Treatment of AIDS and HIV-Related Conditions—1997

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Extraordinary developments in antiretroviral therapy against the human immunodeficiency virus (HIV) have profoundly changed the way patients, their families, their physicians, and society now view HIV disease. Only one decade after discovery of the virus, new medications and pharmacologic strategies appear to be able to retard the proliferation of the virus and slow the progression of disease. Although long-term studies of the clinical impact of antiretroviral therapy are not yet available, all indications are that treatment of this chronic disease will be dramatically more promising during the next decade.

The prospect of markedly slowing the progression of HIV disease and the acquired immunodeficiency syndrome (AIDS) challenges all clinicians to provide their patients with the most helpful guidance and the most effective therapies. These challenges include selecting antiretroviral strategies, offering prophylaxis against opportunistic infections, treating the major complications of AIDS, and providing comprehensive primary care.

This Current Report—HIV is an update of our annual treatment guidelines.[1] It is based on our clinical experience at San Francisco General Hospital, a review of the medical literature, and experience gained from answering calls to our National HIV Telephone Consultation Service. Its purpose is to provide treatment recommendations for most of the medical problems of adults and adolescents with HIV disease and AIDS.

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Antiretroviral Therapy

The recent consensus guidelines on antiretroviral strategies and monitoring HIV disease serve as an excellent resource for clinicians in managing HIV disease.[2] Additional studies[3-8] and reviews[9-11] published since these guidelines were released do not substantially change those recommendations. Recent unpublished reports add strong evidence for using triple drug antiretroviral therapy early in the course of HIV disease.

Monitoring HIV Disease Progression

Quantitative measurement of HIV RNA (viral load) is now available through most commercial laboratories. With careful handling of specimens and high-quality laboratory testing, viral load measurements can add information about the amount of virus in the blood. The patient's clinical status can then be evaluated by assessing the viral load, the CD4+ (T-helper) lymphocyte count, and the patient's symptomatic and physical manifestations of HIV disease.

Viral load measurements give an indication of the amount of current viral activity, whereas the CD4+ lymphocyte count gives an indication of the degree of immunologic destruction. Viral load measurements have been shown to correlate with disease progression[12] and are now being used routinely in making antiretroviral treatment decisions.[13,14] Effects of drug intervention on viral loads can be noted in about 2 to 6 weeks. When used to assess response to therapy, the viral load can be measured at 1 month and every 3 to 4 months thereafter. Variability in both viral load measurements and CD4+ counts occurs frequently; consistent trends of both of these surrogate markers can be important when using these measurements to interpret prognosis and assess therapeutic efficacy.

A key study showed that viral loads greater than 30,000 to 50,000 HIV RNA copies per milliliter of plasma correlate with poor prognosis; viral loads of less than 5,000 copies/mL correlate with

better prognosis.[12] The goal of achieving undetectable levels of HIV RNA in the plasma seems highly desirable, but has not been proved to be the necessary endpoint of antiretroviral therapy at this time. Decreases in viral load measurements by at least 0.5 log can be interpreted as beneficial effects of therapies, whereas rises of 0.5 log or more can indicate progressive disease (and possibly therapeutic failure). A 0.5 log change is roughly a threefold difference. For example, a change from 60,000 to 20,000 is a 0.5 log difference.

Initiating and Changing Antiretroviral Therapy

There is general agreement that all persons with symptomatic HIV disease should receive antiretroviral therapy regardless of CD4+ count or viral load. There is less agreement, however, about treating asymptomatic persons. Therapy is generally recommended for asymptomatic persons with a CD4+ cell count of fewer than 500/μL, although some experts do not initiate therapy as long as the viral load is low (less than 5,000 or 10,000 copies/mL). For asymptomatic patients with CD4+ cell counts greater than 500/μL, a range of strategies can be appropriate. Some experts recommend treating if any virus is detectable. Others do not initiate antiretroviral therapy unless the viral load is more than 30,000 to 50,000 copies/mL or the CD4+ count is decreasing consistently.

Decisions about initiating antiretroviral therapy must be individualized. Because the natural history of HIV disease in general is that of a slowly progressive disease with about one decade between infection and clinical AIDS, different therapeutic strategies are acceptable. Some patients wish to have aggressive therapy early in the course of HIV disease, whereas others wish to withhold medication therapy until indications of advancing disease are clearer. Because long-term efficacy and safety of antiretroviral therapy are not known, no specific strategy—from the hit hard, hit early approach[15] to a more conservative approach in which antiretroviral drug therapy is initiated later—is now known to be correct. Although the current trend is toward earlier and more aggressive therapy based on the hope that decreased viral replication will produce better long-term benefits, it cannot be stated with certainty that this approach is better than one designed to avoid the possibility of inducing early drug resistance and producing cumulative drug toxicity.

When clinically important drug toxicity or signs of progressive disease occur, the medication regimen should be changed. The signs of progressive disease include opportunistic infections or other complications of AIDS, substantial decreases in CD4+ cell counts, and rises in viral loads of 0.5 to 1.0 log difference. When a regimen is considered to be failing, at least two drugs should be changed or added, because changing or adding only one drug might be equivalent to (ineffective) monotherapy.

Drug Treatment

Antiretroviral Drugs

The most potent antiretroviral effects, as measured by changes in the quantity of virus in blood and lymphatic tissue, have been produced by combining nucleoside analog drugs with protease inhibitors. Triple drug therapy with two nucleoside analogs plus a protease inhibitor is generally recommended for patients able to tolerate and fully adhere to these difficult and complicated regimens. Combination therapy is preferred to monotherapy (although didanosine monotherapy was equivalent to combination therapy in one important nucleoside analog study) despite the lack of consistency among the studies that measure clinical endpoints. Benefits of monotherapy, however, are clearly time limited.

Nucleoside Analogs

Five nucleoside analog drugs (zidovudine, didanosine, zalcitabine, lamivudine, and stavudine) are now available. Reasonable combinations that can be recommended are zidovudine plus lamivudine, didanosine, or zalcitabine; lamivudine plus stavudine; and stavudine plus didanosine. Lamivudine plus didanosine or lamivudine plus zalcitabine can be used, but studies assessing safety and efficacy of these combinations have not been performed. Zidovudine and stavudine should not be used together, as CD4+ counts declined significantly in one study of this drug combination. Stavudine plus didanosine has been recommended, but peripheral neuropathy can be a problem, especially in advanced disease. Monotherapy with didanosine, or in some cases zidovudine, can be considered an acceptable option for patients unable to take combination therapy.

Protease Inhibitors

The introduction of the protease inhibitors is the most powerful intervention against HIV to date. Marked reductions in viral load, striking clinical improvement, and reduction in mortality have been observed among patients able to take these medications properly. Whether to initiate protease inhibitor therapy in the very early stages of HIV disease is controversial. We do not believe that adding a protease inhibitor is mandatory when combination nucleoside therapy has been effective in decreasing the viral load to less than about 5,000 copies/mL. The protease inhibitors do not work for all HIV-infected persons; the reasons for this lack of efficacy are not completely understood. Long-term adverse effects of protease inhibitors are not known at this time. It is hoped that cumulative toxicities from years of protease inhibitor therapy will not offset the benefits. Drug resistance to protease inhibitor therapy can occur de novo during regular use and especially when the drugs are taken intermittently. Resistance to one protease inhibitor can also confer cross-resistance to other protease inhibitors, although cross-resistance has not yet been established for the new protease inhibitors currently under investigation. These factors will need to be considered when discussing antiretroviral strategies with patients and their families.

The protease inhibitors must be given together with nucleoside analogs, as rapid resistance develops to protease inhibitor monotherapy. The protease inhibitor drugs are not easy to take. They must be taken regularly and without interruption to avoid drug resistance. Saquinavir is well-tolerated but must be taken with a high-fat meal to ensure absorption and is the least effective protease inhibitor; a new preparation might be more efficacious. Ritonavir has numerous drug interactions that make therapy problematic for patients with more advanced disease who are receiving multiple drugs. In addition, ritonavir must be refrigerated to retain potency. Indinavir, the most commonly used protease inhibitor, has the disadvantage of requiring administration every 8 hours, not three times daily. It needs to be taken on an empty stomach or with a light meal. In addition, indinavir can cause nephrolithiasis and hyperbilirubinemia. Combination protease inhibitor therapy with ritonavir and saquinavir has also been studied; marked reductions in viral load levels have been observed.

Nonnucleoside Reverse Transcriptase Inhibitors (NNRTIs)

The NNRTIs, nevirapine and delavirdine, have antiretroviral activity when used in combination with at least one other nucleoside analog. At the present time their usual role has been as a substitute when excessive drug toxicity prevents the use of protease inhibitors, or when the antiretroviral regimen is failing. Drug-drug interactions between the NNRTIs and protease inhibitors are complex.

Opportunistic Infections

Prophylaxis and treatment of opportunistic infections remain critical elements in managing HIV disease. The Centers for Disease Control and Prevention (CDC) guidelines for prevention of opportunistic infections[16] remains the single best source of information about prophylaxis.

Prophylaxis against *Pneumocystis carinii* pneumonia (PCP) is essential for all persons with symptomatic HIV disease or AIDS (including those with CD4+ cell counts less than 200/μL). PCP prophylaxis with trimethoprim-sulfamethoxazole (and possibly with dapsone-trimethoprim, dapsone-pyrimethamine, or clindamycin-primaquine) also provides prophylaxis against toxoplasmosis. Prophylaxis against *Mycobacterium avium* complex (MAC) is recommended when the CD4+ cell count falls to less than 75 or 50/μL. The macrolides, clarithromycin and azithromycin, are preferred as prophylaxis against MAC disease rather than rifabutin, which poses drug-drug interaction problems. There is some evidence that clarithromycin prophylaxis decreases mortality. When MAC is identified at sterile sites (i.e., bone marrow, blood, or biopsied tissue), active MAC disease is present. Identification of MAC in stool or pulmonary secretions alone in many instances is actually colonization rather than parenchymal disease. Although treatment for acute MAC disease might not be necessary, the problem of drug resistance induced by single-drug prophylaxis probably mandates treating patients who have sputum or stool isolates alone with two drugs. Primary prophylaxis against candidal and other fungal diseases is not required, although many patients receive fluconazole therapy for oral candidiasis. Likewise, primary prophylaxis against cytomegalovirus disease is not currently recommended despite the availability of oral ganciclovir.

Table 1. Treatment Regimens for HIV Disease

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL/SYSTEMIC			
Antiretroviral (Anti-HIV)			
Combination therapies	*Combination therapy of two nucleoside analogs, with or without a protease inhibitor, is recommended. Nucleoside analog combinations are: zidovudine plus lamivudine, didanosine, or zalcitabine; lamivudine plus stavudine; didanosine plus stavudine. Lamivudine plus either didanosine or zalcitabine can be used for patients unable to take other combinations, but safety and efficacy have not been studied. Zidovudine and stavudine should not be used in combination. The most common triple drug combination at this time is indinavir plus zidovudine plus either lamivudine or didanosine. Monotherapy with zidovudine or didanosine offers time-limited benefits but is reserved for patients unable to take combination therapy. See text for further discussion*		
Nucleoside analogs			
Zidovudine (AZT, Retrovir) 200 mg po tid or 300 mg po bid; lower dosages (eg, 100 mg tid) for patients unable to tolerate higher dosages and patients with renal failure or cirrhosis	Until efficacy wanes or toxicity occurs	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	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 neutrophil count (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 po bid as 2 100-mg tablets or 250-mg po bid powder for patients > 60 kg; 125 mg (tablets) or 167 mg (powder) po bid for patients < 60 kg. Dosage reduction (ie, 200 mg/d) in renal failure	Until efficacy wanes or toxicity occurs	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, indinavir, tetracyclines, quinolone antibiotics). Oral and intravenous ganciclovir increases 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, indinavir, 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	Until efficacy wanes or toxicity occurs	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)	
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	Until efficacy wanes or toxicity occurs	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	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 Do not use in combination with zidovudine
Lamivudine (3TC, Epivir) 150 mg po bid; 2 mg/kg po bid for patients < 50 kg. Dosage reduction in renal failure	Until efficacy wanes or toxicity occurs	Headache, fatigue, insomnia; peripheral neuropathy, muscle aches; rash; aphthous ulcers; nausea; rare neutropenia, thrombocytopenia	Not to be used as monotherapy
Protease inhibitors			
Indinavir (Crixivan) 800 mg po q 8 h on empty stomach or with milk, juice, coffee, tea, toast; dosage adjustment to 600 mg po q 8 h in hepatic disease	Until efficacy wanes or toxicity occurs	Nephrolithiasis; nausea, vomiting, diarrhea, abdominal pain; asymptomatic hyperbilirubinemia, aminotransferase elevations; rash; insomnia, headache, taste disturbances *Drug interactions* Avoid concomitant use of indinavir with rifampin, rifabutin (or decrease rifabutin dosage to 150 mg po qd), astemizole (Hismanal), cisapride (Propulsid), triazolam (Halcion), or midazolam (Versed). Decrease indinavir dosage to 600 mg po q 8 h when given with ketoconazole. Didanosine and indinavir administration must be at least 1 hour apart. Increase indinavir dosage to 1 g po q 8 h when given with nevirapine	Can be ordered from Stadtlander Pharmacy 1-800-927-8888. Take with at least 6 glasses of noncaffeinated liquid daily to avoid nephrolithiasis. Must be taken q 8 h, not tid. Not to be used as monotherapy
Ritonavir (Norvir) 600 mg po bid with meals; can increase from 300-600 mg po bid over 4-6 days to minimize gastrointestinal symptoms	Until efficacy wanes or toxicity occurs	Nausea, vomiting, diarrhea, anorexia in more than 50% of patients; aminotransferase elevations; hypercholesterolemia, hypertriglyceridemia; fatigue, weakness, headache, dizziness, circumoral paresthesias; increased creatine phosphokinase	Capsules must be refrigerated; solution is stable at room temperature for 30 days. Combination protease inhibitor therapy with ritonavir 400-600 mg po bid plus saquinavir 400-600 mg po bid has been used with indications of increased viral activity. Not to be used as monotherapy

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL/SYSTEMIC			
Antiretroviral (Anti-HIV) (cont.)			
Ritonavir (Norvir) (cont.)		*Drug interactions* Potent hepatic P-450 enzyme inhibitor. Avoid concomitant use with rifampin, rifabutin, astemizole, cisapride, and benzodiazepines except lorazepam and temazepam. Dosages of desipramine and other antidepressants and narcotics might need adjustment	
Saquinavir (Invirase) 600 mg po tid within 2 hours of a high-fat meal to increase absorption	Until efficacy wanes or toxicity occurs	Headache, confusion; nausea, diarrhea, abdominal pain; fever *Drug interactions* Ketoconazole, ritonavir, delavirdine, and grapefruit juice increase saquinavir serum concentration. Avoid concomitant use of saquinavir with rifampin, rifabutin, phenytoin, carbamazepine, phenobarbital, dexamethasone, nevirapine and other enzyme inducers	Poor bioavailability (4%) even when taken with high-fat meal. Higher dosages (3600-7200 mg po qd) might be more effective; safety and efficacy data not available. Improved drug formulation being developed. Combination therapy with ritonavir (see above). Not to be used as monotherapy
Nelfinavir (Viracept) 750 mg po tid with meals	Until efficacy wanes or toxicity occurs	Diarrhea *Drug interactions* P-450 enzyme inhibitor. Avoid concomitant use with rifampin, rifabutin, astemizole, terfenadine, and cisapride. Benzodiazepine interactions under investigation	Available by expanded access protocol at 1-800-621-7111. Expected to be approved in 1997. Not to be used as monotherapy
Nonnucleoside reverse transcriptase inhibitors			
Nevirapine (Viramune) 200 mg po qd for 14 days; if no rash develops, increase to 200 mg po bid	Until efficacy wanes or toxicity occurs	Maculopapular rash; nausea, vomiting, diarrhea; fatigue, fever, headaches; aminotransferase elevations; rare hematologic toxicity; Stevens-Johnson syndrome *Drug interactions* P-450 enzyme inducer. Avoid concomitant use with protease inhibitors, rifampin and rifabutin. Protease inhibitor interactions	Use in combination with at least one nucleoside analog to avoid rapid development of resistance Increased indinavir dosage might be necessary
Delavirdine (Rescriptor) 200 mg po tid for 14 days; if no rash develops increase to 400 mg po tid	Until efficacy wanes or toxicity occurs	Maculopapular rash; nausea; headache; aminotransferase elevations especially when used with saquinavir *Drug interactions* P-450 enzyme inhibitor. Avoid concomitant use of astemizole, rifampin, rifabutin, phenytoin, carbamazepine. Ketoconazole, fluconazole, clarithromycin, and fluoxetine can increase delavirdine serum concentrations; dosage reduction might be necessary	Food and Drug Administration (FDA) approval expected in early 1997. Use in combination with at least one nucleoside analog to avoid rapid development of resistance. Safety of use with protease inhibitors not established. Delavirdine increases saquinavir and indinavir levels by 50%. Reduce indinavir dosage to 400-600 mg po tid when used in combination with delavirdine
Postexposure prophylaxis Zidovudine 200 mg po tid plus lamivudine 150 mg po bid with or without Indinavir 800 mg po q 8 h	4 weeks	See above adverse effects and drug interactions. Zidovudine and lamivudine appear safe in pregnancy	Administration within 1-2 hours or as soon as possible after exposure. Can substitute other antiretroviral agents when source patient has received extensive treatment with zidovudine or lamivudine. Add indinavir or other protease inhibitor for high-risk exposures and when source patient suspected to have developed antiretroviral drug resistance

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 adverse effects and drug interactions. Serious adverse effects on fetus not demonstrated in studies to date	Zidovudine therapy, initiated at 14-34 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. Other agents (didanosine, lamivudine, nevirapine, protease inhibitors) under investigation
Wasting Syndrome			
Megestrol (Megace) suspension (40 mg/mL) 800 mg po qd	Indefinitely	Nausea, vomiting; edema; adrenal suppression; 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 number of tablets are required for administration and are more expensive
Dronabinol (Tetrahydrocannabinol [THC], Marinol) 2.5 mg po bid 30 minutes to 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 (r-hGH, Serostim) 0.1 mg/kg/d SQ (average dosage 6 mg/d)	Unknown	Arthralgias, joint stiffness, carpal tunnel syndrome; hyperglycemia; hypertriglyceridemia	Can improve exercise endurance and increase weight, characterized by increased lean body mass and decreased fat
Anabolic steroids (eg, testosterone 200 mg IM every 2 weeks, oxandrolone [Oxandrin] 2.5 mg po bid-tid or testosterone patches [Testoderm, Androderm]). Preparation and dosage not established	Unknown	Edema; cholestatic jaundice, peliosis hepatis, aminotransferase elevations; increased libido, testicular atrophy, priapism; insomnia	Unknown whether anabolic steroid therapy improves health. Not indicated for patients with normal testosterone levels. Treatment must be accompanied by exercise
***Mycobacterium avium* complex (MAC)**			
Prophylaxis			
Clarithromycin (Biaxin)500 mg po bid	Indefinitely	Clarithromycin and azithromycin side effects include nausea, vomiting, dyspepsia, diarrhea, hearing loss, aminotransferase elevations	Survival benefits shown for clarithromycin. Prophylaxis can be offered to patients with CD4+ cell counts < 50 or 75/μL
OR			
Azithromycin (Zithromax) 1200 mg po once weekly or 500 mg po qd	Indefinitely	*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 astemizole in combination with azole antibiotics because of increased risk of torsades de pointes and ventricular tachyarrhythmias	
OR			

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL/SYSTEMIC			
***Mycobacterium avium* complex (MAC) (cont.)**			
Rifabutin (Mycobutin) 300 mg po qd or 150 mg po bid	Indefinitely	Nausea (can be reduced by adminstering 150 mg po bid). Rash. Uveitis with dosages greater than 300 mg po qd and in patients receiving concomitant clarithromycin, fluconazole, or indinavir therapy. Red-orange discoloration of body fluids. Rare neutropenia, thrombocytopenia, anemia; flu-like syndrome; elevated bilirubin and alkaline phosphatase levels, hepatitis *Drug interactions* Multiple interactions with protease inhibitors (see Antiretroviral drugs, above). 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 rifabutin therapy
Acute MAC disease Ethambutol (Myambutol) 15 mg/kg po qd (1 g po qd maximum); dosage reduction in renal failure plus either Clarithromycin 500 mg po bid. Higher dosages associated with higher mortality or Azithromycin 500 mg po qd	Indefinitely, if tolerated (minimum of 12 weeks)	Optic neuritis (if > 25 mg/kg/d); hyperuricemia; nausea, vomiting	Treatment indicated for documented MAC disease and patients with progressive signs, symptoms, and laboratory abnormalities consistent with MAC disease. Clinical improvement might take 2-4 weeks. Isolation of MAC in stool or sputum might not indicate systemic disease but is usually treated with ethambutol plus a macrolide antibiotic When both *M tuberculosis* and MAC infections are suspected, add isoniazid, rifampin, and pyrazinamide to ethambutol and clarithromycin pending culture results. See *M tuberculosis*
For serious illness or failure to respond within 1 month, can add one or two of the following:			
Rifabutin 300 mg po qd	Indefinitely		Rifampin (Rimactane, Rifadin) 450-600 mg po qd can substitute for rifabutin if concern about *M tuberculosis* infection
Ciprofloxacin (Cipro) 500-750 mg po qd-bid	Indefinitely	Nausea, diarrhea, vomiting, abdominal pain, headache, anxiety, insomnia, euphoria, rash, tremor, hallucinations, seizures *Drug interactions* Binds to cations, resulting in decreased ciprofloxacin absorption. Administer 2-4 hours after antacids, sucralfate, dairy products, and didanosine	
Amikacin (Amikin) 7.5-10.0 mg/kg IM/IV qd	2-8 weeks	Nephrotoxicity, ototoxicity	Monitor drug levels in patients with renal failure

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL/SYSTEMIC			
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 6 months, and 6 months beyond culture conversion	See individual drug adverse effects and drug interactions Rifampin causes red-orange discoloration of body secretions and fluids; elevated bilirubin and alkaline phosphatase, 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	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 until 15 mg/kg total dosage has been administered. Decrease to 0.7-0.8 mg/kg qd if not tolerated	6-8 weeks total acute therapy (amphotericin plus itraconazole)	See CENTRAL NERVOUS SYSTEM, *Cryptococcus neoformans*	Amphotericin B recommended initially; oral therapy does not appear as effective. Itraconazole 200 mg po bid might be effective
followed by			
Itraconazole (Sporanox) 200 mg po bid	See above	Nausea, vomiting; hypokalemia; hypertension; aminotransferase elevations; adrenal insufficiency; rhabdomyolysis. Teratogenic *Drug interactions* Potent hepatic enzyme inducers, such as rifampin and phenytoin, increase metabolism of itraconazole; higher itraconazole dosages might be required. Avoid concurrent use with triazolam, alprazolam (Xanax), antacids, H_2 blockers, and omeprazole	
Maintenance			
Itraconazole 200 mg po qd	Indefinitely		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

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Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL/SYSTEMIC			
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. Liposomal preparations might have some advantages in specific cases	Therapy can help control disease but does not alter prognosis. Consultation by oncologist or AIDS specialist usually required
OR			
Interferon alfa 3 mU SQ 3 times weekly; increase by 3 mU/d every 2 weeks as tolerated (maximum 27 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			
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
Mucocutaneous herpes simplex			
Acute			
Acyclovir (Zovirax) 200-400 mg po 5 times a day	7-10 days	Oral: nausea, vomiting, diarrhea, dizziness	Topical acyclovir ineffective for most episodes
Maintenance			
Acyclovir 200-400 mg po bid-tid	Indefinitely		Chronic maintenance therapy might 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; maintenance as above	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

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
SKIN/MUCOCUTANEOUS			
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 intravenous acyclovir for renal failure	7-10 days or until lesions resolve		Alternate drugs are foscarnet, vidarabine, cidofovir, and trifluridine (Viroptic) applied to skin covered with polymyxin B-bacitracin (Polysporin) ointment q 8 h. Keratoconjunctivitis requires more frequent (q 2 h) trifluridine application
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. 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 q 2 h, maximum 9 drops a day) trifluridine application
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 (eg, hepatic, splenic, central nervous system, bone) or cutaneous recurrences require treatment for 4 months or indefinitely. Azithromycin 1 g po qd and clarithromycin 500-1000 mg po qd can be used as alternatives
OR			
Doxycycline 100 mg po bid	2 months		
Eosinophilic folliculitis			
High-potency fluorinated corticosteroid cream bid	Indefinitely		Itraconazole 200 mg po qd 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. Topical metronidazole might be helpful
plus			
Antihistamine (eg, diphenhydramine [Benadryl], hydroxyzine [Atarax, Vistaril], doxepin [Sinequan])	Indefinitely		Avoid astemizole 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 Corticosteroids can increase immunodeficiency	Treatment not required in absence of bleeding. Consider platelet transfusions prior to invasive procedures. High-dosage zidovudine, corticosteroids (eg, prednisone 60 mg po qd), splenectomy, intravenous gamma globulin, and interferon alfa can raise platelet count
OPHTHALMOLOGIC			
Cytomegalovirus (CMV)			
Prophylaxis			
Ganciclovir (Cytovene) 1 g po tid	Indefinitely	See OPHTHALMOLOGIC, CMV, maintenance	Oral ganciclovir primary prophylaxis is not currently recommended

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
OPHTHALMOLOGIC			
Cytomegalovirus (CMV) (cont.)			
Acute retinitis			
Induction			
Ganciclovir 5 mg/kg/dose 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	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 (filgrastim, Neupogen) 300 μg SQ qd to 3 times a week for ganciclovir-induced neutropenia (ANC < 500/μL on two consecutive measurements)
OR			
Foscarnet 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 500-1000 mL 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
OR			
Ganciclovir plus foscarnet		See below	Continue maintenance drug, induce with the alternative drug, then continue maintenance therapy with both drugs
Alternative to ganciclovir or foscarnet			
Cidofovir (Vistide) 5 mg/kg IV with probenecid (2 g po 3 hours before and 1 g po 2 and 8 hours after infusion) each week for 2 weeks, then every 2 weeks thereafter; contraindicated in renal insufficiency (serum creatinine ≥ 1.5 mg/dL, CrCl ≤ 55 mL/min, 2+ proteinuria)	14-day induction period	Life-threatening nephrotoxicity; fever; nausea, diarrhea; rash; proteinuria. Persons allergic to sulfa compounds can be allergic to probenecid; metabolic acidosis; neutropenia *Drug interactions* Avoid concomitant administration with any potentially nephrotoxic agent, including nonsteroidal anti-inflammatory drugs	Not known whether cidofovir is as effective as ganciclovir or foscarnet. Indwelling catheter not required Prehydrate with 1 L normal saline. Do not administer within 7 days of other potentially nephrotoxic agents. Patients previously treated with foscarnet are at increased risk for renal failure
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			
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			

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
OPHTHALMOLOGIC			
Cytomegalovirus (CMV) (cont.)			
Acute retinitis			
Maintenance (cont.)			
Foscarnet	Indefinitely		Combination therapy not routinely recommended as initial therapy. 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
plus			
Ganciclovir			
OR			
Ganciclovir 1 g po tid		Anemia, neutropenia; nephrotoxicity; neuropathy *Drug interactions* Oral ganciclovir therapy causes 50% increase in didanosine blood levels; reduce didanosine dosage by 50%	Oral ganciclovir is not as effective for maintenance therapy as intravenous regimens, but is more convenient. Oral absorption is erratic when diarrhea is present. Administer on empty stomach to improve absorption
OR			
Cidofovir 5 mg/kg as 1-hour infusion every 2 weeks at infusion center	Indefinitely	Life-threatening nephrotoxicity; cannot be given with potentially nephrotoxic drugs	Does not require indwelling catheter; quality of life might be improved
ORAL CAVITY			
Candida albicans			
Clotrimazole (Mycelex) troches 10 mg 5 times a day or vaginal suppositories 100 mg qd-bid. Dissolve troches 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 q 6 h or 1 500,000-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 is 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 testosterone levels; gynecomastia; adrenal suppression	

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
ORAL CAVITY			
Candida albicans (cont.)			
Ketoconazole (cont.)		*Drug interactions* Need gastric acidity to be effective; avoid antacids, H_2 antagonists; administer 2 hours apart from didanosine. Higher dosages might be necessary if taking rifampin. Avoid concurrent use with triazolam or alprazolam	
OR			
Amphotericin B mouthwash 100 mg/mL, swish and swallow 1 mL qid	Same	Unpalatable; nausea, vomiting, diarrhea; rare urticaria	Not absorbed. No systemic effects. 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	
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; see ORAL CAVITY, *Candida albicans*	Same as above		
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

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
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. Haloperidol (Haldol) can also be effective
Metoclopramide (Reglan) 10 mg po 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
Granisetron (Kytril) 1 mg po q 12 h, or 10 µg/kg/bid IV, or 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 or granisetron in combination with droperidol helpful for intractable nausea and vomiting
Dronabinol (Marinol) 2.5-10.0 mg po q 8-12 h	As needed	See GENERAL/SYSTEMIC, wasting syndrome	Effective in drug-induced nausea. Marijuana can be helpful
Droperidol (Inapsine) 2.5 mg IM/IV q 4-6 h	As needed	Similar to prochlorperazine	
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 until 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, 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. 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

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GASTROINTESTINAL (cont.)			
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	No evidence of efficacy. Expensive. No drug effectively eradicates Cryptosporidium
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 OPHTHALMOLOGIC, CMV	14-21 days	See OPHTHALMOLOGIC, CMV	Long-term suppressive therapy not routinely indicated. Consider only after multiple recurrences. Beware of drug resistance
PULMONARY			
***Pneumocystis carinii* pneumonia (PCP)**			
Prophylaxis for patients with AIDS (including CD4+ cell count < 200/μL), unexplained fever, or oral candidiasis			
Trimethoprim-sulfamethoxazole 1 DS tablet po qd or qod or 3 times a week (eg, M-W-F)	Indefinitely	See TMP-SMX below	TMP-SMX considered most effective for prophylaxis. Multiple TMP-SMX regimens have been used and all appear effective. TMP-SMX provides additional prophylaxis against toxoplasmosis
Alternatives to TMP-SMX for prophylaxis			
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 below. 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	Bronchospasm and coughing are common; pretreatment with inhaled bronchodilator (eg, albuterol) can help. Increased risk of spontaneous pneumothorax. Minimal systemic effects. Rare pancreatitis, hypoglycemia; rare nephrotoxicity	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 (Cleocin) 450-600 mg po bid-tid plus primaquine 15 mg po qd	Indefinitely	See Alternatives to TMP-SMX for acute PCP below	Efficacy and proper dosages for PCP prophylaxis unknown
OR			

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
PULMONARY			
***Pneumocystis carinii* pneumonia (PCP) (cont.)**			
Prophylaxis (cont.)			
Atovaquone (Mepron) suspension (750 mg/ 5 mL) 750 mg po bid with or without pyrimethamine 25-75 mg po q wk	Indefinitely	Rash, drug fever; headaches; nausea, diarrhea, aminotransferase elevations; neutropenia, anemia; transient conjunctivitis; erythema multiforme	Efficacy and proper dosages for PCP prophylaxis unknown. For patients who fail or are intolerant to TMP-SMX, pentamidine, dapsone-TMP, or clindamycin-primaquine. Take with food to increase drug absorption. Patients with enteropathy might not absorb a sufficient amount of atovaquone for adequate treatment
OR			
Pyrimethamine 25 mg-sulfadoxine 500 mg (Fansidar) 1 tablet po q 2 wk	Indefinitely	Stevens-Johnson syndrome, toxic epidermal necrolysis; bone marrow suppression; gastrointestinal, central nervous system toxicity	No studies clearly demonstrate efficacy
Acute PCP			
TMP-SMX; TMP 15 mg/kg/d given in 3 divided doses either po or as 1-2-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, Stevens-Johnson syndrome) are of concern. Oral and intravenous routes equally effective
		Rashes: maculopapular, exfoliative, Stevens-Johnson syndrome	Mild rash does not necessitate stopping or changing treatment: institute antihistamine or rechallenge with lower dosage of TMP-SMX. Desensitization protocol might not be necessary
Note: Patients with substantial hypoxemia require concomitant corticosteroids (see below)		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. 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; 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

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
PULMONARY (cont.)			
Alternatives to TMP-SMX for acute PCP			
Pentamidine isethionate (Pentam) 4 mg/kg/d as 1-2-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	
		Renal failure; hyperkalemia. Concomitant nephrotoxic agents (eg, nonsteroidal anti-inflammatory agents) and dehydration increase risk of 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
		Rare: neutropenia, thrombocytopenia; hypocalcemia, hypomagnesemia; aminotransferase elevations; cardiac arrhythmias (rare) with prolongation of QT interval and T wave flattening	
OR			
Clindamycin 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 50 mg po bid 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 often tolerate dapsone. Methemoglobinemia, dose-related hemolysis, bone marrow suppression; rash; fever; nausea, abdominal pain; hyperkalemia; proteinuria, papillary necrosis	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% (13-20% 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
		Drug interactions Drug interactions with 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 as salvage therapy
plus			
Dapsone 50 mg po bid	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			

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
PULMONARY			
Alternatives to TMP-SMX for acute PCP (cont.)			
Atovaquone suspension (750 mg/5mL) 750 mg po bid with food plus Pyrimethamine 50-75 mg po qd	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 food to increase drug absorption. Patients with enteropathy might not absorb a sufficient amount of atovaquone for adequate treatment
Adjunctive corticosteroid therapy for acute PCP with PaO_2 ≤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 ≤ 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; leukopenia, thrombocytopenia; crystalluria with renal failure	Sulfadiazine probably provides effective prophylaxis against PCP. Ensure adequate fluid intake
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			
Alternative (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			Other agents used for acute toxoplasmosis might be effective at lower dosage for maintenance
Sulfadiazine 1 g po q 12 h	Indefinitely		
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
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 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. Liposomal amphotericin B might decrease toxicity. Fever, chills; anemia, thrombophlebitis. Granulocytopenia; nausea, vomiting, diarrhea, aminotransferase elevations; rash from flucytosine. Flucytosine toxicities (rash, metallic taste, leukopenia, thrombocytopenia) limit its usefulness	Pretreatment with diphenhydramine, acetaminophen or IV morphine can decrease amphotericin-induced fevers, chills, and rigors. Administer for 4-6 hours in D5W. Addition of heparin 500 U and hydrocortisone 50 mg to amphotericin IV solution can decrease phlebitis. Infusion of 500-1000 mL 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 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 400-800 mg po qd. Dosage reduction in renal failure	8-12 weeks	Nausea, vomiting, diarrhea; dizziness; aminotransferase elevations; rare cutaneous reactions, skin pigmentation, alopecia *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 increase efficacy. 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	10-14 days	Same. Probenecid rash	
plus			
Probenecid 500 mg po qid	10-14 days		
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

Current antiretroviral therapies can raise CD4+ lymphocyte counts considerably. There is debate, therefore, as to whether to continue prophylaxis against PCP and other opportunistic infections if antiretroviral therapy causes the CD4+ count to rise above prophylaxis threshold levels. Although opportunistic infections generally do not occur at these higher CD4+ counts, studies to date do not support discontinuing prophylaxis. We recommend the conservative approach of continuing PCP prophylaxis (and possibly MAC prophylaxis) if CD4+ cell counts increase above prophylaxis threshold levels as a result of antiretroviral therapy.

The Table

Table 1 gives our recommendations for treating specific diseases and the 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 include articles about pulmonary disease,[17-19] tuberculosis and other mycobacterial diseases,[20-22] herpesvirus infections,[23-26] dermatologic problems,[27-29] oropharyngeal,[30-31] ophthalmologic,[24-26,32] and gastrointestinal[33-34] problems and the AIDS wasting syndrome,[35-36] neurologic disease,[37-40] and other bacterial[40,41] and fungal[42] infections. Additional references are intended to assist providers with the broad spectrum of HIV/AIDS problems,[43] including drug reactions,[44] other sexually transmitted diseases,[45] and special treatment considerations for occupational exposures[46-49] and pregnancy.[50]

Other Sources of Information

Information about clinical trials is available through the AIDS Clinical Trials Information Service of the Centers for Disease Control and the National Institutes of Allergy and Infectious Diseases, 1-800-TRIALS A, and through the AIDS Treatment Information Service (ATIS), 1-800-HIV-8440, which also has printed guidelines and information about approved therapies and management protocols. 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 (SFGH) provides clinical consultation and education for health care providers; the Warmline is in operation weekdays at 1-800-933-3413. 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. Additional information can be accessed at the SFGH website [hivinsite.ucsf.edu].

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