Current Report — HIV

Treatment Of AIDS And HIV-Related Conditions — 1995

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The cornerstones of primary care for human immunodeficiency virus (HIV) disease are prophylaxis against *Pneumocystis carinii* pneumonia (PCP), antiretroviral therapy, treatment of opportunistic infections and other complications of the acquired immunodeficiency syndrome (AIDS), and a productive provider-patient-family relationship. Although much of HIV/AIDS treatment has now become standardized, guidelines can be helpful, especially for primary care providers treating small populations of HIV-infected persons. The Current Report — HIV series attempts to provide timely updates and comprehensive treatment reviews for family physicians and other primary care providers. This Current Report — HIV article, based on our clinical experience at San Francisco General Hospital and a review of the medical literature, updates our annual treatment recommendations.[1]

Antiretroviral Strategies

Antiretroviral therapy can delay the development of AIDS and probably prolongs life. The benefits of antiretroviral therapy, however, are time-limited to a period of about 1 year or perhaps longer.[2,3] It is not clear that different antiretroviral strategies (e.g., combination therapy versus monotherapy or earlier versus later therapy) produce different long-term outcomes and prolong survival. Because no single approach to antiretroviral therapy has been shown to be superior, a wider acceptance that patient choice is key to selecting antiretroviral treatment strategies has emerged.[4-6] The reader is referred to the January 1995 issue of *JABFP*, which provides an extensive discussion of factors that patients, families, and their providers must consider in making decisions about antiretroviral strategies.[6]

Studies to date do not show long-term benefits of antiretroviral therapy for patients who have more than 500 CD4+ (T-helper) lymphocytes per microliter. Antiretroviral treatment is not recommended in this group of patients.[7] Treatment is recommended for all patients with symptomatic disease and patients with fewer than 200 CD4+ cells/μL.[4,6] For asymptomatic patients with 200 to 500 CD4+ cells/μL considerable controversy about therapy exists. Long-term studies of clinical end points have not found that initiating antiretroviral therapy earlier, rather than later, in the course of asymptomatic HIV disease is beneficial.[8-10] Patients who desire an aggressive approach might wish to initiate antiretroviral therapy when their CD4+ cell count is at or close to the 500 cells/μL threshold, whereas patients preferring a conservative approach might wish to initiate antiretroviral treatment when their CD4+ cell count approaches the 200/μL threshold or when symptomatic disease occurs. Similarly, an aggressive approach would likely include combination therapy, whereas a more conservative approach would be more likely to begin with monotherapy. There are strong proponents for each of these approaches. When patients or providers do not have strong feelings about a specific antiretroviral strategy, we recommend the more conservative approach, initiating monotherapy when the patient's CD4+ cell count is closer to the 200/μL threshold than the 500/μL threshold. Zidovudine[11] remains the first-choice antiretroviral agent. Didanosine, zalcitabine, and stavudine are generally used for combination therapy and following zidovudine intolerance or failure.[12-15]

Changing antiretroviral therapy is also an inexact science. Viral resistance (of unknown clinical importance) to antiretroviral agents increases with the duration of treatment. Drug effect

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wanes with time, apparently independent of viral resistance. These factors, coupled with findings from some short-term studies that show improvements in surrogate markers when new antiretroviral agents are added or substituted, support changing therapy when clinical or laboratory deterioration occurs. Thresholds for changing therapy are arbitrary. We recommend changing or adding another antiretroviral agent when the CD4+ cell count has decreased to 50 percent of the initial threshold chosen. Continuing antiretroviral therapy during progressive end-stage disease is not required.

Prophylaxis against Opportunistic Infections

Because opportunistic infections cause most of the morbidity and mortality in AIDS, prophylaxis against these infections is a major emphasis of HIV management. Prophylaxis against PCP is the single most important drug intervention for HIV-infected persons.[16,17] All persons with AIDS (including those with a CD4+ count of $\leq$200 cells/μL as the only reason for their AIDS case designation) should receive prophylaxis against PCP. The incidence of PCP as the initial AIDS diagnosis has decreased markedly since PCP prophylaxis became standard. In addition, persons who receive PCP prophylaxis live considerably longer than those who have not received it. Trimethoprim-sulfamethoxazole (TMP/SMX) is the agent of choice. Trimethoprim-sulfamethoxazole also provides prophylaxis against toxoplasmic encephalitis,[18] although there is no evidence that prophylaxis against toxoplasmosis is essential.

Treatment of oral candidiasis with fluconazole provides limited prophylaxis against other serious fungal diseases, such as cryptococcal meningitis, but has not been shown to change long-term outcomes. Cryptococcal meningitis and serious fungal diseases are not universal among patients with HIV disease, and when these infections occur, they usually respond to standard treatment. Providing fluconazole antifungal prophylaxis to all patients, therefore, is not necessary. Because resistance to this essential drug can occur, we do not recommend routine antifungal prophylaxis for all HIV-infected persons.

Rifabutin prophylaxis against *Mycobacterium avium* complex (MAC) disease has been recommended.[19-21] The necessity of prophylaxis against MAC disease and the threshold at which that prophylaxis might best occur, as well as risks of rifabutin therapy (e.g., uveitis, gastrointestinal side-effects, and drug-drug interactions) make rifabutin prophylaxis controversial.[22-24] Prophylaxis against MAC disease has not been shown to provide survival benefits.[21] MAC disease usually occurs in patients with severe immunodeficiency and end-stage AIDS. The strategy of MAC prophylaxis for all persons with advanced immunodeficiency has not been compared with the strategy of treating active MAC disease in the minority of patients who develop symptomatic disease. We continue to recommend offering, but not strongly encouraging, MAC prophylaxis for patients who have fewer CD4+ cells than 50/μL, although national recommendations strongly recommend rifabutin prophylaxis for patients with a higher CD4+ cell threshold.

Combining multiple medications to provide prophylaxis against a wide range of opportunistic infections has the potential for incurring multiple drug toxicities and drug interactions without long-term benefits. No studies show that prophylaxis against multiple possible infections is a wise treatment strategy, especially when these opportunistic infections might never occur in that individual patient. Further research is needed to determine the best strategies for prophylaxis.

Opportunistic Infections

Treatment of the major opportunistic infections continues to be beneficial in most instances. PCP remains the most important single opportunistic infection in AIDS. Treatment with trimethoprim-sulfamethoxazole is first-line therapy; a variety of equivalent choices for second-line therapy are available.[17,25-27] Concomitant corticosteroid therapy is beneficial for persons with substantial hypoxemia ($PaO_2 \leq 70$ mmHg).[28]

Serious herpes simplex and zoster infections remain responsive to acyclovir therapy in most instances. Alternate treatments are available for acyclovir resistance.[29,30] Treatment of cytomegalovirus retinitis and cytomegaloviral gastrointestinal and neurologic disease can be extremely beneficial.[31-33] Ganciclovir or foscarnet therapy are indicated; combination therapy with ganciclovir plus foscarnet has been reported to be effective.[34] Favorable results of oral ganciclovir maintenance therapy (after initial intravenous therapy for acute

Table 1. Treatment Regimens for HIV Disease.

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL			
Antiretroviral (Anti-HIV)			
Asymptomatic and symptomatic patients			
Zidovudine (AZT, Retrovir) 200 mg po tid; lower dosages (e.g., 100 mg 3-5 times daily) for patients unable to tolerate higher dosages and patients with renal failure or cirrhosis	Indefinitely	Malaise, headache, nausea, insomnia, seizures, myalgias. Anemia, granulocytopenia, thrombocytopenia; macrocytosis is an expected effect of zidovudine therapy and requires no intervention. Toxic myopathy (with elevated creatine phosphokinase [CPK]) with long-term use. Lactic acidosis. Hepatomegaly with steatosis; aminotransferase elevations (alanine transaminase [ALT], aspartate transaminase [AST]). Blue to black discoloration of nails and skin in pigmented races *Drug interactions* Careful monitoring required when used with other myelosuppressive drugs (i.e., trimethoprim-sulfamethoxazole, ganciclovir). Probenecid can increase levels of zidovudine. Acetaminophen (Tylenol) administration does not increase zidovudine toxicity	Ideal time to initiate antiretroviral treatment uncertain. Recommend treatment for all symptomatic patients and asymptomatic patients with repeated CD4+ lymphocyte counts <200 cells/μL; can be offered to patients with CD4+ counts as high as 500 cells/μL. Zidovudine is the usual first-choice antiretroviral agent Monitor for signs of zidovudine toxicity and reduce dosage if required. Transfusions or erythropoietin (if endogenous erythropoietin level <500 IU/L) therapy can be used if anemia (e.g., hemoglobin <8.0 g/dL) occurs in patients who require zidovudine therapy. Decrease dosage or interrupt for absolute neutrophil count (ANC) <500 cells/μL; consider granulocyte colony-stimulating factor (G-CSF). Transfusions and erythropoietin and G-CSF therapies are expensive; changing to alternate agent preferred Thrombocytopenia and HIV dementia have been reported to respond at times to zidovudine therapy. High-dosage (1200 mg po qd) zidovudine therapy can be considered for HIV dementia. Didanosine and zalcitabine do not penetrate the blood-brain barrier as well as zidovudine Change to alternate agent if unable to tolerate or marked progression of disease
OR			
Didanosine (ddI, Videx) 200-mg tablet po or 250-mg powder bid for patients >60 kg; 125 mg-tablet or 167-mg powder po bid for <60 kg. Dosage reduction (i.e., 200 mg/d) in renal failure	Indefinitely	Pancreatitis; painful peripheral neuropathy (dosage related, reversible); nausea, abdominal cramps, diarrhea related to antacid in formulation; rash; hyperglycemia; hyperuricemia; aminotransferase elevations; headache, insomnia, seizures; elevated triglyceride and amylase levels; thrombocytopenia; retinal atrophy	Can be used in combination with zidovudine or as monotherapy in patients who fail or are intolerant to zidovudine. Monitor for signs of neuropathy. Two tablets must be given per dose to provide adequate buffer for absorption. Can be difficult to chew; tablets do not dissolve readily in water, can be crushed manually

Continued

Table 1. ***Continued***

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL **Antiretroviral (Anti-HIV) (cont.)**		*Drug interactions* Concomitant administration of H_2 antagonists, antacids, and omeprazole (Prilosec) can increase didanosine absorption, resulting in additional toxicity. Avoid alcohol and other pancreatic toxins (e.g., systemic pentamidine). Avoid concomitant neurotoxic drugs (e.g., zalcitabine, stavudine, isoniazid). Oral ganciclovir increases didanosine toxicity. Didanosine decreases absorption of drugs whose absorption is impaired by buffered products (e.g., dapsone, ketoconazole, itraconazole, tetracyclines, quinolone antibiotics)	Administer didanosine on empty stomach 2 hours apart from antacids, H_2 antagonists, and drugs (e.g., dapsone, ketoconazole, itraconazole, tetracyclines, quinolone antibiotics) whose absorption is impaired by buffered products; breakthrough episodes of *Pneumocystis carinii* pneumonia (PCP) have been reported in patients receiving concomitant didanosine therapy and dapsone PCP prophylaxis
OR			
Zalcitabine (ddC, Hivid) 0.75 mg po tid; 0.375 mg po tid for patients <30 kg. Dosage reduction in renal failure	Indefinitely	Painful peripheral neuropathy (dosage related, reversible); rash, stomatitis, aphthous ulcers; pancreatitis; esophageal ulceration; seizures; aminotransferase elevations; cardiomyopathy *Drug interactions* Avoid alcohol and other pancreatic toxins (e.g., systemic pentamidine). Avoid concomitant neurotoxic drugs (e.g., didanosine, stavudine, isoniazid)	Can be used in combination with zidovudine or as monotherapy in patients who fail or are intolerant to zidovudine. Not as effective as zidovudine for monotherapy. Neurotoxicity can improve with zalcitabine "rest periods"
OR			
Stavudine (d4T, Zerit) 20 mg po bid for patients >60 kg; 15 mg po bid for patients 40-60 kg; reduce dosage for patients <40 kg and patients with renal failure	Indefinitely	Painful peripheral neuropathy; aminotransferase elevations; anemia, macrocytosis. Psychological disturbances: insomnia, anxiety, panic attacks *Drug interactions* Avoid concomitant use of drugs that can cause neurotoxicity (including didanosine and zalcitabine) or pancreatic toxicity. See didanosine	Consider for patients intolerant to zidovudine, didanosine, and zalcitabine. Dosages listed in this table are lower than the original Food and Drug Administration (FDA)-approved dosages. Studies suggest that these lower dosages are associated with equivalent efficacy and a lower incidence of peripheral neuropathy than current FDA-approved dosages
OR			
Combination therapy (zidovudine plus didanosine or zidovudine plus zalcitabine). Unclear whether combination of zidovudine plus acyclovir provides additional antiretroviral benefit	Indefinitely	Additive toxicities can complicate management, especially for patients with late-stage disease and patients receiving multiple medications	No clear evidence of added benefit or survival from combination therapy or from sequential therapy (e.g., alternating regimens of zidovudine plus didanosine or zalcitabine). Studies of zidovudine plus stavudine combination therapy are in progress Other experimental agents, such as protease inhibitors and lamivudine (3TC), are available through clinical trials and expanded access programs; no long-term studies show clinical efficacy

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Table 1. ***Continued***

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL			
Antiretroviral (Anti-HIV) (cont.)			
Postexposure prophylaxis			
Zidovudine 1200 mg po qd in divided doses for 3 days, followed by 1000 mg po qd in divided doses for 25 days	4 weeks	See above	Not known whether postexposure prophylaxis is effective. Failures have been reported. Administration within 1–2 hours of needlestick or other injury appears best (in animal models). Appears safe in pregnancy. One-month treatment with didanosine or zalcitabine alone or in combination with zidovudine recommended by some experts when index case is receiving zidovudine. Counseling required
Pregnancy			
Zidovudine 100 mg po 5 times/d followed by intrapartum zidovudine 2 mg/kg IV for 1 h, then 1 mg/kg/h until delivery	Until end of pregnancy	See above. Serious adverse effects on fetus not demonstrated in studies to date	Zidovudine therapy, initiated at 14 to 34 weeks' gestation, combined with intrapartum intravenous zidovudine plus oral zidovudine 2 mg/kg qid to infants for first 6 weeks of life, decreased transmission to infants (AIDS Clinical Trials Group Study 076[75])
Wasting syndrome			
Megestrol (Megace) suspension 40 mg/mL, 400 mg po qd. Higher dosages (800 mg po qd) might be necessary	Indefinitely	Nausea, vomiting; edema; depression. Progestin side effects (hyperglycemia, decreased testosterone levels)	Megestrol can increase appetite and cause fat accumulation with weight gain. Uncertain whether this weight gain improves health. Usually well tolerated. Available also as tablets, but a large number of tablets are required for administration and are more expensive
Dronabinol (Tetrahydrocannabinol [THC], Marinol) 2.5 mg po bid 30 min–1 h before meals. Maximum 20 mg qd	Indefinitely	Restlessness, irritability, insomnia, dizziness, loss of coordination, psychotomimetic effects; fatigue; tachycardia	Increases appetite and can cause weight gain. Uncertain whether this weight gain improves health. Antinauseant. Not recommended for persons sensitive to marijuana effects
Human growth hormone. Preparation, dosage, and indications not established	Unknown	Arthralgias, joint stiffness, carpal tunnel syndrome; hyperglycemia; hypertriglyceridemia	Studies of a recombinant human growth hormone (r-hGH, Serostim) 0.1 mg/kg/d SQ (average dosage 6 mg/d) demonstrated increased exercise endurance and weight gain characterized by increased lean body mass and decreased fat. Experimental. Not approved by FDA
Anabolic steroids. Preparation, dosage, and indications not established	Unknown	Edema; jaundice	No satisfactory studies to date. Not indicated for patients with normal testosterone levels. Treatment must be accompanied by exercise. Unknown whether anabolic steroid therapy improves health

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Table 1. *Continued*

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL (cont.)			
***Mycobacterium avium* complex (MAC)**			
Prophylaxis			
Observe for signs and symptoms of MAC disease	Indefinitely		
OR			
Rifabutin (Mycobutin) 300 mg po qd or 150 mg po bid	Indefinitely	Nausea (can be reduced by administering 150 mg po bid). Rash. Uveitis with dosages greater than 300 mg po qd and in patients receiving concomitant clarithromycin or fluconazole therapy. Rare neutropenia, thrombocytopenia, anemia; flu-like syndrome; elevated bilirubin and alkaline phosphatase levels, hepatitis. Red-orange discoloration of body fluids	Survival benefits not demonstrated. Rifabutin can be offered as primary prophylaxis for patients with advanced immunodeficiency (e.g., CD4+ <50 or 100 cells/μL). Patients who do not wish to receive or are unable to tolerate MAC prophylaxis can be monitored for signs and symptoms of active disease. Clarithromycin 500 mg po qd-bid can substitute for rifabutin
		Drug interactions Rifabutin increases metabolism of methadone, zidovudine, and clarithromycin; higher dosage of these drugs might be required. Clarithromycin and fluconazole increase rifabutin blood levels and can lead to rifabutin toxicity	Exclude *Mycobacterium tuberculosis* infection before initiating MAC prophylaxis
Acute			
Ethambutol (Myambutol) 15 mg/kg po qd (1 g po qd maximum); dosage reduction in renal failure		Optic neuritis (if >25 mg/kg/d); hyperuricemia; nausea, vomiting	
plus either			
Clarithromycin (Biaxin) 500 mg po bid. Higher dosages (maximum 1 g po bid) might be necessary	Indefinitely, if tolerated (minimum of 12 weeks)	Clarithromycin and azithromycin side effects include nausea, vomiting, dyspepsia, diarrhea, hearing loss, aminotransferase elevations	Treatment indicated for patients with progressive signs, symptoms, and laboratory abnormalities consistent with MAC disease. Evaluate benefits and risks of multidrug regimen before treating
or		*Drug interactions* Clarithromycin increases serum levels of rifabutin and can lead to rifabutin toxicity, including severe anterior uveitis. Clarithromycin and azithromycin increase levels of carbamazepine and theophylline. Avoid terfenadine (Seldane), astemizole (Hismanol), or loratadine (Claritin) in combination with azole antibiotics because of increased risk of torsades de pointes and ventricular tachyarrhythmias	
Azithromycin (Zithromax) 500 mg po qd			At least two drugs including either clarithromycin or azithromycin should be used
			When both *M. tuberculosis* and MAC infections are suspected, add isoniazid, rifampin, and pyrazinamide to MAC treatment
For serious illness or failure to respond within 1 month can add one or two of the following:			
Clofazimine (Lamprene) 100 mg po qd	Indefinitely	Nausea, vomiting, diarrhea, reversible pink to brown-black discoloration of skin, eyes, body secretions; rash; hyperglycemia; retinal degeneration	

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Table 1. *Continued*

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL			
***Mycobacterium avium* complex (MAC) (cont.)**			
Ciprofloxacin (Cipro) 500–750 mg po qd	Indefinitely	Nausea, vomiting, abdominal pain; anxiety, insomnia, euphoria; tremor; hallucinations; seizures *Drug interactions* Binds to aluminum, calcium, and magnesium, resulting in decreased absorption	Administer ciprofloxacin 4 hours before or 6 hours after antacids, sucralfate, dairy products, and didanosine
Rifampin (Rimactane, Rifadin) 450–600 mg po qd or rifabutin 300 mg po qd	Indefinitely	Red-orange discoloration of body secretions and fluids; elevated bilirubin and alkaline phosphatase levels, hepatitis; anorexia; flu-like syndrome; thrombocytopenia *Drug interactions* Rifampin is a potent hepatic P-450 enzyme inducer; higher dosages of dapsone, methadone, zidovudine, clarithromycin, fluconazole, ketoconazole, itraconazole, warfarin, and estrogens might be required	Rifabutin might provide better activity than rifampin in multidrug therapy against MAC
Amikacin 7.5 mg/kg IM/IV qd	2–8 weeks	Nephrotoxicity, ototoxicity	Monitor drug levels in patients with renal failure
Mycobacterium tuberculosis *Prophylaxis*			
Isoniazid (INH) 300 mg po qd	12 months	Aminotransferase elevations and hepatitis; administer with pyridoxine to prevent peripheral neuropathy; sedation and mental status changes *Drug interactions* Isoniazid increases metabolism of ketoconazole; larger dosages of ketoconazole might be required. Increased phenytoin and carbamazepine toxicity; monitor levels	INH prophylaxis for all HIV-infected persons with ≥5-mm intermediate strength tuberculin skin test induration and those with strong history of tuberculosis exposure, regardless of skin test reactivity
Active tuberculosis			
Isoniazid 300 mg po qd plus	Begin with 4-drug therapy. After 2 months can continue INH and rifampin only, depending upon susceptibility testing results. Total treatment: at least 9 months, and 6 months beyond culture conversion	See above	Directly observed therapy can permit more flexible (e.g., 3 times/wk) treatment schedules. Consultation with tuberculosis experts and coordination with tuberculosis control agencies often required
Rifampin 600 mg po qd plus		See MAC	
Pyrazinamide (PZA) 15–30 mg/kg po qd (2 g po qd maximum) plus		Aminotransferase elevations, abdominal pain; rash; arthralgia; hyperuricemia	

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Table 1. *Continued*

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL			
***Mycobacterium tuberculosis* (cont.)**			
Ethambutol 15 mg/kg po qd (2.5 g po qd maximum)		See MAC	
or			
Streptomycin 15 mg/kg IM qd (1 g IM qd maximum)		Hearing loss, nephrotoxicity; nystagmus, ataxia	
Histoplasmosis			
Acute			
Amphotericin B (Fungizone) 1.0 mg/kg IV qd. Decrease to 0.7–0.8 mg/kg qd if not tolerated	Until 15 mg/kg total dosage has been administered or can change from amphotericin B to itraconazole when patient sufficiently stable. Total acute therapy 6–8 weeks	See CENTRAL NERVOUS SYSTEM, *Cryptococcus neoformans*	Amphotericin B recommended as initial treatment for serious illness; oral therapy does not appear as effective. Fluconazole 400 mg po bid might be effective. Ketoconazole not indicated
OR			
Itraconazole (Sporanox) 200 mg po bid		Nausea, vomiting; hypokalemia; hypertension; aminotransferase elevations; adrenal insufficiency; rhabdomyolysis. Teratogenic *Drug interactions* Potent hepatic enzyme inducers, such as isoniazid, rifampin, and phenytoin, increase metabolism of itraconazole; higher itraconazole dosages can be required	
Maintenance			
Itraconazole 200 mg po qd	Indefinitely		Fluconazole 400 mg po qd might be effective
OR			
Amphotericin B 50 mg IV q week	Indefinitely		Optimum frequency of administration not determined
SKIN/MUCOCUTANEOUS			
Kaposi sarcoma			
Observation	Indefinitely		Treatment not required unless lesions are symptomatic or cosmetically bothersome
OR			
Local treatment (radiation therapy, cryotherapy, excision, or intralesional vinblastine)	Until lesions and symptoms are resolved or controlled	Mucositis in head and neck regions from radiation therapy	Treatment effective for cosmetic purposes, to relieve symptoms, and to help reduce edema caused by lymphatic obstruction
OR			
Systemic chemotherapy with vinblastine and vincristine, vincristine alone, or combination of doxorubicin, bleomycin, and vincristine	Same	Usual chemotherapeutic agent side effects	Multidrug therapy can help control disease but does not alter prognosis. Consultation by oncologist or AIDS specialist usually required
OR			

Continued

Table 1. *Continued*

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
SKIN/MUCO-CUTANEOUS			
Kaposi sarcoma (cont.)			
Interferon-alpha 5 mU/d SQ, increase by 5 mU/d every 2 weeks as tolerated to a maximum of 35 mU/d	Indefinitely	Fatigue, myalgia, asthenia; neutropenia, thrombocytopenia; aminotransferase elevations	Hematologic toxicities increased in patients taking zidovudine. Dosages greater than 10 mU/d necessary for efficacy
Seborrheic dermatitis			
Acute			
Hydrocortisone (HC) cream 2.5% plus ketoconazole cream 2% bid; severe cases can require ketoconazole 200–400 mg po qd for 3–4 weeks	Until resolved	See ORAL CAVITY, *Candida albicans*, ketoconazole	Commonly involves face, eyebrows, retroauricular areas, nasolabial folds, and scalp. Addition of antifungal cream enhances therapeutic response and reduces the frequency of steroid application
Maintenance			
HC cream 1% and ketoconazole cream 2% bid	Indefinitely		
Mucocutaneous herpes simplex			
Acute			
Acyclovir (Zovirax) 200–400 mg po 5 times/d	7–10 days	Oral: nausea, vomiting, diarrhea, dizziness	Topical acyclovir ineffective for most episodes
Maintenance			
Acyclovir 200–400 mg po 3–5 times/d	Indefinitely		Chronic maintenance therapy can be necessary for repeated episodes
Disseminated, extensive, or persistent herpes simplex			
Acute			
Acyclovir 5 mg/kg/dose IV q 8 h; dosage reduction in renal failure	7–14 days or until lesions resolve	Intravenous: lethargy, tremors, confusion, hallucinations; phlebitis; increased serum creatinine, reversible crystalline nephropathy	Severe herpes infections (e.g., esophagitis, colitis, encephalitis) require intravenous acyclovir. Maintain good urine output and hydration to prevent acyclovir crystallization
Maintenance			
Acyclovir 200–400 mg po 3–5 times/d	Indefinitely		
Herpes zoster (shingles, disseminated, or persistent zoster)			
Acyclovir 10 mg/kg/dose IV q 8 h; or acyclovir 800 mg po 5 times/d; dosage reduction in renal failure for intravenous acyclovir	7–10 days or until lesions resolve		Intravenous therapy preferred. Oral therapy not generally recommended because higher acyclovir levels are required for efficacy (oral bioavailability=25%). Alternate drugs are foscarnet and vidarabine
or			

Continued

Table 1. *Continued*

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
SKIN/MUCOCUTANEOUS			
Herpes zoster (shingles, disseminated, or persistent zoster) (cont.)			
Famciclovir (Famvir) 500 mg po q 8 h; dosage reduction in renal failure	Same	Headache, nausea, fatigue	Only approved for herpes zoster infection. Appears as effective as acyclovir, but no studies in immunocompromised patients. Better bioavailability than acyclovir
Acyclovir-resistant herpes infections			
Foscarnet (Foscavir) 40 mg/kg/dose IV q 8 h; dosage reduction in renal failure	10–14 days or until lesions clear	See OPHTHALMOLOGIC, CMV	See OPHTHALMOLOGIC, CMV. Trifluridine might be effective. See SKIN/MUCOCUTANEOUS, herpes zoster
or			
Trifluridine (Viroptic) 1% solution q 8 h	Same	Rare hypersensitivity reactions	Apply to affected areas and cover with antibiotic ointment such as bacitracin or polymyxin B. Keratoconjunctivitis requires more frequent (as often as 2 h, maximum 9 drops qd) trifluridine application
Bacillary angiomatosis			
Erythromycin 500 mg po qid	2 months	See GENERAL, MAC, clarithromycin, azithromycin. Jarisch-Herxheimer reaction with systemic disease	Skin lesions can resolve in 1–3 weeks, but 2 months' treatment needed. Systemic disease (i.e., hepatic, splenic, central nervous system, bone, or other organ involvement) or cutaneous recurrences require treatment for 4 months or indefinitely. Azithromycin 1 g po qd and possibly clarithromycin 500 mg–1 g po qd can be used as alternatives, but less information about efficacy is available
or			
Doxycycline 100 mg po bid	2 months		
Eosinophilic folliculitis			
High-potency fluorinated corticosteroid cream bid	Indefinitely		Itraconazole 200 mg po once daily with food sometimes effective. If no response in 2 weeks, increase dosage to 200 mg po bid for 2 additional weeks. If no response after 4 weeks, discontinue itraconazole. See GENERAL, histoplasmosis. Topical metronidazole might be helpful
plus			
Antihistamine (e.g., diphenhydramine [Benadryl], hydroxyzine [Atarax, Vistaril], doxepin [Sinequan])	Indefinitely		Avoid terfenadine, astemizole, or loratadine in combination with azole antibiotics because of increased risk of torsades de pointes and ventricular tachyarrhythmias
HEMATOLOGIC			
Thrombocytopenia			
Observe		Discontinue drugs that can cause thrombocytopenia	Treatment not required in absence of bleeding. Consider platelet transfusions prior to invasive procedure that causes bleeding. Splenectomy, high-dosage zidovudine, intravenous gammaglobulin, and alpha interferon can raise platelet count
or			
Prednisone 60 mg po qd	Discontinue as soon as possible	Long-term corticosteroid therapy increases immunodeficiency	

Continued

Table 1. *Continued*

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
OPHTHALMOLOGIC			
Cytomegalovirus (CMV)			
Induction			
Ganciclovir (Cytovene) 5 mg/kg IV q 12 h; dosage reduction in renal failure	14 days for acute retinal infection; 14–21 days usually required for extraocular infection	Neutropenia, leukopenia, anemia, thrombocytopenia (avoid if platelet count < 30,000/μL); aminotransferase elevations; renal failure; phlebitis; rash; nausea. Discontinue zidovudine during induction to minimize additive hematologic toxicity (neutropenia). To avoid hematologic toxicity, substitute didanosine or zalcitabine for zidovudine, or change to foscarnet plus zidovudine	CMV retinitis can be arrested or improved with IV ganciclovir therapy. Intravitreal ganciclovir appears effective if IV causes unacceptable toxicity. Ganciclovir can also be effective in CMV esophagitis, colitis, and proctitis; not usually effective in CMV lung infection Start G-CSF (filgastrim, Neupogen) 150–300 μg SQ 3 times weekly for persistent ganciclovir-induced neutropenia (ANC < 500 cells/μL)
OR			
Foscarnet (Foscavir) 90 mg/kg/dose IV q 12 h as 2-h infusion; discontinuation or dosage reduction in renal failure	14-day induction	Nephrotoxicity common; tremors, headaches, occasional seizures, muscle spasms; hypocalcemia, hypercalcemia, hypophosphatemia, hyperphosphatemia; anemia, granulocytopenia; aminotransferase elevations; phlebitis, penile ulcerations *Drug interactions* Avoid concurrent use of nephrotoxic agents when possible	Administered by infusion pump via central line. Infusion of 500 mL–1L normal saline before each foscarnet administration can minimize nephrotoxicity. Twenty-four–hour creatinine clearance should be measured in cachectic patients and in patients with renal insufficiency to ensure proper use of administration nomogram
Maintenance			
Ganciclovir 5 mg/kg IV as 1-h infusion 7 times/wk or 6 mg/kg IV 5 times/wk; dosage reduction in renal failure	Indefinitely		Lifelong suppressive therapy required to prevent recurrence of retinitis. Daily administration is optimal. Administer G-CSF or change to foscarnet if ANC consistently < 500 cells/μL
or			
Ganciclovir 1 g po tid	Indefinitely	Anemia, leukopenia; nephrotoxicity; neuropathy *Drug interactions* Oral ganciclovir therapy causes 80% increase in didanosine blood levels; reduce didanosine dosage by 50%	Oral ganciclovir might be as effective for maintenance therapy as intravenous regimens. Not recommended for induction therapy or for primary prophylaxis. Administer on empty stomach to improve absorption
OR			
Foscarnet 90–120 mg/kg IV qd as 2-h infusion 7 times/wk; discontinuation or dosage reduction in renal failure	Indefinitely		Maintenance with 120 mg/kg/d might be more effective but also more toxic
OR			
Foscarnet plus ganciclovir	Indefinitely		Combination therapy not routinely recommended. Can be used after resistance to both drugs demonstrated. Continue maintenance dosage of current drug (foscarnet or ganciclovir); provide standard induction with alternate drug, followed by maintenance with both drugs

Continued

Table 1. *Continued*

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
ORAL CAVITY			
Candida albicans			
Ketoconazole (Nizoral) 400 mg po qd; can follow with maintenance therapy 200 mg po qd–bid for 7 consecutive days per month	1–2 weeks or until resolved; maintenance might be required (with lowest effective dosage)	Nausea, vomiting; aminotransferase elevations; anaphylaxis, urticaria. Higher dosages can suppress testosterone levels; gynecomastia; adrenal suppression *Drug interactions* Need gastric acidity to be effective; avoid antacids, H_2 antagonists, and didanosine. Higher dosages might be necessary if taking rifampin	Improvement within 2–3 days
OR			
Fluconazole (Diflucan) 100–200 mg po qd; can follow with maintenance therapy 50–100 mg po qd or 100–200 mg po once weekly	Same	See CENTRAL NERVOUS SYSTEM, *Cryptococcus neoformans*	More expensive than other agents. Effective in oral candidiasis unresponsive to above oral agents. Increased frequency or higher dosages might be required. Fluconazole-resistant organisms reported
OR			
Clotrimazole (Mycelex) troches 10 mg 5 times/d or vaginal suppositories 100 mg qd–bid. Dissolve slowly in mouth	Same	Minimal toxicity. Unpleasant taste, nausea, vomiting; aminotransferase elevations	Improvement within 2–3 days
OR			
Nystatin (Mycostatin) 100,000 U/mL, swish and swallow 5 mL po q 6 h or one 500,000-unit tablet dissolved slowly in mouth q 6 h	Same	Large oral doses can produce diarrhea, nausea, vomiting	Generally less effective than ketoconazole, fluconazole, or clotrimazole. Can be effective in fluconazole-resistant candidal infection
OR			
Amphotericin B mouthwash 0.1 mg/mL, swish and swallow 5 mL qid	Same	Unpalatable; nausea, vomiting	Not absorbed. No systemic effects. Must be prepared from IV solution
OR			
Amphotericin B 0.3–0.4 mg/kg IV qd	10 days or until resolution	See CENTRAL NERVOUS SYSTEM, *Cryptococcus neoformans*	Candidal esophagitis unresponsive to oral agents requires low-dose IV amphotericin B
Periodontal disease			
Hydrogen peroxide gargles for 30 sec bid	Indefinitely		Less expensive than chlorhexidine. Listerine gargles can be effective
OR			Oral hygiene measures with manual removal of plaque is essential. Severe periodontal disease can require antibiotic therapy with metronidazole 250 mg po tid for 7–10 days (alternatives: clindamycin or augmentin)
Chlorhexidine gluconate (Peridex) oral rinse 15 mL swished in mouth for 30 sec bid	Indefinitely	Staining of teeth	

Continued

Table 1. *Continued*

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
ESOPHAGEAL			
Candida albicans			
Fluconazole 200–400 mg po qd; higher dosages might be required OR Ketoconazole 200 mg po bid; amphotericin B; see ORAL CAVITY, *Candida albicans*	14–21 days; maintenance with lowest effective dosage	See CENTRAL NERVOUS SYSTEM, *Cryptococcus neoformans*	Empiric treatment for patients with dysphagia or odynophagia who have oral thrush. Endoscopy with biopsy and cultures appropriate for patients who fail to respond within 1 week. Ketoconazole less expensive than fluconazole and effective in most patients. Fluconazole effective in more patients than ketoconazole; can be reserved for ketoconazole-resistant esophageal candidiasis
Cytomegalovirus			
Ganciclovir; foscarnet; see OPHTHALMOLOGIC, CMV	14–21 days	See OPHTHALMOLOGIC, CMV	Diagnose by endoscopic appearance plus biopsy showing CMV inclusion bodies and positive culture. Long-term suppressive therapy not routinely indicated
Herpes simplex			
IV acyclovir; see SKIN/MUCOCUTANEOUS, disseminated, extensive, or persistent herpes simplex	10–14 days; maintenance required	See SKIN/MUCOCUTANEOUS, herpes simplex	Diagnose by endoscopic appearance plus positive culture
GASTROINTESTINAL			
Nausea and vomiting			
Prochlorperazine (Compazine) 2.5–10 mg IV or 5–10 mg po or IM q 6 h or 25 mg pr q 12 h	As needed	Fatigue, drowsiness, dizziness, depression; extrapyramidal reactions; dystonic reactions; aminotransferase elevations; constipation	Nausea is most often caused by drugs; pretreatment or concurrent treatment can permit administration of necessary drugs. Central nervous system, biliary tract, pancreatic, or other gastrointestinal disease must be considered. Combinations of these agents often necessary
Metoclopramide (Reglan) 10 mg po qid or 1 mg/kg IV q 3 h or 10 mg IM q 4–6. Dosage reduction in renal failure	As needed	Same as above	Same as above
Lorazepam (Ativan) 0.5–2 mg po or SL tid-qid	As needed	Similar to benzodiazepines; antegrade amnesia	Effective for anticipatory nausea
Ondansetron (Zofran) 0.15 mg/kg IV infusion for 15 min q 6 h or 4–10 mg po q 6 h	As needed	Constipation, diarrhea, abdominal pain; fever, chills; headache; sedation	Reserved for intractable nausea and vomiting unresponsive to other agents. Ondansetron, metoclopramide, and dexamethasone (4–10 mg po qd) combination helpful for intractable nausea and vomiting
Dronabinol 2.5–10 mg po q 8–12 h	As needed	See GENERAL, wasting syndrome	Effective in drug-induced nausea

Continued

Table 1. *Continued*

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GASTROINTESTINAL (cont.)			
Diarrhea			
Symptomatic treatment Loperamide (Imodium) 4 mg po initially then 2 mg q 6 h around the clock and prn (maximum 16 mg pd)	As needed	Abdominal cramps, nausea, abdominal distention, vomiting; dizziness, drowsiness	Around-the-clock regimen more effective than prn. Treat to 2–3 bowel movements per day
Diphenoxylate-atropine (Lomotil) 2.5–5 mg po 3–6 times daily for 24–48 h; then 2.5–5 mg tid and prn to control diarrhea (maximum 20 mg qd)	As needed	Ileus; nausea, vomiting, abdominal discomfort; anticholinergic side effects secondary to atropine	Same as above. 2.5 mg diphenoxylate-atropine is equivalent to 2 mg morphine sulfate
Paregoric 0.4 mg morphine/mL, 5–10 mL qd–qid or tincture of opium 10 mg morphine/mL, 0.3–1.0 mL po qid and prn (maximum 1 mL/dose or 6 mL/d), or equivalent	As needed	Ileus; altered mental status, hallucinations, other adverse effects common to narcotic analgesics	Same as above. 5 mL paregoric and 0.2 mL tincture of opium are equivalent to 2 mg morphine sulfate
Octreotide (Sandostatin) 100 μg SQ tid, increase by 100–200 μg q 1–2 weeks until maximum of 500 μg SQ tid or until 50% decrease of stool output	Indefinitely	Nausea, steatorrhea; hyperglycemia; pain at injection site	Not approved by FDA. Short-term efficacy demonstrated. Long-term safety and efficacy unknown. Malabsorption not improved
Cryptosporidium			
See Diarrhea, above	Indefinitely	See Diarrhea	No drug effectively eradicates Cryptosporidium
Paromomycin (Humatin) 750 mg po tid	10–14 days or indefinitely	Nausea, vomiting, diarrhea; rare ototoxicity and nephrotoxicity (similar to other aminoglycosides) only if absorbed through ulcerative bowel lesions	Nonabsorbable aminoglycoside. Effective in some patients. Azithromycin might be effective
Isospora belli			
Trimethoprim-sulfamethoxazole (TMP-SMX) 1 DS (double-strength) tablet po qid	21 days	See PULMONARY, *Pneumocystis carinii* pneumonia	Usually effective
Cytomegalovirus			
Ganciclovir; foscarnet; see OPHTHALMOLOGIC, CMV	14–21 days	See OPHTHALMOLOGIC, CMV	Diagnose by endoscopic appearance plus biopsy showing CMV inclusion bodies and positive culture. Long-term suppressive therapy not routinely indicated. Consider only after multiple recurrences. Beware of drug resistance

Continued

Table 1. *Continued*

System, Problem and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
PULMONARY			
***Pneumocystis carinii* pneumonia (PCP)**			
Prophylaxis or suppression of PCP for patients with CD4+ <200 cells/μL, prior episode of PCP, or constitutional symptoms of HIV disease			
Trimethoprim-sulfamethoxazole (TMP-SMX, Septra, Bactrim) 1 DS tablet po qd or qod or 3 times/wk (e.g., MWF) or 1 tablet po bid	Indefinitely	See *acute* PCP, TMP-SMX below	TMP-SMX considered most effective for prophylaxis or suppression. Once-daily administration is easiest to remember. Three-day-per-week regimen might be best tolerated. Multiple TMP-SMX regimens have been used and all appear effective. TMP/SMX provides additional prophylaxis against toxoplasmosis
Alternatives to TMP-SMX for prophylaxis or suppression			
Dapsone 50 mg po bid or 100 mg po qd with or without TMP 2.5–5 mg/kg/d or pyrimethamine (Daraprim) 25–75 mg po q wk	Indefinitely	See *acute* PCP dapsone plus TMP below	Probably less effective than TMP-SMX; might be less toxic, but some cross-sensitivity with TMP-SMX likely. Lower dosages (e.g., 100 mg po 2 times per week) might be effective
OR			
Inhaled pentamidine (Aeropent) 300 mg q 4 weeks or 150 mg q 2 weeks; requires specially designed nebulizer system, e.g., Respirgard II	Indefinitely	Adverse systemic effects are minimal because of low pentamidine serum concentrations. Bronchospasm and coughing are common, especially in smokers. Pretreatment with inhaled bronchodilator (e.g., albuterol) can help. Rare pancreatitis, hypoglycemia; rare nephrotoxicity. Increased risk of spontaneous pneumothorax	Effective for prophylaxis against primary PCP. Does not prevent extrapulmonary disease. Efficacy for secondary prophylaxis inferior to TMP-SMX. Upper lobe recurrences probably due to poor drug distribution when inhaled in upright position. Consider monthly IM or IV injections of pentamidine 4 mg/kg if other options are not available. Do not use in patients with possible *M. tuberculosis* infection because of risk of *M. tuberculosis* spread by aerosolization
OR			
Clindamycin 450–600 mg po bid–tid plus primaquine 15 mg po qd	Indefinitely	See above	Efficacy and proper dosages for PCP prophylaxis unknown
OR			
Atovaquone 750 mg po qd–bid with or without pyrimethamine 25–75 mg po q week	Indefinitely	See above	Efficacy and proper dosage for PCP prophylaxis unknown
OR			
Pyrimethamine 25 mg-sulfadoxine 500 mg (Fansidar) 1–2 po q week	Indefinitely	Stevens-Johnson syndrome, toxic epidermal necrolysis; leukopenia, bone marrow suppression; GI, CNS toxicity	No studies clearly demonstrate efficacy

Continued

Table 1. *Continued*

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
PULMONARY			
Pneumocystis carinii **pneumonia (PCP) (cont.)**			
Acute Pneumocystis carinii pneumonia			
TMP-SMX, 15 mg TMP per kg daily given in 3 divided doses po or for 1–2 h IV infusion; lower dosages (12 mg TMP per kg daily) can be effective and less toxic	21 days	Adverse effects commonly appear between 7 and 14 days in more than 50% of patients	TMP-SMX is the drug of choice and should be used unless severe reactions (e.g., anaphylaxis, severe rashes, Stevens-Johnson syndrome) are of concern. Oral and intravenous routes equally effective. Can provide prophylaxis against toxoplasmosis
		Rashes: maculopapular, exfoliative, Stevens-Johnson syndrome	Mild rash does not necessitate stopping or changing treatment: institute antihistamine or consider oral desensitization
		Hematologic: neutropenia, leukopenia, thrombocytopenia, anemia	If ANC <500 cells/μL or if platelet count $<30\times10^9$/L and bleeding occurs, consider alternative treatment. Concurrent leucovorin calcium therapy associated with increased rate of therapeutic failure
		Gastrointestinal: nausea, vomiting, aminotransferase elevations. Aminotransferase elevations 4–5 times normal require treatment change	Pretreatment with lorazepam, prochlorperazine, metoclopramide, or dronabinol to reduce nausea. See GASTROINTESTINAL. Nausea can be less with oral TMP-SMX
		Renal: increased blood urea nitrogen (BUN) and creatinine; hyperkalemia secondary to hypoaldosterone effects of TMP	TMP decreases creatinine tubular secretion and can falsely elevate serum creatinine levels. Discontinue TMP-SMX if serum creatinine >3.0 mg/dL
		Hyponatremia	Can be caused by large volume of 5% dextrose in water (D5W) needed for IV administration; can dilute each 80 mg TMP in 75 mL D5W or change to oral TMP-SMX. For severe hyponatremia ($Na^+ <115$ mEq/dL) can dilute in normal saline; administer within 1 hour of preparation to avoid TMP-SMX precipitation
		Drug fever; sepsis-like syndrome, especially upon rechallenge	Drug fever can herald onset of neutropenia, rash, hepatitis, and bone marrow toxicity
Alternatives to TMP-SMX for acute PCP			
Pentamidine isethionate (Pentam) 4 mg/kg/d as 1–2-h IV infusion once daily; 3 mg/kg/d might also be effective	21 days	Orthostatic hypotension can be severe and occur with initial infusion	Slow IV infusion for 2 hours can prevent hypotension. Check blood pressure at end of infusion
		Pancreatitis; avoid concomitant pancreatic toxins, such as didanosine, zalcitabine, and alcohol. Early or delayed hypoglycemia (can occur after discontinuation of therapy); hyperglycemia	Hypoglycemia can be profound and prolonged, requiring immediate IV D50W followed by D10W glucose infusions. Permanent diabetes can occur

Continued

Table 1. ***Continued***

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
PULMONARY ***Pneumocystis carinii*** **pneumonia (PCP) (cont.)**			
		Renal: increased BUN and creatinine; hyperkalemia. Concomitant nephrotoxic agents and dehydration increase risk of pentamidine nephrotoxicity	Obtain accurate patient weight every 2–3 days to adjust pentamidine dosage. Discontinue pentamidine if creatinine >3.0 mg/dL. Can resume administration if creatinine <2 mg/dL
		Other: neutropenia, thrombocytopenia; hypocalcemia, hypomagnesemia; aminotransferase elevations; cardiac arrhythmias	
OR			
Clindamycin (Cleocin) 450–600 mg IV or po tid	21 days	Maculopapular rash (day 10–12 most common, usually self-limiting), fever; diarrhea, nausea, vomiting, abdominal cramps, *Clostridium difficile* colitis, aminotransferase elevations	Consider in patients with mild-to-moderate PCP, intolerant of or unresponsive to TMP-SMX
plus			
Primaquine 30-mg base po qd		Methemoglobinemia from primaquine, hemolysis in glucose-6-phosphate dehydrogenase (G6PD)-deficient patients, leukopenia	Check G6PD before initiating primaquine therapy. Check methemoglobin levels when clinically indicated (see dapsone). Lower dosage of primaquine (15 mg po qd) can be effective
OR			
Dapsone 100 mg po qd plus either TMP 15 mg/kg/d po in 3–4 divided doses or pyrimethamine 50–75 mg po qd	21 days	See toxicities for TMP-SMX. Methemoglobinemia, dose-related hemolysis, bone marrow suppression; rash; fever; nausea, abdominal pain; hyperkalemia; proteinuria, papillary necrosis. Patients allergic to TMP-SMX might tolerate dapsone-TMP	Proved effective in mild-to-moderate PCP only. Check G6PD before starting dapsone. Check methemoglobin levels if suggested by discrepancy between oxygen saturation and simultaneous arterial PaO_2. Pulse oximetry is inaccurate in presence of methemoglobinemia. Treat methemoglobinemia >20% with methylene blue 1% solution 2 mg/kg IV once; treat methemoglobinemia <20% with vitamin C 1 g po tid
		Drug interactions Drug interactions with didanosine, rifampin, and rifabutin can render dapsone ineffective	
OR			
Trimetrexate (Neutrexin) 45 mg/m^2 IV qd	21 days	Granulocytopenia, fever, rash; aminotransferase elevations	Can be effective in some patients intolerant to or refractory to TMP-SMX therapy. Addition of dapsone might be beneficial
plus			
Leucovorin calcium (folinic acid) 20 mg/m^2 IV or po q 6 h	24 days		Administered for 72 hours after the last dose of trimetrexate. Large IV fluid load with leucovorin administration can result in volume overload
OR			
Atovaquone (Mepron) 750 mg po tid with high-fat meal plus pyrimethamine 50–75 mg po qd		Rash, drug fever; headaches; nausea, diarrhea, aminotransferase elevations; neutropenia, anemia; transient conjunctivitis; erythema multiforme	For patients who fail or are intolerant to other PCP regimens. Patients with enteropathy might not absorb a sufficient amount of atovaquone to treat PCP adequately

Continued

Table 1. *Continued*

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
PULMONARY			
***Pneumocystis carinii* pneumonia (PCP) (cont.)**			
Adjunctive corticosteroid therapy for acute PCP with $PaO_2 \leq 70$ mmHg			
Prednisone po or methylprednisolone (Solu-Medrol) IV: 40 mg bid for 5 days followed by 40 mg qd for 5 days, followed by 20 mg qd for 11 days (can be tapered to zero for last 11 days also)	21 days	Hyperglycemia, sodium retention, potassium wasting. Psychiatric syndromes. Exacerbation of Kaposi sarcoma, thrush, herpes infections, and other opportunistic infections	Corticosteroids indicated in conjunction with antipneumocystis therapy in all patients with $PaO_2 \leq 70$ mmHg. Begin corticosteroids concurrent with PCP treatment or if PaO_2 decreases to ≤ 70 mmHg within 72 hours of initiating PCP treatment
CENTRAL NERVOUS SYSTEM			
Toxoplasma gondii			
Prophylaxis			
Most PCP prophylaxis regimens provide some protection against toxoplasmosis	Indefinitely	See PULMONARY, *Pneumocystis carinii* pneumonia	Prophylaxis against PCP with TMP-SMX, dapsone with TMP or pyrimethamine, clindamycin plus primaquine, atovaquone with pyrimethamine, and pyrimethamine-sulfadoxine probably provide some prophylaxis against toxoplasmosis
Acute			
Pyrimethamine 75–100 mg po qd plus leucovorin calcium (folinic acid) 10–25 mg po qd	6–8 weeks for acute therapy	Leukopenia, anemia, thrombocytopenia	Clinical response or regression of lesions on imaging studies is usually noted within 2 weeks. Maintenance required indefinitely to prevent relapse. Every other day pyrimethamine administration and daily leucovorin calcium administration might delay onset of bone marrow toxicity
plus either			
Clindamycin 600–900 mg po or IV qid		See PULMONARY, PCP	
or			
Sulfadiazine 1–1.5 g po q 6 h	Same	Rash, drug fever; bone marrow suppression, leukopenia, thrombocytopenia	Sulfadiazine probably provides effective prophylaxis and suppression against PCP
Alternative when intolerant of clindamycin and sulfadiazine Pyrimethamine plus leucovorin calcium as above	Same	See above	See above
plus one of the following			
Clarithromycin 1 g po bid or azithromycin 1200–1500 mg po qd	Same	See GENERAL, MAC	
or			
Atovaquone 750 mg po qid with high-fat meal	Same	See PULMONARY, PCP	Appears less effective than other agents
or			

Continued

Table 1. *Continued*

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
CENTRAL NERVOUS SYSTEM			
***Toxoplasma gondii* (cont.)**			
Doxycycline 100 mg po tid–qid or minocycline 200 mg po bid	Same	Tetracycline side effects	Not proved effective
or			
Dapsone 100 mg po qd	Same	See PULMONARY, PCP	
OR			
Pyrimethamine alone 100–200 mg po qd	Same	See PULMONARY, PCP	Not as effective as above regimens
OR			
TMP/SMX as for acute PCP	Same	See PULMONARY, PCP	
Maintenance			
Pyrimethamine 25–50 mg po qd	Indefinitely		Add leucovorin calcium if evidence of leukopenia
plus either			
Sulfadiazine 1 g po q 12 h or Clindamycin 300–450 mg po q 6–8 h			Other agents used for acute toxoplasmosis might be effective at lower dosages for maintenance
Cryptococcus neoformans			
Prophylaxis			
Fluconazole provides limited prophylaxis			Primary prophylaxis not required. No long-term survival benefit. Fluconazole resistance reported
Meningitis or disseminated cryptococcosis			
Acute			
Amphotericin B 0.7–1.0 mg/kg/d IV with or without 5-flucytosine (Ancobon) 100 mg/kg po qd in 4 divided doses for first 2–4 weeks. If clinically improved or after 7.5 mg/kg total amphotericin B administration can change to fluconazole 400 mg po qd or itraconazole 200 mg po bid	6–8 weeks; amphotericin total dosage not to exceed 2 g	Renal failure, hypokalemia, hypomagnesemia; fever, chills; anemia, thrombophlebitis. Pretreatment with diphenhydramine, acetaminophen, or IV meperidine (Demerol, Mepergon) can decrease amphotericin B-induced fevers, chills, and rigors Flucytosine; granulocytopenia; nausea, vomiting, diarrhea, aminotransferase elevations; rash; not indicated if granulocytopenia or thrombocytopenia is present	Administer for 4–6 h in D5W. Addition of heparin 500 U and hydrocortisone 50 mg to amphotericin B IV solution can decrease phlebitis. Infusion of 500 mL–1L normal saline before administration of amphotericin B can minimize renal toxicity. Maintain 5-flucytosine levels between 50–100 μg/dL Markedly increased intracranial pressure (>300 mm) might require acetazolamide (Diamox) 250–500 mg po or IV qid, cerebrospinal fluid drainage (5–15 mL), or possibly corticosteroid or mannitol therapy
OR			

Continued

Table 1. ***Continued***

System, Problem and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
CENTRAL NERVOUS SYSTEM			
Cryptococcus neoformans **(cont.)**			
Fluconazole 400 mg po qd	8–12 weeks	Nausea, vomiting, diarrhea; dizziness; aminotransferase elevations; rare cutaneous reactions *Drug interaction* Increased phenytoin (Dilantin) and warfarin (Coumadin) levels; higher fluconazole dosages might be necessary for patients taking rifampin	As effective as amphotericin B against mild or moderate disease; unknown whether equally effective against severe disease. Higher dosages (e.g., 800–1200 mg po qd) might be necessary in severe disease. Fluconazole penetrates the central nervous system (CNS) and most body tissues, including prostate
Maintenance			
Fluconazole 200–400 mg po qd	Indefinitely	Same	Higher dosages might be necessary for recurrent disease
OR			
Amphotericin B 0.5–0.8 mg/kg/d 3–5 times q week	Indefinitely	Same	
Syphilis			
Aqueous crystalline penicillin G 2–4 mU IV q 4 h (total 12–24 mU/d)	10–14 days	Usual penicillin adverse effects; Jarisch-Herxheimer reaction; seizures from high-dosage penicillin in renal failure	Treatment failures reported; continued serologic and clinical follow-up required to assess adequacy of treatment. Persons with ophthalmic, auditory, cranial nerve abnormalities, or other syndromes consistent neurosyphilis should receive daily penicillin therapy for 10–14 days. Intravenous penicillin preferred for adequate CNS penetration. Consultation with a syphilis expert advised when treating penicillin-allergic patients. Administer benzathine penicillin 2.4 mμ IM once after completion of neurosyphilis treatment
OR			
Procaine penicillin G 2.4 mU IM qd plus Probenecid 500 mg po qid	10–14 days	Same. Probenecid rash	
Peripheral neuropathy			
Amitriptyline (Elavil) or desipramine (Norpramin) 25–150 mg po hs	Indefinitely	Usual tricyclic side-effects; drowsiness; orthostatic hypotension; anticholinergic symptoms	Desipramine causes less sedation and fewer anticholinergic effects. Other tricyclic drugs might be equally effective
Carbamazepine (Tegretol) 100–300 mg po bid	Indefinitely	Leukopenia, bone marrow suppression, rare agranulocytosis; rash; drowsiness, dizziness; aminotransferase elevations	Less desirable because of bone marrow effects. Need to monitor carbamazepine levels to avoid toxicity
Mexiletine (Mexitil) 50–150 mg po bid–tid	Indefinitely	Nausea, vomiting, epigastric pain; dizziness, tremor; bradycardia; rare seizures, leukopenia, agranulocytosis	Less desirable because of side effects
Capsaicin (Axsain, Zostrix-HP)0.075% topical cream qid	Indefinitely	Minor burning sensation, skin irritation, erythema	Pain relief delayed 2–4 weeks. No systemic effects
CMV polyradiculopathy			
Ganciclovir and/or foscarnet induction and maintenance therapy	Indefinitely	See OPHTHALMOLOGIC, CMV	Response to therapy can be slow (3–4 weeks)

disease) and of oral ganciclovir prophylaxis have been discussed at scientific conferences. Oral ganciclovir is now approved for maintenance therapy; the proper role of this agent in preventing cytomegalovirus disease remains uncertain. Treatment of toxoplasmic encephalitis,[35,36] cryptococcal meningitis,[37-39] and cryptococcemia remains effective with standard therapy.

Concern about the adequacy of standard treatment for syphilis among HIV-infected persons continues. Recent reports again confirm that standard therapy can be inadequate in both early and late syphilis.[40,41] Aggressive treatment and careful follow-up are essential.[42,43]

The Table

Table 1 provides our recommendations for treating the major signs, symptoms, and specific complications of HIV disease and AIDS. The table is organized by organ systems to suggest a general overview of different diagnostic possibilities. In general, our drug recommendations are in order of efficacy. Where more than one drug is effective for a specific condition, recommendations are usually in an order that favors the least expensive choice among equally effective options. The most common and clinically important adverse effects and drug interactions are listed.

References

A selected bibliography for this article highlights the most important management and therapeutic problems in HIV/AIDS. References for dermatologic problems,[44-47] the AIDS wasting syndrome,[48-50] diarrhea,[51,52] endocrine abnormalities,[53] tuberculosis[54-59] and other mycobacterial diseases,[60,61] fungal diseases,[62-66] neurologic complications of HIV disease,[67] and drug toxicity[68-71] are included. Additional references are intended to assist providers with health care maintenance,[72,73] special considerations in pregnancy,[74,75] and a broad range of HIV therapeutics.[42,76-79]

Other Sources of Information

A wide range of resources is available to assist providers who care for HIV-infected patients. Information about clinical trials is available through the AIDS Clinical Trials Information Service of the Centers for Disease Control and Prevention and the National Institutes of Allergy and Infectious Diseases (1-800-TRIALS A). The AIDS Education and Training Centers (AIDS ETCs) of the Health Resources and Services Administration (HRSA) offer regional educational, training, and consultation services to health care providers, and HRSA offers a bimonthly teleconference service. Information about these programs can be obtained by calling the national AIDS ETC office at 1-301-443-6364. Our national HIV Telephone Consultation Service (Warmline) in the University of California, San Francisco, Department of Family and Community Medicine at San Francisco General Hospital provides clinical consultation and education for health care providers; the Warmline is in operation on weekdays at 1-800-933-3413.

Conclusion

HIV disease is a chronic disease with a long latency period between infection and AIDS. An excellent provider-patient-family relationship, antiretroviral therapy, and prophylactic and acute treatment interventions addressed in this article form the basis of primary HIV care. Treatment to avoid or delay most of the major complications of HIV disease is within the purview and responsibility of family physicians and other primary care providers.

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