew WL, Ives D, Lalezari J, et al. Oral ganciclovir as maintenance treatment for cytomegalovirus retinitis in patients with AIDS. N Engl J Med 1995; 333:615.

61. Studies of Ocular Complication of AIDS Research Group in collaboration with the AIDS Clinical Trials Group. Parenteral cidofovir for cytomegalovirus retinitis in patients with AIDS: the HPMPC Peripheral Cytomegalovirus Retinitis Trial. Ann Intern Med 1997; 126:264.

62. Palestine AG, Polis MA, De Smet MD, et al. A randomized, controlled trial of foscarnet in the treatment of cytomegalovirus retinitis in patients with AIDS. Ann Intern Med 1991; 115:665.

63. Studies of the Ocular Complications of AIDS (SOCA) in collaboration with the AIDS Clinical Trials Group. Cytomegalovirus (CMV) culture results, drug resistance, and clinical outcomes in patients with AIDS and CMV retinitis treated with either

foscarnet or ganciclovir. J Infect Dis 1997; 176:50.

64. Whitcup SM, Fortin E, Lindblad AS, et al. Successful discontinuation of specific anti-cytomegalovirus therapy in persons with HIV infection and cytomegalovirus retinitis: results of a longitudinal intervention trial. Pending.

65. Vrabec TR, Baldassano VF, Whitcup SM. Discontinuation of maintenance therapy in patients with quiescent cytomegalovirus retinitis and elevated CD4+ counts. Ophthalmology 1998; 105:1259-64.

66. Schacker T, Zeh J, Hu HL, et al. Frequency of symptomatic and asymptomatic herpes simplex virus type 2 reactivations among human immunodeficiency virus-infected men. J Infect Dis 1998; 178:1616-22.

67. Schacker T, Hu HL, Koelle DM, et al. Famciclovir for the suppression of symptomatic and asymptomatic herpes simplex virus reactivation in HIV-infected persons – a double-blind placebo-controlled trial. Ann Intern Med 1998; 128:21.

68. Kurman RJ, Henson DE, Herbst AL, Noller KL, Schiffman MH. Interim guidelines for management of abnormal cervical cytology. The 1992 National Cancer Institute workshop. JAMA 1994; 271:1866-9.

69. Golde S, et al. Clinical effectiveness and cost effectiveness of screening for anal squamous and intraepithelial lesions in homosexual and bisexual HIV positive men. JAMA (in press).

70. Centers for Disease Control and Prevention. Recommendations for prevention and control of hepatitis C virus (HCV) infection and HCV-related chronic disease. MMWR 1998; 47 (No. RR-19).

71. Thomas DL, Shih JW, Alter HJ, et al. Effect of human immunodeficiency virus on hepatitis C virus infection among injecting drug users. J Infect Dis 1996; 174:690.

72. United States Public Health Service. HIV prevention bulletin: medical advice for persons who inject illicit drugs. May 8, 1997, Atlanta, Georgia and Rockville, Maryland.

73. Centers for Disease Control and Prevention. Prevention of hepatitis A through active or passive immunization: recommendations of the Advisory Committee on

Immunization Practices (ACIP). MMWR 1996; 45 (No. RR-15):1-30.

74. Centers for Disease Control and Prevention. Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1999; 48 (No. RR-4):1-28.

75. Nielsen H, Kvinesdal B, Benfield TL, Lundgren JD, Konradsen HB. Rapid loss of specific antibodies after pneumococcal vaccination in patients with human immunodeficiency virus-1 infection. Scand J Infect Dis 1998; 30:597-601.

76. Centers for Disease Control and Prevention. Hepatitis B virus: a comprehensive strategy for eliminating transmission in the United States through universal childhood vaccination: recommendations of the Immunization Practices Advisory Committee (ACIP). MMWR 1991; 40 (No. RR-13).