Current Report - HIV

Treatment of AIDS and HIV-Related Conditions — 1996

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Human immunodeficiency virus (HIV) care, including antiretroviral therapy, treatment of opportunistic infections and other complications of the acquired immunodeficiency syndrome (AIDS), and general care of HIV/AIDS patients and their families will continue to be important primary care problems. The dramatic shift toward primary care in the United States reinforces the importance of managing clinical problems rationally and efficiently without sacrificing quality. About 750,000 Americans are infected with HIV. AIDS is the leading cause of death for men 25 to 44 years old.

HIV/AIDS treatment guidelines can be helpful, especially for primary care clinicians caring for small numbers of HIV-infected persons. 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 for adults and adolescents.[1]

Antiretroviral Therapy

Initiating and Changing Therapy

All patients with symptomatic HIV disease and AIDS, including persons with 200 or fewer CD4+ (T-helper) lymphocytes per microliter, should be encouraged to take antiretroviral therapy. Antiretroviral therapy for asymptomatic patients with CD4+ cell counts greater than 500/μL is not recommended unless patients indicate such a preference. A recent study showed that zidovudine (AZT, ZDV) monotherapy for asymptomatic patients with CD4+ cell counts of more than 500/μL offered no advantage to waiting until CD4+ cell counts decreased to fewer than 500/μL.[2] Some experts argue, however, that combination drug therapy at these high CD4+ levels might be beneficial. The optimal time to initiate antiretroviral therapy for asymptomatic patients with CD4+ cell counts of 200-500/μL is controversial. A cell count near the midrange (350/μL) is as good a threshold as any and is our personal choice when patients have no strong opinions.

Benefits of antiretroviral therapy are time limited.[3-7] Changing therapy after a period of time should be expected, as no drug or combination of drugs has been shown to halt the progression of HIV disease. Antiretroviral therapy should be changed when drug toxicities occur or new clinical manifestations (opportunistic infections, malignancies, and other clinical signs of advancing disease) develop. Decreasing CD4+ cell counts, such as a decrease of 100/μL or a 50 percent decline during treatment with a particular antiretroviral regimen, also indicate the need to change drugs.

Antiretroviral Drugs

Six antiretroviral drugs are now approved by the Food and Drug Administration for use against HIV.[8-12] These drugs include the reverse transcriptase inhibitors zidovudine, didanosine (ddI), zalcitabine (ddC), stavudine (d4T), and lamivudine (3TC), and the protease inhibitor saquinavir. Two other protease inhibitors, indinavir and ritonavir, will be probably approved early this year.

Lamivudine and saquinavir have been approved on the basis of surrogate marker studies. No clinical end point (ie, opportunistic infections, AIDS, death, etc) studies have been reported for either drug. Neither lamivudine nor saquinavir should be used alone, as viral resistance can occur rapidly. The lamivudine studies showed modest increases in CD4+ cell counts (30-50/μL) and decreases in viral load. Saquinavir and other protease inhibitors

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are associated with increases in CD4+ cell counts and decreases in viral load.

During the past year the findings of two important studies have been presented at conferences and in the news media. Although the results have not been published in the peer-reviewed medical literature, these reports have been influential in generating trends in HIV care. These studies, the AIDS Clinical Trials Group 175 (ACTG 175)[13] trial and the Delta trial,[14] compared zidovudine monotherapy with other therapies.

The ACTG 175 trial compared four separate treatments: zidovudine alone, didanosine alone, zidovudine plus didanosine, and zidovudine plus zalcitabine. The study included persons who had no prior zidovudine treatment (zidovudine-naive) and those who had received zidovudine (zidovudine-experienced). A total of 2500 persons with mean CD4+ cells counts of about 350/μL (range 200-500/μL) were enrolled for a median of 3 years. Among zidovudine-experienced subjects, changing from zidovudine monotherapy to didanosine alone or to didanosine plus zidovudine lowered the death rate from 10 percent to 5 percent and 6 percent, respectively. For zidovudine-naive subjects, zidovudine plus zalcitabine was associated with a statistically significant lower rate of developing the combined end point of new AIDS-defined conditions or death when compared with zidovudine monotherapy. In addition, there was a trend toward more deaths among the zidovudine monotherapy subjects (7 percent) than the other groups (3 to 4 percent), but this difference was not statistically significant.

The Delta trial compared zidovudine alone with zidovudine plus didanosine or zidovudine plus zalcitabine among more than 3000 subjects with a CD4+ cell count of about 200/μL for a median of 26 months. The Delta trial showed a statistically significant improvement in survival for combination therapy for zidovudine-naive persons. Death rates were 16.5 percent for zidovudine alone, 9.6 percent for zidovudine plus didanosine, and 11.6 percent for zidovudine plus zalcitabine.

These two studies provide some support for the concept of changing therapies after a period of time and suggest that the rationale for combination therapy has clinical validity. The ACTG 175 trial shows that adding didanosine to zidovudine therapy or changing to didanosine is beneficial for zidovudine-experienced persons with CD4+ cell counts around 350/μL. For zidovudine-naive persons with CD4+ cell counts around 200/μL, the Delta trial indicates that combination therapy with zidovudine plus didanosine or zidovudine plus zalcitabine is superior to zidovudine monotherapy. These and other studies have prompted many AIDS experts to conclude that combination therapy should always be used, preferably early in the course of HIV disease (at or near CD4+ cell counts of 500/μL) when the viral burden is smaller, rather than later in the course of HIV disease. Although theoretically sound, clinical studies have not yet established that this approach is the best strategy. Combination therapy certainly appears more promising than monotherapy, but monotherapy might also be appropriate for those in whom drug toxicities or interactions are of concern or who are reluctant to take drugs.

Antiretroviral Drug Selection

An entire spectrum of approaches to antiretroviral therapy[15,16] remains acceptable. Patients and their primary care clinicians need to discuss and individualize strategies of care. For example, some patients will prefer early intervention with multiple agents, whereas others will prefer to withhold medications as long as possible.

Most combination regimens should include the best studied drug, zidovudine, if tolerated. Preliminary reports of prolonged and substantial decreases in viral loads with ritonavir and indinavir therapies support adding a protease inhibitor to antiretroviral drug regimens. Because of potential interactions, zidovudine and stavudine should not be used together. The toxicity profiles of didanosine and zalcitabine prevent their concurrent use. Neurologic toxicity might limit concurrent use of stavudine with either didanosine or zalcitabine.

Depending upon individual patient characteristics and individual drug toxicities, the following reverse transcriptase-inhibitor regimens are reasonable: zidovudine in combination with didanosine, lamivudine, or zalcitabine; didanosine or stavudine alone; possibly lamivudine in combination with stavudine, didanosine, or zalcitabine. Zidovudine or zalcitabine alone could also be considered if other regimens are not acceptable. A protease inhibitor can be added to any of these above regimens.

Table 1. Treatment Regimens for HIV Disease

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL/SYSTEMIC			
Antiretroviral (Anti-HIV)			
Combination or monotherapy with the following drugs	Indefinitely, unless toxicities exceed potential benefits	See individual agents	See text. Therapy indicated for all patients with AIDS (including CD4+ lymphocytes < 200/μL) and those with symptomatic HIV disease. Initiation of therapy for asymptomatic persons with CD4+ cell counts of 200–500/μL at discretion of patient and primary care clinician
Zidovudine (AZT, Retrovir) 200 mg po tid; lower dosages (eg, 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 (ie, trimethoprim-sulfamethoxazole, ganciclovir). Probenecid can increase levels of zidovudine. Acetaminophen (Tylenol) administration does not increase zidovudine toxicity	Zidovudine is the common first-choice agent, usually in combination with other retroviral drugs 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 (eg, hemoglobin < 8.0 g/dL) occurs in patients who require zidovudine therapy. Decrease dosage or interrupt for absolute neutrophilcount (ANC) < 500/μL; consider granulocyte colony-stimulating factor (G-CSF). Transfusions and erythropoietin and G-CSF therapies are expensive; changing to alternate agent preferred High-dosage (1200 mg po qd) zidovudine therapy can be considered for HIV dementia and thrombocytopenia. Toxicity of high-dosage zidovudine can be substantial
Didanosine (ddI, Videx) 200-mg tablet po or 250-mg powder bid for patients > 60 kg; - 125-mg tablet or167-mg powder po bid for patients < 60 kg. Dosage reduction (ie, 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 *Drug interactions* Concomitant administration of H_2 antagonists, antacids, and omeprazole (Prilosec) can increase didanosine absorption, resulting in toxicity. Avoid alcohol and other pancreatic toxins (eg, systemic pentamidine). Avoid concomitant neurotoxic drugs (eg, zalcitabine, stavudine, vinca alkaloids, oral ganciclovir). Decreases absorption of drugs whose absorption is impaired by buffered products (eg, ketoconazole, itraconazole, tetracyclines, quinolone antibiotics). Oral and intravenous ganciclovir increase didanosine toxicity	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 Administer didanosine on empty stomach 2 hours apart from antacids, H_2 antagonists, and drugs (eg, ketoconazole, itraconazole, tetracyclines, quinolone antibiotics) whose absorption is impaired by buffered products

Continued

Table 1. *Continued*

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL/SYSTEMIC			
Antiretroviral (Anti-HIV) (cont.)			
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 (eg, systemic pentamidine). Avoid concomitant neurotoxic drugs (eg, didanosine, stavudine, isoniazid, vinca alkaloids, oral ganciclovir)	Not as effective as zidovudine, didanosine, or stavudine for monotherapy. Neurotoxicity can improve with zalcitabine "rest periods"
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 for 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 standard dosages (30–40 mg po bid), as studies suggest these lower dosages are associated with equivalent efficacy and a lower incidence of peripheral neuropathy
Lamivudine (3TC, Epivir) 150 mg po bid; 2 mg/kg po bid for patients < 50 kg	Indefinitely	Headache, fatigue, insomnia; peripheral neuropathy, muscle aches; rash; aphthous ulcers	Not to be used as monotherapy; approved for use with zidovudine. Some evidence that combination therapy with lamivudine plus zidovudine is most effective therapy for zidovudine-naive patients
Saquinavir (Invirase) 600 mg po tid	Indefinitely	Headache, confusion; nausea; fever; abdominal pain *Drug interactions* Ketoconazole and grapefruit juice increase saquinavir serum concentration. Avoid concomitant use of saquinavir with rifampin or rifabutin	Decreases viral load. Resistance to saquinavir develops with time
Indinavir (Crixivan) 800 mg po tid	Indefinitely	Nausea, vomiting, diarrhea, asymptomatic hyperbilirubinemia, aminotransferase elevations. Rash, dry skin; nephrolithiasis; insomnia *Drug interactions* Avoid concomitant use of indinavir with rifampin or rifabutin	Decreases viral load
Ritonavir (Norvir) 600 mg po bid	Indefinitely	Nausea, vomiting, diarrhea, aminotransferase elevations; hypercholesterolemia, hypertriglyceridemia; paresthesias *Drug interactions* Avoid concomitant use of ritonavir with rifampin or rifabutin	Decreases viral load. Preliminary results of one study of ritonavir in patient with advanced disease suggests improvement in disease progression
Postexposure prophylaxis Zidovudine 200 mg po tid plus lamivudine 150 mg po bid	4 weeks	See above	Administration within 1–2 hours of needlestick or other injury advised. Zidovudine appears safe in pregnancy. Some experts recommend treatment with lamiduvine or didanosine in combination with zidovudine. Counseling required

Continued

Table 1. *Continued*

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL/SYSTEMIC			
Antiretroviral (Anti-HIV) (cont.)			
Pregnancy			
Zidovudine 100 mg po 5 times daily followed by intrapartum zidovudine 2 mg/kg IV for 1 hour, 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, decreases transmission to infants
Wasting Syndrome			
Megestrol (Megace) suspension (40 mg/mL) 800 mg po qd	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 large numbers of tablets are required for administration and are more expensive
Dronabinol (Tetrahydrocannabinol [THC] Marinol) 2.5 mg po bid 30 minutes–1 hour 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 Food and Drug Administration (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
***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 therapy. Red-orange discoloration of body fluids. Rare neutropenia, thrombocytopenia, anemia; flu-like syndrome; elevated bilirubin and alkaline phosphatase levels, hepatitis	Survival benefits of MAC prophylaxis not demonstrated. Prophylaxis can be offered for patients with advanced immunodeficiency (eg, CD4+ cell count < 50 or 75/μL). Azithromycin 1200 mg po q wk appeared effective in preliminary results from one study
or			
Clarithromycin (Biaxin) 500 mg po qd-bid	Indefinitely		
or			

Continued

Table 1. *Continued*

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL/SYSTEMIC			
***Mycobacterium avium* complex (MAC) (cont.)**			
Azithromycin (Zithromax) 500 mg po qd	Indefinitely	*Drug interactions* Rifabutin increases metabolism of methadone, zidovudine, and clarithromycin; higher dosage of these drugs might be required. Clarithromycin increases 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	Indefinitely, if tolerated (minimum of 12 weeks)	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		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. Clinical improvement might take 2–4 weeks
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 (Hismanal), or loratadine (Claritin) in combination with azole antibiotics because of increased risk of torsades de pointes and ventricular tachyarrhythmias	
Azithromycin 500 mg po qd			At least two drugs (preferably ethambutol plus clarithromycin or azithromycin) should be used When both *M tuberculosis* and MAC infections are suspected, add isoniazid, rifampin, and pyrazinamide to ethambutol and clarithromycin. See *M tuberculosis*
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	
Ciprofloxacin (Cipro) 500–750 mg po qd-bid	Indefinitely	Nausea, vomiting, abdominal pain. Anxiety, insomnia, euphoria; tremor; hallucinations; seizures	
		Drug interactions Ciprofloxacin binds to cations, resulting in decreased absorption.	Administer 2–4 hours after antacids, sucralfate, dairy products, and didanosine

GENERAL/SYSTEMIC *Continued*

Table 1. *Continued*

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL/SYSTEMIC			
***Mycobacterium avium* complex (MAC) (cont.)**			
Rifampin (Rimactane, Rifadin) 450–600 mg po qd or rifabutin 300 mg po qd	Indefinitely	Rifampin causes red-orange discoloration of body secretions and fluids; elevated bilirubin and alkaline phosphatase levels, hepatitis; anorexia; flu-like syndrome; thrombocytopenia *Drug interactions* Rifampin induces hepatic P-450 enzyme; higher dosages of dapsone, methadone, zidovudine, clarithromycin, fluconazole, ketoconazole, itraconazole, warfarin, protease inhibitors and estrogens might be required	Not clear whether rifampin or rifabutin provides better activity in multidrug therapy against MAC
Amikacin (Amikin) 7.5–10.0 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 *Drug interactions* 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 Rifampin 600 mg po qd plus Pyrazinamide (PZA) 15–30 mg/kg po qd (2 g po qd maximum) plus either Ethambutol 15 mg/kg po qd (2.5 g po qd maximum) or Streptomycin 15 mg/kg IM qd (1 g IM qd maximum)	Begin with 4 drugs. 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 individual drug adverse effects and drug interactions	Directly observed therapy can permit more flexible (eg, 3 times a week) treatment schedules. Consultation with tuberculosis experts and coordination with tuberculosis control agencies often required
Histoplasmosis and coccidioidomycosis			
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	See CENTRAL NERVOUS SYSTEM, *Cryptococcus neoformans*	Amphotericin B recommended initially; oral therapy does not appear as effective. Itraconazole 200 mg po bid or fluconazole 400 mg po bid might be effective. Ketoconazole not indicated

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Table 1. *Continued*

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL/SYSTEMIC			
Histoplasmosis and coccidioidomycosis (cont.)			
Maintenance			
Itraconazole (Sporanox) 200 mg po qd	Indefinitely	Nausea, vomiting. Hypokalemia; hypertension; aminotransferase elevations; adrenal insufficiency; rhabdomyolysis. Teratogenic *Drug interactions* Potent hepatic enzyme inducers, such as rifampin and phenytoin, increase metabolism of intraconazole; higher itraconazole dosages can be required	Fluconazole 400 mg po qd might be effective
OR			
Amphotericin B 50 mg IV each week, 2 times a week, or every other week			Optimum frequency of administration not determined
Cryptococcosis		See CENTRAL NERVOUS SYSTEM, *Cryptococcus neoformans*	
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, for relief of 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			
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

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
SKIN/MUCOCUTANEOUS			
Seborrheic dermatitis (cont.)			
Maintenance			
HC cream 1% and ketoconazole cream 2% bid	Indefinitely		
Mucocutaneous herpes simplex			
Acute			
Acyclovir (Zovirax) 200–400 mg po 5 times a day	7–10 days	Oral: nausea, vomiting, diarrhea,	Topical acyclovir ineffective for most episodes
Maintenance			
Acyclovir 200–400 mg po 2-3 times a day	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 (eg, esophagitis, colitis, encephalitis) require intravenous acyclovir. Maintain good urine output and hydration to prevent acyclovir crystallization
Maintenance			
Acyclovir 200–400 mg po 2-3 times a day	Indefinitely		
Herpes zoster (shingles, disseminated, or persistent zoster)			
Acyclovir 10 mg/kg/dose IV q 8 h; or acyclovir 800 mg po 5 times a day; dosage reduction in renal failure for intravenous acyclovir	7-10 days or until lesions resolve		Intravenous therapy preferred. Alternate drugs are foscarnet, vidarabine, and cidofovir (available via compassionate use) and trifluridine (Viroptic) applied to skin covered with polymyxin B-bacitracin (Polysporin) ointment q 8 h. Keratoconjunctivitis requires more frequent (q 2 h) trifluiridine application
or			
Famciclovir (Famvir) 500 mg po tid; dosage reduction in renal failure	Same	Headache, nausea, fatigue	Approved only for herpes zoster infection. Appears as effective as acyclovir, but no studies in immunocompromised patients. Better bioavailability than acyclovir
Acyclovir-resistant herpes infections			
Foscarnet 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. Cidofovir might be effective. See CMV
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 hours, maximum 9 drops a day) trifluridine application

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
SKIN/MUCOCUTANEOUS (cont.)			
Bacillary angiomatosis			
Erythromycin 500 mg po qid	2 months	See GENERAL/SYSTEMIC, MAC, clarithromycin, azithromycin. Jarisch-Herxheimer reaction with systemic disease	Skin lesions can resolve in 1–3 weeks, but 2 months' treatment needed. Systemic disease (ie, 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 clarithyromycin 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 might be 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/SYSTEMIC, histoplasmosis. Topical metronidazole might be helpful
plus			
Antihistamine (eg, 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			
Observation		Discontinue drugs that can cause thrombocytopenia	Treatment not required in absence of bleeding. Consider platelet transfusions prior to invasive procedures. Splenectomy, high-dosage zidovudine, intravenous gammaglobulin, and interferon-alpha can raise platelet count
OR			
Prednisone 60 mg po qd	Discontinue as soon as possible	Long-term corticosteroid therapy increases immunodeficiency; discontinue as soon as possible	
OPHTHALMOLOGIC			
Cytomegalovirus (CMV)			
Prophylaxis			
Gancyclovir (Cytovene) 1 g po tid	Indefinitely	See OPHTHALMOLOGIC, CMV, maintenance	Oral gancyclovir primary prophylaxis can be considered but is not currently recommended
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 < 20,000/μL; aminotransferase elevations; renal failure; phlebitis, rash; nausea. Discontinue zidovudine during induction to minimize additive hematologic toxicity (neutropenia). To avoid hematologic toxicity, substitute didanosine, zalcitabine, or stavudine for zidovudine, or change to foscarnet plus zidovudine	Intravitreal ganciclovir by injection or implant appears effective if IV causes unacceptable toxicity. Does not provide systemic therapeutic effect or protection of contralateral eye Start G-CSF (filgastim, Neupogen) 300 μg SQ qd to 3 times a week for ganciclovir-induced neutropenia (ANC < 500/μL) on two consecutive measurements
or			

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
OPHTHALMOLOGIC			
Cytomegalovirus (CMV) (cont.)			
Foscarnet (Foscavir) 90 mg/kg/dose IV q 12 h as 2-hour infusion; discontinuation or dosage reduction in renal failure	14-day induction	Nephrotoxicity common; tremors, headaches, occasional seizures, muscle spasms; hypocalcemia, hypercalcemia, hypokalemia, 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–1 L 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
Alternative to ganciclovir or foscarnet			
Cidofovir (Vistide) 5 mg/kg IV with probenecid each week for 2 weeks, then every 2 weeks; dosage reduction in renal failure	Same	Nephrotoxicity; fever; nausea; rash; proteinuria. Persons allergic to sulfa compounds can be allergic to probenecid	Not known whether cidofovir is as effective as ganciclovir or foscarnet. Available by compassionate use
Maintenance			
Ganciclovir 5 mg/kg IV as 1-hour infusion. 7 times a week or 6 mg/kg IV 5 times a week; 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/μL
or			
Ganciclovir 1 g po tid		Anemia, leukopenia; nephrotoxicity; neuropathy *Drug interactions* Oral ganciclovir therapy causes 50% increase in didanosine blood levels; reduce didanosine dosage by 50%	Oral ganciclovir might be as effective for maintenance therapy as intravenous regimens. Oral absorption is erratic when diarrhea is present. Administer on empty stomach to improve absorption
OR			
Foscarnet 90 mg/kg IV qd as 2-hour infusion 7 times a week; 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; induce alternate drug, followed by maintenance with both drugs. Reinduction with ganciclovir or foscarnet might be helpful for recurrences when alternative drug cannot be administered

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
ORAL CAVITY			
Candida albicans			
Clotrimazole (Mycelex) troches 10 mg 5 times a day or vaginal suppositories 100 mg qd-bid. Dissolve slowly in mouth	1–2 weeks or until resolved; maintenance (with lowest effective dosage) might be required for severe or frequent recurrences	Minimal toxicity. Unpleasant taste, nausea, vomiting; aminotransferase elevations	Troches have high sugar content and often require frequent administration. Suppositories can be more convenient
OR			
Nystatin (Mycostatin) 100,000 U/mL, swish and swallow 5 mL po q 6 h or one 500,000-U tablet dissolved slowly in mouth q 6 h	Same	Large oral doses can produce diarrhea, nausea, vomiting	Generally less effective than ketoconazole, fluconazole, and clotrimazole. Can be effective in fluconazole-resistant candidal infection
OR			
Fluconazole (Diflucan) 100–200 mg po qd followed by maintenance therapy 50–100 mg po qd; 100–200 mg po once weekly less effective	Same	See CENTRAL NERVOUS SYSTEM, *Cryptococcus neoformans*	More expensive than other agents. Effective in oral candidiasis unresponsive to above oral agents. Higher dosages might be required. Itraconazole 200 mg po qd might be effective against fluconazole-resistant *Candida albicans*
OR			
Ketoconazole (Nizoral) 400 mg po qd followed by maintenance therapy 200 mg po qd-bid for 7 consecutive days per month	Same	Nausea, vomiting; aminotransferase elevations; anaphylaxis, urticaria. Higher dosages can suppress testerone levels; gynecomastia; adrenal suppression *Drug interactions* Need gastric acidity to be effective; avoid antacids, H2 antagonists; administer 2 hours apart from didanosine. Higher dosages might be necessary if taking rifampin	
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. Intravenous amphotericin B might be necessary for severe disease
Periodontal disease			
Hydrogen peroxide gargles for 30 sec bid	Indefinitely		Less expensive than chlorhexidine. Listerine gargles can be effective Oral hygiene measures with manual removal of plaque are essential. Severe periodontal disease can require antibiotic therapy with metronidazole 250 mg po tid for 7–10 days (alternatives: clindamycin or amoxicillin/clavulanate [Augmentin])
OR			
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	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
OR			
Ketoconazole 200 mg po bid; amphotericin B; see ORAL CAVITY, *Candida albicans*			
OR			
Amphotericin B 0.3–0.4 mg/kg IV qd	10 days or until resolution		Candidal esophagitis unresponsive to oral agents requires low-dose IV amphotericin B
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
Herpes simplex			
IV acyclovir; see SKIN/MUCOCUTANEOUS, disseminated, extensive, or persistent herpes simplex	10–14 days; maintenance required	See SKIN/MUCOCUTANEOUS, disseminated, extensive, or persistent herpes simplex	Diagnose by endoscopic appearance plus positive culture
GASTROINTESTINAL			
Nausea and vomiting			
Prochlorperazine (Compazine) 2.5–10.0 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	Combinations of these agents often necessary
Metoclopramide (Reglan) 10 mg po qid qid or 1 mg/kg IV q 3 h or 10 mg IM q 4–6 h. Dosage reduction in renal failure	As needed	Same as above	Same as above
Lorazepam (Ativan) 0.5-2.0 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 or granisetron (Kytril) 1 mg po bid	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 2.5–10.0 po q 8–12 h	As needed	See GENERAL/SYSTEMIC, wasting syndrome	Effective in drug-induced nausea
Droperidol (Inapsine) 2.5 mg IM/IV q 4–6 h	As needed	Similar to prochlorperazine	

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GASTROINTESTINAL			
Diarrhea			
Symptomatic treatment			
Loperamide (Imodium) 4 mg po initially then 2 mg q 6 h around the clock and prn (maximum 16 mg qd)	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) 2.5–5.0 mg po 3–6 times daily for 24–48 hours; then 2.5–5.0 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, 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. 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 wk until maximum of 500 µg SQ tid	Indefinitely	Nausea, steatorrhea; hyperglycemia; pain at injection site	Not approved by FDA. Efficacy not demonstrated. Long-term safety unknown. Octreotide does not improve malabsorption
Cryptosporidium			
See Diarrhea, symptomatic treatment	Indefinitely	See Diarrhea, symptomatic treatment	No drug effectively eradicates *Cryptosporidium*. Azithromycin, clarithromycin, atovaquone, and bovine colostrum (investigational) might be effective
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
Isospora belli			
Trimethoprim-sulfamethoxazole (TMP-SMX, Septra, Bactrim) 1 DS (double-strength) tablet po qid	21 days	See PULMONARY, PCP	Usually effective
Cytomegalovirus			
Ganciclovir; foscarnet; see OPHTHALOMOLOGIC, CMV	14-21 days	See OPHTHALMOLOGIC, CMV	Diagnose by endoscopic appearance plus biopsy showing CMV inclusion bodies and positive culture. Recurrences should be re-treated as acute disease. 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 AIDS (including CD4+ cell count < 200/μL), unexplained fever, or oral candidiasis			
TMP-SMX 1 DS tablet po qd or qod or 3 times a week (eg, M-W-F) or 1 tablet po bid	Indefinitely	See TMP-SMX, below	TMP-SMX considered most effective for prophylaxis or suppression. Once-daily administration is easiest to remember. Three-days-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 (Trimpex) 15 mg/kg/d or pyrimethamine (Daraprim) 25–75 mg po q wk	Indefinitely	See dapsone plus TMP. Patients allergic to sulfa might tolerate dapsone; some cross-sensitivity	Probably less effective than TMP-SMX; might be less toxic. Check glucose-6-phosphate dehydrogenase (G6PD) before starting dapsone. Lower dosages (eg, 100 mg po 2 times a week) might be effective
OR			
Inhaled pentamidine (Aeropent) 300 mg q 4 wk using Respirgard II nebulizer	Indefinitely	Adverse systemic effects are minimal because of low pentamidine serum concentrations. Bronchospasm and coughing are common, especially in smokers. Pretreatment with inhaled bronchodilator (eg, albuterol) can help. Rare pancreatitis, hypoglycemia; rare nephrotoxicity. Increased risk of spontaneous pneumothorax	Effective for prophylaxis against primary PCP when CD4+ cell count > 150/μL. Does not prevent extrapulmonary disease. Upper lobe recurrences from poor drug distribution when inhaled in upright position. 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	Indefinitely	See above	Efficacy and proper dosages for PCP prophylaxis unknown
plus			
Primaquine 15 mg po qd		See above	
OR			
Atovaquone (Mepron) suspension (750 mg/5 mL) 750 mg po bid with or without pyrimethamine 25–75 mg po q wk	Indefinitely	See above	Efficacy and proper dosages for PCP prophylaxis unknown
OR			
Pyrimethamine 25 mg-sulfadoxine 500 mg (Fansidar) 1 po q 2 wk	Indefinitely	Stevens-Johnson syndrome, toxic epidermal necrolysis; bone marrow suppression; gastrointestinal, central nervous system toxicity	No studies clearly demonstrate efficacy

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
PULMONARY, PCP			
Acute PCP			
TMP-SMX. TMP 15 mg/kg/d given in 3 divided doses either po or as 1-hour to 2-hour IV infusions; lower dosages (TMP 12 mg/kg/d) 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 (eg, 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/μL or if platelet count < 30×10^9/L and bleeding occurs, consider alternative treatment
		Drug interactions Concurrent leucovorin calcium therapy associated with increased rate of therapeutic failure	
		Gastrointestinal: nausea, vomiting, aminotransferase elevations	Pretreatment with lorazepam, prochlorperazine, metoclopramide, or dronabinol to reduce nausea. See GASTROINTESTINAL, nausea and vomiting. Nausea can be less with oral TMP-SMX. Aminotransferase elevations 4–5 times normal require treatment change
		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-hour to 2-hour IV infusion once a day; 3 mg/kg/d might also be effective	21 days	Adverse effects commonly appear between 7 and 14 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; 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
		Drug interactions Avoid concomitant pancreatic toxins such as didanosine, zalcitabine, and alcohol	

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
PULMONARY, PCP			
Alternatives to TMP-SMX for acute PCP (cont.)		Renal: increased BUN and creatinine; hyperkalemia. Concomitant nephrotoxic agents (eg, nonsteroidal anti-inflammatory agents) and dehydration increase risk of nephrotoxicity Rare: neutropenia, thrombocytopenia; hypocalcemia, hypomagnesemia; aminotransferase elevations; cardiac arrhythmias (rare) with prolongation of QT interval and T wave flattening	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
OR			
Clindamycin (Cleocin) 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 G6PD-deficient patients, leukopenia	Check G6PD before initiating primaquine therapy. Check methemoglobin levels when clinically indicated (see Dapsone). Vitamin C 1 g po tid might prevent methemoglobinemia. 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. Patients allergic to sulfa might tolerate dapsone. Methemoglobinemia, dose-related hemolysis, bone marrow suppression; rash; fever; nausea, abdominal pain; hyperkalemia; proteinuria papillary necrosis *Drug interactions* Drug interactions with rifampin and rifabutin can render dapsone ineffective	Effective in mild-to-moderate PCP only. Check G6PD before starting dapsone. Check methemoglobin levels if symptomatic or discrepancy between oxygen saturation and simultaneous arterial PaO_2. Treat methemoglobinemia > 20% (15% if anemic or respiratory compromise) with methylene blue 1% solution 2 mg/kg IV once; methylene blue contraindicated in G6PD deficiency. Vitamin C 1 g po tid might prevent methemoglobinemia
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
plus			
Dapsone 100 mg po qd	21 days	See above	
plus			
Leucovorin calcium (folinic acid) 20 mg/m^2 IV or po q 6 h	24 days		Must be administered for 72 hours after the last dose of trimetrexate. Large IV fluid load with leucovorin administration can result in volume overload
OR			
Atovaquone suspension (750 mg/5mL) 750 mg po bid with food	21 days	Rash, drug fever; headaches; nausea, diarrhea, aminotransferase elevations; neutropenia, anemia; transient conjunctivitis; erythema multiforme	Higher therapeutic failure rate than TMP-SMX. For patients who fail or are intolerant to TMP-SMX, pentamidine, dapsone-TMP, or clindamycin-primaquine. Take with high-fat diet to increase drug absorption. Patients with enteropathy might not absorb a sufficient amount of atovaquone to treat adequately
plus			
Pyrimethamine 50–75 mg po qd			

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
PULMONARY, 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, PCP	TMP-SMX, dapsone plus TMP or pyrimethamine, clindamycin plus primaquine, atovaquone plus pyrimethamine, and pyrimethamine-sulfadoxine provide some prophylaxis against toxoplasmosis. Other PCP regimens (eg, aerosolized pentamidine) not effective; adding another agent to provide toxoplasmosis prophylaxis not required. Clarithromycin and azithromycin provide some benefit
Acute			
Pyrimethamine 75–100 mg po qd (every other day if bone marrow suppression) 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
plus either			
Sulfadiazine 1.0-1.5 g po q 6 h	Same	Rash, drug fever; bone marrow suppression, leukopenia,	Sulfadiazine probably provides effective prophylaxis and suppression against PCP
or			
Clindamycin 600–900 mg po or IV qid	Same	See PULMONARY, PCP	
Alternative when intolerant of sulfadiazine and clindamycin			
Pyrimethamine plus leucovorin as above	Same	See above	
plus one of the following			
Clarithromycin 1 g po bid or azithromycin 1200–1500 mg po qd	Same	See GENERAL/SYSTEMIC, MAC	
or			

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
CENTRAL NERVOUS SYSTEM			
Toxoplasma gondii			
Alternatives (cont.)			
Atovaquone suspension (750 mg/5 mL) 750 mg po qid with meals	Same	See PULMONARY, PCP	Not proved effective
or			
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	Indefinitely		Other agents used for acute toxoplasmosis might be effective at lower dosage for maintenance
or			
Clindamycin 300–450 mg po q 6 h	Indefinitely		
Cryptococcus neoformans			
Prophylaxis			
Fluconazole provides limited prophylaxis			Primary prophylaxis not routinely recommended. Can be considered for patients with CD4+ cell counts < 50 /μL. No long-term survival benefit. Fluconazole resistance reported
Acute meningitis or disseminated cryptococcosis			
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 after 7.5 mg/kg total amphophotericin 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 Granulocytopenia; nausea, vomiting diarrhea, aminotransferase elevations; rash from flucytosine Flucytosine toxicities (rash, leukopenia), in absence of clear benefits, limit its use	Pretreatment with diphenhydramine, acetaminophen, or IV meperidine can decrease amphotericin-induced fevers, chills, and rigors. Administer for 4–6 h in D5W. Addition of heparin 500 U and hydrocortisone 50 mg to amphotericin IV solution can decrease phlebitis. Infusion of 500 mL–1 L normal saline before administration of amphotericin B can minimize renal toxicity. 5-Flucytosine not indicated if granulocytopenia or thrombocytopenia is present Markedly increased intracranial pressure (> 300 mm) might require acetazolamide (Diamox) 250–500 mg po or IV qid, cerebrospinal fluid drainage (15 mL or more per day) or possibly corticosteroids 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 interactions* 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 (eg, 800–1200 mg po qd) might be necessary in severe disease. Fluconazole penetrates central nervous system 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 a 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	Continued serologic and clinical follow-up required to assess adequacy of treatment. Persons with ophthalmic, auditory or cranial nerve abnormalities or other syndromes consistent with neurosyphilis should receive daily penicillin therapy for 10–14 days. Intravenous penicillin preferred for adequate central nervous system penetration. For penicillin-allergic patients, consultation with an expert advised. Administer additional benzathine penicillin 2.4 mu IM weekly after completion of neurosyphilis treatment to ensure 3 weeks total penicillin therapy
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	Pain relief occurs in 3–5 days. Desipramine causes less sedation and fewer anticholinergic effects. Other tricyclic drugs might be equally effective
Phenytoin (diphenylhydantoin, Dilantin) 100 mg po tid	Indefinitely	Usual side effects and drug-drug interactions	Generally ineffective
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) 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

Viral Load Measurements

HIV viral loads are correlated with disease progression. Many clinicians are using viral load measurements to monitor antiretroviral efficacy or development of drug resistance. Although reduction of viral load has been observed after starting or changing antiretroviral therapies, studies have not adequately correlated these changes with clinical outcomes. It is unclear whether the benefits of viral load measurements justify the routine use of this expensive ($200) test. We believe that monitoring the patient's clinical course and CD4+ cell counts remains critical.

Prophylaxis and Treatment of Opportunistic Infections

New guidelines for prevention of opportunistic infections have been published by the Centers for Disease Control and Prevention (CDC).[17] These guidelines are available from the CDC National AIDS Clearinghouse at 1-800-458-5231.

Pneumocystis carinii pneumonia (PCP) remains the single most important opportunistic infection in AIDS because of its frequency, its substantial morbidity and mortality, and its susceptibility to prophylaxis and treatment.[18,19] PCP prophylaxis should be given to all persons with CDC-defined AIDS (including a CD4+ cell count of less than 200/μL on two occasions) and other manifestations of advanced immunodeficiency, such as recurrent oral candidiasis and persistent unexplained fever greater than 100°F for 2 or more weeks.

Toxoplasmosis prophylaxis, recommended by the CDC for patients with CD4+ cell counts less than 100/μL, is achieved with most PCP prophylaxis regimens except dapsone alone and aerosolized pentamidine.[20-22] For those receiving dapsone alone or pentamidine, we recommend treating toxoplasmosis in the small number of patients who develop it rather than administering specific prophylaxis.

Mycobacterium avium complex (MAC) prophylaxis is recommended by the CDC for persons with a CD4+ cell count of less than 75/μL.[17,23-25] We do not consider MAC prophylaxis an essential part of HIV primary care.[26,27] An alternative strategy is to treat clinical MAC disease if it occurs. Similarly, because of the expense and lack of clear benefit, prophylaxis against candidal and other fungal diseases, as well as prophylaxis against cytomegalovirus retinitis, is not recommended.

The Table

Table 1 gives our recommendations for treating most specific diseases and major symptoms of HIV/AIDS. The recommendations are principally 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 highlights the most important management and therapeutic problems in HIV/AIDS. References including articles about pulmonary disease,[18-22,28-35] herpesvirus infections,[36-44] dermatologic problems,[45-48] the AIDS wasting syndrome,[49-53] diarrhea,[54-57] neurologic disease,[44,58-69] tuberculosis,[70-72] and other mycobacterial [23-27,73,74] and fungal diseases[75-80] are included. Additional references are intended to assist providers with drug reactions[33,34,81-83] and prevention[84,85] including special considerations in pregnancy,[86,87] and for health care workers sustaining percutaneous exposure to blood.[88]

Other Sources of Information

To assist clinicians in providing HIV care, many local, regional, state, university, and national information services are available. 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. Information about clinical trials is available through the AIDS Clinical Trials Information Service of the CDC and the National Institutes of Allergy and Infectious Diseases at 1-800-TRIALS A and through the AIDS Treatment Information Service (ATIS) at 1-800-HIV-8440, which also has printed guidelines and information about approved therapies and management protocols. The AIDS Education and Training Centers (AIDS ETCs) of the Health Resources and Services Administration (HRSA) at 1-301-443-6364 offers education, training, and consultation services to health care providers; HRSA also offers a bimonthly teleconference service.

Conclusion

For the family physician and other clinicians, key elements of HIV care are antiretroviral therapy, prophylaxis against opportunistic infections, and treatment of acute complications of AIDS. The importance of the provider-patient-family relationship in providing this care cannot be underestimated. The Current Report - HIV treatment guidelines are intended to help family physicians and other primary care clinicians provide interventions that will delay or prevent many of the complications of HIV/AIDS.

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