Treatment of AIDS and HIV- Related Conditions: 2000

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Managing human immunodeficiency virus (HIV) disease and the acquired immunodeficiency syndrome (AIDS) has changed dramatically during the past few years. Potent combination antiretroviral therapy has produced dramatic improvement in the clinical status of many persons living with HIV disease, decreased the incidence of opportunistic infections, and reduced mortality from AIDS. For the patient, the family, and the primary care clinician, the major challenges are achieving suppression of viral replication to obtain clinical benefits, preventing the development of drug resistance, maintaining adherence to complicated medication regimens, and avoiding toxicities and drug-drug interactions.

Excellent care of persons with HIV disease requires applying the principles of primary care and chronic care management to a disease that is somewhat different from other primary care diseases. Not only are HIV disease and AIDS unique in their potential lethality and infectiousness,[1] but suboptimal antiretroviral therapy can lead to irreversible drug resistance. Multidisciplinary care, therefore, has great advantages in managing HIV infection and AIDS. Collaboration among a team consisting of a primary care clinician, pharmacists, case workers, nurses, and AIDS experts can offer the best opportunity to provide excellent comprehensive care. Pharmacists can be especially helpful in assessing and improving treatment adherence.

This Current Report—HIV updates our annual treatment guidelines.[2] The recommendations (Table 1) are based on our experience at San Francisco General Hospital, published guidelines, a review of the medical literature, and experience gained from answering calls to our National HIV Telephone Consultation Service (Warmline). Because HIV disease management changes rapidly, clinicians are advised to refer to the excellent federal guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents[3] and for prevention of opportunistic infections.[4] The guidelines are updated frequently on the Internet (Table 2), and these and other federal guidelines are available at http://www.hivatis.org.

Antiretroviral Therapy

The key determinants of effective antiretroviral therapy are the selection of a potent regimen and the patient's ability to adhere to the medication regimen. Antiretroviral regimens can be difficult to take. Multiple daily doses, a large pill burden, drug side effects, and the necessity to administer some medicines either with or without food can make adherence difficult even for the most well-intentioned and motivated patient. The commitment must be to take these drugs daily without interruption on a lifelong basis. The primary care clinician and the patient must acknowledge these inherent difficulties and develop realistic expectations before antiretroviral treatment begins. Adherence should be reevaluated regularly during treatment because inadequate adherence can rapidly lead to virologic resistance to the entire class of drugs as well as the specific drugs used. Although there might be some temporary improvement in laboratory values or even in some clinical manifestations of HIV disease when less potent treatment regimens are used or regimen adherence is poor, such suboptimal approaches appear to be poor long-term strategies. It is better to withhold antiretroviral therapy if careful adherence to potent treatment regimens cannot be maintained.

Embarking on antiretroviral therapy is a major decision. Patients need to understand that the first regimen is usually the simplest and most effective regimen. Subsequent regimens after failed therapy (salvage regimens) are often more difficult to take,

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Table 1. Treatment Regimens for HIV Disease.

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Hematologic p. 285 | **Esophageal p. 288** | **Central Nervous System p. 292**

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL/SYSTEMIC **Antiretroviral (Anti-HIV)**			
Combination therapies	*Combination antiretroviral therapy is always recommended. Preferred regimens include two nucleoside reverse transcriptase inhibitors (NRTIs) along with 1 or 2 protease inhibitors (PIs) or one of the nonnucleoside reverse transcriptase inhibitors (nNRTIs). Combinations of all 3 classes of antiretroviral drugs have also been used. Cross-resistance among PIs is common, as is cross-resistance among nNRTIs. NRTI combinations are: zidovudine plus lamivudine, didanosine, abacavir, or zalcitabine; or stavudine plus lamivudine, didanosine, or abacavir; or didanosine plus lamivudine or abacavir; zidovudine and stavudine should not be used in combination. Protease inhibitor therapy is usually with nelfinavir, indinavir, amprenavir, or saquinavir soft-gel capsules. Dual PI combinations include ritonavir plus either indinavir, saquinavir, nelfinavir, or amprenavir; or nelfinavir plus indinavir. Indinavir and saquinavir should not be used in combination. Preferred nNRTIs are efavirenz and nevirapine. See text for further discussion*		
Nucleoside reverse transcriptase inhibitors (NRTIs)			
Zidovudine (AZT, Retrovir) 200 mg PO tid or 300 mg PO bid; lower dosages (eg, 100 mg 3 times daily) for patients unable to tolerate higher dosages and patients with renal failure or cirrhosis. Available as liquid formulation. Available also as fixed-dose combination (Combivir) consisting of zidovudine (300 mg) with lamivudine (150 mg) given as one capsule bid. Take with or without food	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, mitochondrial toxicity. Aminotransferase elevations (alanine transaminase [ALT], aspartate transaminase [AST]), hepatomegaly with steatosis. 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) 400 mg PO qhs as 2 200-mg tablets, or 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. Take on an empty stomach	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. Lactic acidosis, mitochondrial toxicity *Drug interactions* Avoid alcohol and other pancreatic toxins (eg, systemic pentamidine). Avoid concomitant neurotoxic drugs (eg, zalcitabine, vinca alkaloids, oral ganciclovir). Decreases absorption of drugs whose absorption is impaired by buffered products (eg, ketoconazole, itraconazole, indinavir, delavirdine, ritonavir, 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 or given with apple juice Administer didanosine on empty stomach 2 hours apart from antacids, H_2 antagonists, and drugs (eg, ketoconazole, itraconazole, indinavir, delavirdine, ritonavir, tetracyclines, quinolone antibiotics) whose absorption is impaired by buffered products

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
Zalcitabine (ddC, Hivid) 0.75 mg PO tid; 0.375 mg PO tid for patients < 30 kg. Doase reduction in renal failure. Take with or without food	Until efficacy wanes or toxicity occurs	Painful peripheral neuropathy (dosage related, reversible); rash; stomatitis, aphthous ulcers; pancreatitis; esophageal ulceration; seizures; aminotransferase elevations; cardiomyopathy. Lactic acidosis, mitochondrial toxicity *Drug interactions* Avoid alcohol and other pancreatic toxins (eg, systemic pentamidine). Avoid concomitant neurotoxic drugs (eg, didanosine, isoniazid, vinca alkaloids, oral ganciclovir)	Zalcitabine might be less potent than other NRTIs
Stavudine (d4T, Zerit) 20–40 mg PO bid for patients > 60 kg; 15–30 mg PO bid for patients 40–60 kg; reduce dosage for patients < 40 kg and for patients with renal failure. Take with or without food. Available as liquid formulation	Until efficacy wanes or toxicity occurs	Painful peripheral neuropathy; aminotransferase elevations; anemia, macrocytosis; psychological disturbances, insomnia, anxiety, panic attacks. Lactic acidosis, mitochondrial toxicity *Drug interactions* Avoid concomitant use with zidovudine or drugs that can cause neurotoxicity or pancreatic toxicity	Dosage range in this table is lower than standard dosage (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 because of antagonistic antiviral activity
Lamivudine (3TC, Epivir) 150 mg PO bid; 2 mg/kg PO bid for patients < 50 kg. Dosage reduction in renal failure. Available as liquid formulation. Available also as fixed-dose combination (Combivir) consisting of zidovudine (300 mg) with lamivudine (150 mg) given as one capsule bid. Take with or without food	Until efficacy wanes or toxicity occurs	Headache, fatigue, insomnia; peripheral neuropathy, muscle aches; rash; nausea; rare neutropenia, thrombocytopenia; paronychia. Lactic acidosis, mitochondrial toxicity	Provides some efficacy against hepatitis B. Once-daily dosing (300 mg PO qd) might be effective
Abacavir (Ziagen) 300 mg PO bid. Will be available as fixed-dosage combination (Trizivir) consisting of zidovudine 300 mg, lamivudine 150 mg, and abacavir 300 mg, given as one capsule bid. Take with or without food	Until efficacy wanes or toxicity occurs	Nausea, headache, malaise; abdominal pain, diarrhea, rash. Hepatomegaly, steatosis; lactic acidosis, mitochondrial toxicity. Hypersensitivity reaction (2%–5%, usually in first 4 weeks): flu-like symptoms, fever, malaise, fatigue, dyspnea, cough, pharyngitis, abdominal cramping, nausea, vomiting, diarrhea, rash, elevations in transaminases and CPK levels	Symptoms and signs of potentially life-threatening hypersensitivity reaction can be progressive; will resolve if drug stopped. Do not rechallenge, as anaphylactic reactions and deaths reported
Protease inhibitors (PIs)			See also, Dual protease inhibitors, below
Nelfinavir (Viracept) 750 mg PO tid or 1250 mg PO bid. Available as liquid formulation. Take with food. See dual PI combinations below; note dosage differences	Until efficacy wanes or toxicity occurs	Diarrhea; hypertriglyceridemia; hypercholesterolemia, abnormal fat accumulation, hyperglycemia, aminotransferase elevations, hepatitis; osteoporosis *Drug interactions* Moderate hepatic P-450 enzyme inhibitor. Avoid concomitant use with rifampin, rifabutin (or decrease rifabutin dosage to 150 mg PO qd and increase nelfinavir dosage to 1 g PO tid), midazolam (Versed), triazolam (Halcion). Can use lorazepam (Ativan) and temazepam (Restoril). Decreased nelfinavir levels and increased phenobarbital, phenytoin, and carbamazepine levels when used in combination; dosage adjustments probably required. Avoid simvastatin or lovastatin because of rhabdomyolysis; can use pravastatin, fluvastatin, or atorvastatin. Limit sildenafil (Viagra) dosage to 25 mg q 48 h	Resistant strains might be sensitive to other PIs

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL/SYSTEMIC **Antiretroviral (Anti-HIV) (cont.)**			
Indinavir (Crixivan) 800 mg PO q 8 h, dosage adjustment to 600 mg PO q 8 h in hepatic disease. Take on empty stomach or with skim milk, juice, coffee, tea, toast. See dual PI combinations below; note dosage differences	Until efficacy wanes or toxicity occurs	Nephrolithiasis, crystalluria, interstitial nephritis; hypertriglyceridemia, hypercholesterolemia, abnormal fat accumulation, hyperglycemia; nausea, vomiting, diarrhea, abdominal pain; asymptomatic hyperbilirubinemia, aminotransferase elevations; rash; insomnia, headache, dizziness, taste disturbances; thrombocytopenia, osteoporosis *Drug interactions* Moderate hepatic P-450 enzyme inhibitor. Avoid concomitant use of indinavir with rifampin, rifabutin (or decrease rifabutin dosage to 150 mg PO qd and increase indinavir dosage to 1 g PO tid), midazolam, triazolam, and ergotamines. Phenobarbital, phenytoin, and carbamazepine can reduce indinavir levels. Decrease indinavir dosage to 600 mg PO q 8 h when given with ketoconazole. Increase indinavir to 1 g PO q 8 h when given with efavirenz or nevirapine. Indinavir administration must be at least 1 hour apart from didanosine or antacid administration. Avoid simvastatin or lovastatin because of rhabdomyolysis; can use pravastatin, fluvastatin, or atorvastatin. Limit sildenafil dosage to 25 mg q 48 h	Take with at least 6 glasses of noncaffeinated liquid daily to avoid nephrolithiasis Must be taken every 8 hours, not 3 times daily, when used as sole PI
Ritonavir (Norvir) 600 mg PO bid; can increase from 300 mg PO bid to 600 mg PO bid over 4–7 days to minimize gastrointestinal symptoms. Take with food. Available as liquid formulation. See dual PI combinations below; note dosage differences	Until efficacy wanes or toxicity occurs	Nausea, vomiting, diarrhea, anorexia in more than 50% of patients at these dosages; less frequent at the lower dosages used in combination therapy. Aminotransferase elevations; hypertriglyceridemia, hypercholesterolemia, abnormal fat accumulation, hyperglycemia; fatigue, weakness, headache, dizziness, circumoral paresthesias; hyperuricemia, increased creatine phosphokinase; taste disturbances, osteoporosis *Drug interactions* Potent hepatic P-450 enzyme inhibitor. Avoid concomitant use with rifabutin (or decrease rifabutin dosage to 150 mg PO 2–3 times weekly), clozapine, ergotamines, and benzodiazepines except lorazepam and temazepam. Dosages of desipramine and other antidepressants, narcotics, and oral contraceptives might need adjustment. Avoid simvastatin or lovastatin because of rhabdomyolysis; can use pravastatin, fluvastatin, or atorvastatin. Limit sildenafil to 25 mg q 48 h	Not generally used as sole PI Capsules must be refrigerated; solution is stable at room temperature for 30 days Hepatotoxicity might be greater with ritonavir than with other protease inhibitors
Saquinavir soft-gel capsules (Fortovase) 1200 mg PO tid. Take with food. See dual PI combinations below; note dosage differences	Until efficacy wanes or toxicity occurs	Headache, confusion; hypertriglyceridemia, hypercholesterolemia, abnormal fat accumulation, hyperglycemia; nausea, diarrhea, abdominal pain; fever; aminotransferase elevations; osteoporosis	Hard-gel formulation (Invirase, 600 mg PO tid within 2 hours of a high-fat meal to increase absorption) not recommended because of poor bioavailability (4%), even when taken with high-fat meal

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL/SYSTEMIC **Antiretroviral (Anti-HIV) (cont.)**			
		Drug interactions Weak hepatic P-450 enzyme inhibitor. Ketoconazole, ritonavir, delavirdine, and grapefruit juice increase saquinavir serum concentration. Avoid concomitant use of saquinavir with indinavir, rifampin, rifabutin, phenytoin, carbamazepine, phenobarbital, efavirenz (when saquinavir is used as the sole PI), dexamethasone, nevirapine, and other enzyme inducers. Avoid simvastatin or lovastatin because of rhabdomyolysis; can use pravastatin, fluvastatin, or atorvastatin. Limit sildenafil to 25 mg q 48 h	
Amprenavir (Agenerase) 1200 mg PO bid. Take with or without food; avoid high-fat meal. See dual PI combinations below; note dosage differences. Also available as liquid formulation, which should not be used in hepatic or renal failure	Until efficacy wanes or toxicity occurs	Nausea, diarrhea; hypertriglyceridemia, hypercholesterolemia, abnormal fat accumulation, hyperglycemia; headache; rash, Stevens-Johnson syndrome; aminotransferase elevations; osteoporosis *Drug interactions* Moderate hepatic P-450 enzyme inhibitor. Avoid concomitant use with rifampin, rifabutin (or can decrease rifabutin dosage to 150 mg PO qd), and with all benzodiazepines except lorazepam or temazepam. Avoid simvastatin or lovastatin because of rhabdomyolysis; can use pravastatin, fluvastatin, or atorvastatin. Limit sildenafil to 25 mg q 48 h	Use with caution in patients with sulfa allergy. Contains vitamin E; avoid concomitant vitamin E administration. Difficult to take because of large pill burden Increase amprenavir dosage to 1200 mg PO tid when used as sole PI with efavirenz
Dual protease inhibitor combinations (Dual PIs)			
Ritonavir 200 mg PO bid plus Indinavir 800 mg PO bid	Until efficacy wanes or toxicity occurs	See individual agents	Other bid dosing regimens that might be equivalent: ritonavir 400 mg plus indinavir 400 mg; ritonavir 100 mg plus indinavir 800 mg; ritonavir 200 mg plus indinavir 600 mg
Ritonavir 400 mg PO bid plus Saquinavir soft-gel capsules 400 mg PO bid	Until efficacy wanes or toxicity occurs	See individual agents *Drug interactions* Combination can be given with efavirenz without dosage adjustment. Reduce rifabutin dosage to 150 mg PO 2–3 times weekly	Generally well tolerated. Combination therapy provides higher saquinavir levels
Nelfinavir 1250 mg PO bid plus Indinavir 1200 mg PO bid	Until efficacy wanes or toxicity occurs	See individual agents	Data limited
Ritonavir 400 mg PO bid plus Nelfinavir 500–750 mg PO bid	Until efficacy wanes or toxicity occurs	See individual agents	Data limited
Saquinavir soft-gel capsules 800 mg PO tid plus Nelfinavir 750 mg PO tid or 1250 PO bid	Until efficacy wanes or toxicity occurs	See individual agents	Data limited
Ritonavir 200 mg PO bid plus Amprenavir 600 mg PO bid	Until efficacy wanes or toxicity occurs	See individual agents *Drug interactions* Combination can be given with efavirenz without dosage adjustment	Ritonavir 100 mg PO bid might be equally effective Once-daily dosing under investigation

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL/SYSTEMIC			
Antiretroviral (Anti-HIV) (cont.)			
Dual protease inhibitor combinations (Dual PIs) (cont.)			
ABT 378 (Lopinavir) 400 mg plus ritonavir 100 mg combination; given as 3 fixed-dose capsules PO bid	Until efficacy wanes or toxicity occurs	Nausea, diarrhea, skin rash, headache; hyperlipidemia, hyperglycemia; aminotransferase elevations *Drug interaction* See ritonavir, above	Available by expanded access, 1-888-711-7193. Approval expected in 2000
Nonnucleoside reverse transcriptase inhibitors (nNRTIs)			
Efavirenz (Sustiva) 600 mg PO qhs with or without food; 200 mg PO tid if insomnia or nightmares occur	Until efficacy wanes or toxicity occurs	Dizziness, anxiety, inability to concentrate, lightheadedness, headache, dysphoria, nightmares; nausea; rash (less than other nNRTIs). Avoid in pregnancy *Drug interactions* Mixed hepatic P-450 enzyme inducer and inhibitor. Avoid use with either saquinavir or amprenavir when used as sole PI. Increase indinavir dosage to 1 g PO q 8 h when used as sole PI in combination with efavirenz. Increase rifabutin dosage to 450–600 mg qd or 600 mg 2–3 times weekly. Increase in methadone dosage necessary	Good central nervous system penetration; resistance might develop more slowly than other nNRTIs Rash from one nNRTI does not predict rash from other nNRTIs
Nevirapine (Viramune) 200 mg PO qd for 14 days; if no rash develops, increase to 200 mg PO bid. Once-daily dosing (400 mg PO qd) might be effective	Until efficacy wanes or toxicity occurs	Maculopapular rash, Stevens-Johnson syndrome; nausea, vomiting, diarrhea; fatigue, fever, headaches; aminotransferase elevations; rare hematologic toxicity *Drug interactions* Hepatic P-450 enzyme inducer; avoid concomitant use with saquinavir as sole PI, rifampin, and rifabutin. Decreases methadone and estrogen levels; dosage adjustment necessary	Discontinue drug at any time if rash is severe. Do not increase dosage if any rash is present during first 14-day lead-in period Rash from one nNRTI does not predict rash from other nNRTIs
Delavirdine (Rescriptor) 400 mg PO tid. Can dissolve in 3 oz water as slurry	Until efficacy wanes or toxicity occurs	Maculopapular rash; nausea; headache; aminotransferase elevations especially when taken with saquinavir; neutropenia when taken with nelfinavir *Drug interactions* Moderate hepatic P-450 enzyme inhibitor. Avoid concomitant use of rifampin, rifabutin, phenytoin, carbamazepine, simvastatin, lovastatin, alprazolam, benzodiazepines except lorazepam and temazepam, ergot alkaloids. Ketoconazole, itraconazole, fluconazole, clarithromycin, and fluoxetine can increase delavirdine serum concentrations; dosage reduction might be necessary. Increased warfarin effects. Limit sildenafil to 25 mg q 48 h	Not a preferred nNRTI because of poor bioavailability and concerns about delavirdine-drug interaction profile. Delavirdine increases saquinavir and indinavir levels by 50%. Reduce indinavir dosage to 600 mg PO q 8 h when used in combination with delavirdine. Separate didanosine or antacid administration from delavirdine administration by at least 1 hour Rash from one nNRTI does not predict rash from other nNRTIs
Other agents			
Hydroxyurea (Hydrea) 500 mg PO bid	Until efficacy wanes or toxicity occurs	Bone marrow suppression, including $CD4^+$ count decline during hydroxyurea therapy	Can be used in combination with didanosine (and possibly other antiretroviral drugs) as salvage therapy. Long-term risks and benefits unknown
Tenofovir 300 mg PO qd	Until efficacy wanes or toxicity occurs	Creatine phosphokinase elevation; aminotransferase elevation	Nucleotide analog. Role unclear at this time; might offer benefit in salvage therapy. Active against hepatitis B virus. Approval expected in 2001. Available through expanded access at 1-800-276-0231

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL/SYSTEMIC			
Antiretroviral (Anti-HIV) (cont.)			
Postexposure prophylaxis for health care workers			
Zidovudine 200 mg PO tid or 300 mg PO bid plus lamivudine 150 mg PO bid or Combivir one tablet PO bid with or without nelfinavir 750 mg PO tid or 1250 mg PO bid, or indinavir 800 mg PO q 8 h	4 weeks	See above adverse effects and drug interactions. Zidovudine and lamivudine appear safe in pregnancy	Administer within 2 hours or as soon as possible after exposure. Substitute other antiretroviral agents when source patient has received extensive treatment with zidovudine or lamivudine. Add nelfinavir, indinavir, or other PI for high-risk exposures and when source patient suspected to have antiretroviral drug resistance. Can call 1-888-HIV-4911 for additional assistance 24 hours a day
Pregnancy			
Zidovudine-containing antiretroviral regimen during pregnancy, plus 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 Adverse effects on fetus not clear. Reports of possible mitochondrial toxicity with neurologic abnormalities	Zidovudine therapy, combined with intrapartum intravenous zidovudine plus oral zidovudine 2 mg/kg qid to infants for first 6 weeks of life, decreases transmission to infants Cesarean section is controversial. Alternative therapies (eg, nevirapine, short course zidovudine) might be effective
Wasting syndrome			
Anabolic steroids (eg, testosterone 200 mg IM every 2 weeks or 300 mg IM every 3 weeks, oxandrolone [Oxandrin] 2.5 mg PO bid–tid or testosterone patches [Testoderm, Androderm])	Unknown	Edema; cholestatic jaundice, peliosis hepatis, aminotransferase elevations; increased libido, testicular atrophy, priapism; insomnia	Might improve well-being and increase lean body mass. Treatment should be accompanied by exercise
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
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. Available also as tablets, but large number of tablets required for administration and more expensive
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
***Mycobacterium avium* complex (MAC)**			
Primary prophylaxis			
Prophylaxis recommended for patients with $CD4^+$ cell counts < 50/μL			Consider discontinuing MAC prophylaxis in persons whose $CD4^+$ cell count increases to > 100/μL for more than 3–6 months in response to antiretroviral therapy

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL/SYSTEMIC			
***Mycobacterium avium* complex (MAC) (cont.)**			
Clarithromycin (Biaxin) 500 mg PO bid OR	Indefinitely or discontinue as noted in comments section above	Clarithromycin and azithromycin side effects include nausea, vomiting, dyspepsia, diarrhea, hearing loss, aminotransferase elevations *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, theophylline, and digoxin	Clarithromycin might provide prophylaxis against *Cryptosporidium*
Azithromycin (Zithromax) 1200 mg PO once weekly or 500 mg PO qd	Indefinitely or discontinue as noted in comments section above		
OR			
Rifabutin (Mycobutin) 300 mg PO qd	Indefinitely or discontinue as noted in comments section above	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, fluconazole, or PI 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 PIs. See individual PIs, 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 *For serious illness or failure to respond within 1 month, can add one or two of the following:*	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*
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, vomiting, diarrhea. Reversible pink to brown-black discoloration of skin, eyes, body secretions; rash. Hyperglycemia. Retinal degeneration *Drug interactions* Binds to cations, resulting in decreased ciprofloxacin absorption. Administer 2–4 hours after antacids, sucralfate, dairy products, and didanosine	

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL/SYSTEMIC			
***Mycobacterium avium* complex (MAC) (cont.)**			
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 plus pyridoxine 50 mg PO qd or Isoniazid 900 mg PO plus pyridoxine 100 mg po, both taken twice weekly	9 months	Nausea, vomiting, abdominal pain; aminotransferase elevations and hepatitis; seizures; 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	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 must be ruled out Isoniazid can be administered concurrently with NRTIs, PIs, nNRTIs
OR			
Rifampin 600 mg PO qd plus Pyrazinamide 20 mg/kg PO qd	2 months	See individual drug toxicities *Drug interactions* Protease inhibitors should not be administered concurrently with rifampin. Rifabutin dosage adjustment with ritonavir, soft-gel saquinavir, delavirdine, and possibly other antiretroviral drugs	When short-course prophylaxis is administered with or without directly observed therapy (DOT), consultation with tuberculosis experts is recommended. Rifabutin can be substituted for rifampin in consultation with tuberculosis expert. Effective antiretroviral therapy should not be discontinued to permit use of specific antituberculosis drugs
Active tuberculosis			
Combinations of isoniazid, rifampin or rifabutin, pyrazinamide, ethambutol, and streptomycin	Begin with 4 drugs. After 2 months can usually continue 2-drug therapy, depending upon susceptibility testing results	See individual drug adverse effects and drug Multiple drug interactions with antiretroviral agents. See references or consult with expert	Consultation with tuberculosis experts required. Treatment guidelines available on Centers for Disease Control and Prevention Web site
Histoplasmosis			
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 followed by	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
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	Teratogenic
Maintenance			
Itraconazole 200 mg PO qd	Indefinitely		Fluconazole 400 mg PO qd less effective

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL/SYSTEMIC			
Histoplasmosis (cont.)			
OR			
Amphotericin B 50 mg IV each week, 2 times a week, or every other week	Indefinitely		Optimum frequency of administration not determined
Coccidioidomycosis			
Acute			
Amphotericin B (as above)	6–8 weeks	See CENTRAL NERVOUS SYSTEM, *Cryptococcus neoformans*	Fluconazole penetrates central nervous system (CNS) and is preferred initial therapy for CNS coccidioidomycosis
or			
Fluconazole	Indefinitely		
Maintenance			
Fluconazole	Indefinitely		
Cryptococcosis		See CENTRAL NERVOUS SYSTEM, *Cryptococcus neoformans*	
SKIN/MUCOCUTANEOUS			
Kaposi sarcoma			
Observation	Indefinitely		Treatment not required unless lesions are symptomatic or cosmetically bothersome. Effective antiretroviral therapy can improve systemic and localized Kaposi sarcoma
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	Same	Usual chemotherapeutic agent side effects	Therapy can help control disease but does not alter prognosis
OR			
Interferon-alpha 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 itraconazole or ketoconazole cream bid	Until resolved		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 mg PO 5 times a day or 400 mg PO tid	7–10 days	Oral: nausea, vomiting, diarrhea, dizziness	Topical acyclovir ineffective for most episodes
OR			
Valacyclovir (Valtrex) 500 mg–1 g PO bid	7–10 days	Nausea, vomiting, diarrhea; headache, dizziness, fatigue, insomnia. Hemolytic uremic syndrome (if >3 g/d)	
OR			

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
SKIN/MUCOCUTANEOUS (cont.)			
Mucocutaneous herpes simplex (cont.)			
Famciclovir (Famvir) 250 mg PO tid	7–10 days	Nausea, vomiting, diarrhea; headache, dizziness, fatigue, insomnia	
Maintenance			
Acyclovir 200 mg PO bid or 400 mg PO tid or valacyclovir 500 mg PO bid or 1 g PO qd or famciclovir 500 mg PO bid	Indefinitely	See above	Chronic maintenance therapy might be necessary for repeated episodes
Disseminated, extensive, or persistent herpes simplex			
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
OR			
Valacyclovir 1 g PO tid	7–14 days or until lesions resolve	See above	
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; reduce dosage of intravenous acyclovir in renal failure	7–10 days or until lesions resolve	See above	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
OR			
Valacyclovir 1 g PO tid	7–10 days	See above	
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, below	See OPHTHALMOLOGIC, CMV, below
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
OR			Keratoconjunctivitis requires more frequent (as often as 2 hours, maximum 9 drops a day) trifluridine application
Cidofovir (See OPHTHALMOLOGIC, CMV, below)	Same	See OPTHALMOLOGIC, CMV, below	Cidofovir might be effective
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		

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
SKIN/MUCOCUTANEOUS (cont.)			
Eosinophilic folliculitis			
High-potency fluorinated corticosteroid cream bid plus	Indefinitely	Long-term, high-potency fluorinated corticosteroid creams can cause thinning of skin	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. Topical metronidazole might be helpful
Antihistamine (eg, diphenhydramine [Benadryl], hydroxyzine [Atarax, Vistaril], doxepin [Sinequan])	Indefinitely		
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-alpha can raise platelet count
OPHTHALMOLOGIC			
Cytomegalovirus (CMV)			
Prophylaxis			
Ganciclovir (Cytovene) 1 g PO tid		See below	Primary CMV prophylaxis not recommended
Acute retinitis			
Induction			
Ganciclovir 5 mg/kg per 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	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 (Foscavir) 90 mg/kg per 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. Creatinine clearance should be measured in cachectic patients and in patients with renal insufficiency to ensure proper dosage
OR			
Ganciclovir plus foscarnet		See individual agents above. Combination therapy not routinely recommended as initial therapy	Continue maintenance drug, induce with the alternative drug, then continue maintenance therapy with both drugs

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
OPHTHALMOLOGIC (cont.)			
Cytomegalovirus (CMV) (cont.)			
Alternatives 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, creatinine clearance ≤ 55 mL/min, 2^+ proteinuria)	14-day induction period	Life-threatening nephrotoxicity; fever; nausea, diarrhea; rash; uveitis, iritis, ocular hypotonia; proteinuria, metabolic acidosis; neutropenia. Persons allergic to sulfa compounds can be allergic to probenecid *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. Administer G-CSF if absolute neutrophil count consistently < 500/μL
OR			
Ganciclovir implant (Vitasert) q 6–9 months or fomivirsen injection 2 times weekly to q 2 weeks plus	Indefinitely	Surgical complications, including retinal detachment, intravitreal hemorrhage, and endophthalmitis, can impair vision. Cataracts	Intravitreal ganciclovir by injection or implant appears effective if IV causes unacceptable toxicity or patient is unable to take intravenous therapy. Does not provide systemic therapeutic effect or protection of contralateral eye
Ganciclovir 1 g PO tid		Oral ganciclovir: anemia, neutropenia; nephrotoxicity; neuropathy *Drug interactions* Oral ganciclovir therapy causes 50% increase in didanosine blood levels; reduce didanosine dosage by 50%	Oral ganciclovir absorption is erratic when diarrhea is present. Administer on empty stomach to improve absorption
Maintenance (secondary prophylaxis)			
Indicated for persons with prior episode of CMV retinitis			Consider discontinuing secondary CMV prophylaxis in persons with adequate vision and non-sight-threatening lesion whose $CD4^+$ cell count increases to >100–150/μL for 3–6 months in response to antiretroviral therapy
Ganciclovir 5 mg/kg IV qd 5–7 days per week as 1-hour infusion; dosage reduction in renal failure	Indefinitely		Administer G-CSF or change to foscarnet if ANC consistently < 500/μL
OR			
Foscarnet 90–120 mg/kg IV qd as 2-hour infusion; discontinuation or dosage reduction in renal failure	Indefinitely		Maintenance with 120 mg/kg/d might be more effective but also more toxic
OR			
Ganciclovir plus foscarnet	Indefinitely	See individual agents above	Continue maintenance dosage of current drug; reinduce alternate drug, followed by maintenance with both drugs
OR			
Fomivirsen injection or ganciclovir implant plus oral ganciclovir	Indefinitely	See above	
OR			
Ganciclovir 1 g PO tid	Indefinitely	See above	Oral ganciclovir is not as effective for maintenance therapy as other regimens
OR			
Cidofovir 5 mg/kg as 1-hour infusion with oral probenecid 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

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. Vaginal suppositories can be used orally
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 is less effective. Can add 5-flucytosine (Ancobon) 25 mg/kg per dose PO q 6 h if unresponsive to fluconazole	Same	See CENTRAL NERVOUS SYSTEM, *Cryptococcus neoformans*	Effective in oral candidiasis unresponsive to above oral agents. Fluconazole resistance can occur with prolonged use. Amphotericin B solution or itraconazole 200 mg PO qd (or itraconazole solution) might be effective against fluconazole-resistant *Candida albicans*
OR			
Amphotericin B oral suspension 100 mg/mL, swish and swallow 1–5 mL qid	Same	Unpalatable; nausea, vomiting, diarrhea; rare urticaria	Not absorbed. No systemic effects. Intravenous amphotericin B might be necessary for severe disease. If oral formulation is not available from manufacturer, can prepare from intravenous solution
Periodontal disease			
Hydrogen peroxide gargles for 30 sec bid	Indefinitely		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]). Antiseptic mouthwash (Listerine) gargles can be effective
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
OR			

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
ESOPHAGEAL (cont.)			
Candida Albicans (cont.)			
Itraconazole 200 mg PO qd; see GENERAL/SYSTEMIC, Histoplasmosis	Same as above	See GENERAL/SYSTEMIC, Histoplasmosis	
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 indicated only after multiple recurrences. Beware of drug resistance
Herpes simplex			
Acyclovir IV or valacyclovir PO; 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 Haloperidol (Haldol) can also be effective
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	
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
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	Around-the-clock regimen more effective than prn. 2.5 mg diphenoxylate-atropine is equivalent to 2 mg morphine sulfate

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GASTROINTESTINAL (cont.)			
Diarrhea (cont.)			
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	Around-the-clock regimen more effective than prn. 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 shown. Long-term safety unknown. Octreotide does not improve malabsorption
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. Addition of azithromycin 600 mg PO qod might increase effectiveness
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 indicated only after multiple recurrences. Beware of drug resistance
PULMONARY			
***Pneumocystis carinii* pneumonia (PCP)**			
Prophylaxis			
Prophylaxis indicated for patients with AIDS (including $CD4^+$ cell count <200/μL), symptomatic HIV disease, or oral candidiasis			Consider discontinuing PCP primary prophylaxis in persons whose $CD4^+$ cell count increases to >200/μL for more than 3–6 months in response to antiretroviral therapy
Trimethoprim-sulfamethoxazole (TMP-SMX) 1 DS tablet PO qd or qod or 3 times a week (eg, M-W-F)	Indefinitely or discontinue as noted in comments section above	See TMP-SMX below	TMP-SMX considered most effective for prophylaxis. TMP-SMX provides additional prophylaxis against toxoplasmosis and common bacterial infections
Alternatives to TMP-SMX for prophylaxis			
Dapsone 50 mg PO bid or 100 mg PO qd; or dapsone 50 mg PO qd plus pyrimethamine (Daraprim) 50 mg PO q wk plus leucovorin 25 mg PO q wk	Indefinitely or discontinue as noted in comments section above	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			
Atovaquone (Mepron) suspension (750 mg/5 mL) 1500 mg PO qd or 750 mg PO bid, with or without pyrimethamine 25–75 mg PO q wk	Indefinitely or discontinue as noted in comments section above	Headaches; nausea, diarrhea, aminotransferase elevations; rash, drug fever; neutropenia, anemia; transient conjunctivitis; erythema multiforme	Take with food to increase drug absorption. Patients with enteropathy might not absorb a sufficient amount of atovaquone for adequate treatment. Better tolerated than dapsone; efficacy similar
OR			

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
Pulmonary (cont.)			
Pneumocystis pneumonia (PCP) (cont.)			
Inhaled pentamidine (Aeropent) 300 mg q 4 wk using Respirgard II nebulizer	Indefinitely or discontinue as noted in comments section above	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. 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 or discontinue as noted in comments section above	See Acute PCP below	Efficacy and proper dosages for PCP prophylaxis unknown
OR			
Pyrimethamine 25 mg-sulfadoxine 500 mg (Fansidar) 1 PO q 2 wk	Indefinitely or discontinue as noted in comments section above	Stevens-Johnson syndrome, toxic epidermal necrolysis; bone marrow suppression; gastrointestinal, central nervous system toxicity	No studies clearly show efficacy
Acute PCP			
TMP-SMX; TMP 15 mg/kg/d given in 3 divided doses either PO or as 1- 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, 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. Consider desensitization or rechallenge with or without corticosteroids
Note: Patients with substantial hypoxemia require concomitant corticosteroids (see below)		Hematologic: neutropenia, leukopenia, thrombocytopenia, anemia	If absolute neutrophil count <500/μL or if platelet count <30,000/μL 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 effects of TMP	TMP decreases creatinine tubular secretion and can 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
		Neurologic: tremor, psychosis, aseptic meningitis	Tremors can be confused with seizures
		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.)			
Pneumocystis pneumonia (PCP) (cont.)			
Alternatives to TMP-SMX for acute PCP			
Pentamidine isethionate (Pentam) 4 mg/kg/d as 1- 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	
		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/m² 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/m² 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

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
Pulmonary (cont.)			
Pneumocystis pneumonia (PCP) (cont.)			
OR			
Atovaquone suspension (750 mg/5 mL) 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 food to increase drug absorption. Patients with enteropathy might not absorb a sufficient amount of atovaquone for adequate treatment
plus			
Pyrimethamine 50–75 mg PO qd			
Adjunctive corticosteroid therapy for acute PCP with $PaO_2 \leq 70$ mmHg			
Prednisone PO or methylprednisolone (Solu-Medrol) IV, each given as follows: 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 0 mg 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
Maintenance (secondary prophylaxis) with agents used for primary prophylaxis (above)	Indefinitely	Same	Discontinuing secondary prophylaxis appears safe in persons whose $CD4^+$ cell count increases to >200/μL for 3–6 months in response to antiretroviral therapy. This strategy especially helpful for patients experiencing toxicity to drugs for PCP prophylaxis
CENTRAL NERVOUS SYSTEM			
Toxoplasma gondii			
Prophylaxis			
Most PCP prophylaxis regimens provide some protection against toxoplasmosis. Prophylaxis recommended for persons with IgG antibody to *Toxoplasma* and $CD4^+$ count <100/μL	Indefinitely	See PULMONARY, PCP	TMP-SMX, dapsone plus pyrimethamine, clindamycin plus primaquine, atovaquone with or without pyrimethamine, and pyrimethamine-sulfadoxine provide some prophylaxis against toxoplasmosis. Aerosolized pentamidine not effective; adding another agent to provide toxoplasmosis prophylaxis not required. Clarithromycin and azithromycin provide some benefit
Acute			
Pyrimethamine 50–100 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	

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
CENTRAL NERVOUS SYSTEM (cont.)			
Toxoplasma gondii (cont.)			
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 500 mg–1 g PO qd	Same	See GENERAL/SYSTEMIC, MAC	
or			
Atovaquone suspension (750 mg/5 mL) 750 mg PO qid with meals	Same	See PULMONARY, PCP	Not proved effective
Maintenance			
Pyrimethamine 25–75 mg PO qd plus leucovorin 10–25 mg PO qd	Indefinitely		Other agents used for acute toxoplasmosis might be effective at lower dosage for maintenance
plus either			
Sulfadiazine 500 mg–1 g PO qid	Indefinitely		
or			
Clindamycin 300–450 mg PO q 6–8 h	Indefinitely		
Cryptococcus neoformans			
Prophylaxis			
Fluconazole 100–200 mg PO qd 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. Pretreatment not recommended routinely. Administer for 4–6 hours in D5W. Addition of heparin 500 U and hydrocortisone 25 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 (>240 mm) might require cerebrospinal fluid drainage (20–30 mL or more per day by lumbar puncture or continuous lumbar drain), or possibly corticosteroid, mannitol, or acetazolamide (Diamox) therapy
OR			

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
CENTRAL NERVOUS SYSTEM (cont.)			
Cryptococcus neoformans (cont.)			
Fluconazole 400–800 mg PO qd. Dosage reduction in renal failure. Higher dosages (eg, 800–1200 mg PO qd) might increase efficacy	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. Fluconazole penetrates central nervous system and most body tissues, including prostate. Addition of 5-flucytosine might be of benefit
Maintenance			
Fluconazole 200–400 mg PO qd	Indefinitely	Same	Higher dosages might be necessary for recurrent disease. Fluconazole resistance can occur
OR			
Itraconazole 200 mg PO qd	Indefinitely	Same	
OR			
Amphotericin B 0.5–0.8 mg/kg/d 3–5 times a week	Indefinitely	Same	
Syphilis			
Aqueous crystalline penicillin G 3–4 mU IV q 4 h (total 18–24 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 for neurosyphilis. Persons with ophthalmic, auditory, or cranial nerve abnormalities or other syndromes consistent with neurosyphilis should receive daily intravenous 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	10–14 days		
Probenecid 500 mg PO qid	10–14 days	Probenecid rash	
Peripheral neuropathy			
Gabapentin (Neurontin) 300–400 mg PO tid via dose escalation; dosage reduction in renal failure	Indefinitely	Thrombocytopenia; dizziness, ataxia, nystagmus, fatigue, somnolence, headache; nausea, vomiting, diarrhea	Can be helpful when other agents fail. Maximum dosage is 3600 mg/d in divided doses
Desipramine (Norpramin) or amitriptyline (Elavil) 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
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
Phenytoin (diphenylhydantoin, Dilantin) 100 mg PO tid	Indefinitely	Usual side effects and drug-drug interactions	Generally ineffective
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
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

Table 2. Sources of Information for Treatment of AIDS and HIV-Related Conditions.

Information Source	Description
Guidelines	
www.hivatis.org	Extremely easy to use AIDS-specific Web site with access to key federal and other guidelines. Has up-to-date revisions of guidelines as they are announced, as well as some documents in draft form
www.cdc.gov	Contains all guidelines from the Centers for Disease Control and Prevention, including AIDS and Sexually Transmitted Disease
General information, links to guidelines and other Web sites	
www.hivinsite.ucsf.edu	Comprehensive Web site with access to a wide range of resources, including the full text of the *AIDS Knowledge Base*, clinical articles, tables and protocols, and links to other sites. Based in the AIDS Program at San Francisco General Hospital/UCSF
www.hopkins-aids.edu	Comprehensive Web site with access to a wide range of resources, including *Medical Management of HIV Disease*, ask-the-expert question-and-answer series, and links to other sites. Based in the Johns Hopkins University AIDS Service
www.ama-assn.org/special/hiv	Provides news, articles, abstracts, and policy information on AIDS from JAMA and other AMA sources
www.aids-ed.org	Comprehensive Web site based in the AIDS Education and Training Centers
Clinical trials	
www.actis.org	Official AIDS Clinical Trials Information Service (ACTIS) Web site for information on clinical trials. Additional information is available by calling ACTIS at 1-800-TRIALSA; or on the National Institutes of Health Web site: www.niaid.nih.gov

Note: Standard library searches, such as Galen and Grateful Med, and searches on www.medscape.com and others can also be helpful.

have higher pill burdens, are associated with more drug toxicity and drug-drug interactions, and might be less potent. Simulations with placebo medications (or different colored candies, for example) can be useful in helping the patient understand his or her ability to adhere to the therapeutic regimen. Methods of maximizing adherence, such as pillboxes and watches with alarms, can be considered. The clinician should attempt to simplify the regimen without impairing antiretroviral effectiveness.

Goals of Therapy

The principal goal of therapy is to prevent or reverse the progression of clinical illness. Effective antiretroviral therapy is indicated by improvement in the clinical signs and symptoms of HIV disease (such as weight gain, reduction of oral candidiasis, and improved sense of well-being), a rising $CD4^+$ cell count, and decreasing viral load. Some reduction in viral load should be apparent within 4 to 6 weeks of therapy. Ideally, the viral load will decrease to undetectable levels (less than 50 copies/mL by the branched DNA [bDNA] assay) within 4 to 6 months. Patients who obtain substantial decreases in viral loads, but not to undetectable levels, can still obtain clinical benefit from antiretroviral therapy. The goal of therapy, however, should be to achieve viral suppression to undetectable levels or levels as close to undetectable as possible. Effective therapy is usually accompanied by a $CD4^+$ cell count increase of 100–200/μL or more within 2 to 4 months.

Initiating Antiretroviral Therapy

All patients with symptomatic HIV disease, low $CD4^+$ counts, or high HIV RNA (viral load) levels are candidates for antiretroviral therapy. Laboratory markers should be repeated before deciding to treat. Current Department of Health and Human Services recommendations for initiating antiretroviral therapy[3] are a $CD4^+$ cell count of fewer than 500/μL or HIV RNA levels of more than 10,000 copies/mL (bDNA assay) or 20,000 copies/mL (RT-PCR assay). The International AIDS Society – USA[5] recommends an absolute $CD4^+$ cell threshold of 350/μL and viral load of more than 5000 copies/mL for initiating therapy, with the $CD4^+$ cell count range of 350–500/μL being optional. We generally favor either a $CD4^+$ cell count of 350/μL or a (bDNA assay) HIV RNA threshold of 10,000 copies/mL for encouraging antiretroviral therapy. All experts agree that the ideal time to begin therapy should be individualized. For example, persons who wish to have antiretroviral therapy initiated at $CD4^+$ cell count levels greater than 350/μL or with detectable viral loads at any level should be offered antiretroviral therapy if they are committed and able to adhere to the medication regimens. Conversely, the patient who cannot take the medications consistently should

not risk the development of resistance, regardless of laboratory markers.

Recommended Antiretroviral Drug Combinations

Drug combinations of three or four antiretroviral agents are generally required to obtain potent antiretroviral effects. These combination drug regimens, also termed highly active antiretroviral therapy (HAART), usually include 2 nucleoside reverse transcriptase inhibitors (NRTIs) with the addition of either of the following: one or two protease inhibitors (PIs), or one of the nonnucleoside reverse transcriptase inhibitors (nNRTIs), such as efavirenz. No specific regimen is considered the treatment of choice. The preferred NRTI combinations are zidovudine plus lamivudine, didanosine, abacavir, or zalcitabine; or stavudine plus lamivudine, didanosine, or abacavir. Didanosine plus lamivudine or abacavir are optional NRTI combinations. The recommended PIs are nelfinavir, indinavir, amprenavir, or saquinavir, or a combination of two protease inhibitors. The most commonly recommended dual PI combinations are ritonavir plus either indinavir, saquinavir or nelfinavir. Other combinations might be equally effective. Ritonavir is poorly tolerated at high dosages, limiting its use as a sole protease inhibitor, but it is extremely effective in raising the blood levels of other PIs. Because of concerns about the risks of lipid abnormalities and the potential for developing resistance to the protease inhibitor class of drugs, some experts prefer an nNRTI, such as efavirenz or nevirapine, in combination with two NRTIs for initial therapy. This approach can preserve the PI class of drugs for subsequent regimens. Delavirdine is not a preferred nNRTI because of its poor bioavailability and concerns about its drug interaction profile. Triple NRTI therapy with abacavir plus zidovudine and lamivudine also appears effective.

Antiretroviral Therapy Failure and Resistance Testing

New opportunistic infections and other clinical illnesses usually indicate failed therapy regardless of laboratory findings. Laboratory signs of failing therapy are a consistently rising viral load (usually a threefold increase or more) or a falling $CD4^+$ cell count. Virologic failure as indicated by rising viral loads is not always accompanied by clinical progression or decreasing $CD4^+$ counts. Although some patients retain clinical benefit for years after the reemergence of high viral load, this outcome is not predictable, so alternative antiretroviral regimens should be sought.

Antiretroviral therapy can fail because of poor adherence, acquired drug resistance, poor drug absorption, drug-drug interactions, or lack of drug potency. These factors need to be assessed to determine the proper intervention. Regardless of the cause of antiretroviral therapy failure, resistance testing can provide valuable information in selecting antiretroviral regimens.

Resistance Testing

Resistance testing is an important adjunct in making decisions about changing therapies. The test should be obtained while the patient is taking the failing regimen. Some words of caution are in order: genotypic resistance tests are not well standardized, all laboratories do not provide equally accurate information, the reports can be difficult to interpret, the correlation between resistance testing results and clinical effectiveness (or lack of effectiveness) of drugs has not been established adequately, and often only the predominant viral population (not minor strains) is tested. Nevertheless, resistance testing can be most helpful in selecting a new drug regimen by determining drugs to which the patient's predominant virus might be resistant. Phenotypic resistance testing is presumably more accurate than genotypic testing, but it is more expensive, and correlation with clinical outcomes has not yet been established. Current resistance testing methods are expensive ($300 to $1,200) and are variably covered by third party payers. Additional resistance testing and reporting methods are being developed.

Changing Antiretroviral Therapy

All drugs of a failing antiretroviral regimen are usually discontinued. Before doing so, however, it is prudent to obtain resistance tests (while the patient is still receiving that failing regimen) to guide decisions about alternative drug regimens. Multiple drug resistance is often encountered, so antiretroviral regimen selection can be challenging. The new regimen requires at least two (and usually three to five) new agents from different antiretroviral classes, and sometimes drugs from all three classes. Dual protease inhibitor therapy should be considered strongly in these cases. Clinical resistance to stavudine, didanosine, or both is uncommon; these NRTIs can often be included in a salvage regimen. Consultation with an expert AIDS clinician is often required.

The strategy of discontinuing all antiretroviral drugs (scheduled treatment interruptions) is under investigation. There have been several reports describing reversion of the predominant virus to a sensitive (wild type) virus after weeks to months off antiretroviral treatment. This approach is not recommended unless all other options have failed.

Complications of Antiretroviral Therapy

Table 1 lists the major complications of drugs used in HIV disease. As patients survive longer, additional complications have been noted. Some complications are class related. The NRTI drug class appears to be associated with lipodystrophy, hepatomegaly, glucose intolerance, and lactic acidosis. Many NRTI side effects have been attributed to NRTI-induced mitochondrial toxicity. For patients with unexplained systemic illness, the presence of metabolic acidosis with anion gap should prompt an evaluation of the serum lactate level to confirm the diagnosis of lactic acidosis. This condition can be fatal and requires discontinuation of all NRTI drugs. An alternative antiretroviral regimen should be developed, because rechallenge with NRTI drugs is contraindicated. Lipodystrophy, hyperlipidemia, and hyperglycemia have also been associated with the protease inhibitor class of drugs. The clinical importance of the various lipid abnormalities in HIV disease and AIDS has not been fully assessed; long-term development of coronary artery disease is of concern.

Paradoxical responses to effective antiretroviral therapy can occur. As the immune system improves, inflammatory responses to latent opportunistic infections, including uveitis in patients with cytomegalovirus (CMV) disease and acute adenitis in patients with mycobacterial diseases, can occur. These clinical flares should not be considered to be adverse clinical deteriorations; antiretroviral therapy should continue.

Opportunistic Infections

Opportunistic infections have decreased markedly since the introduction of potent antiretroviral therapy. Nevertheless, primary prophylaxis against *Pneumocystis carinii* pneumonia (PCP) and *Mycobacterium avium* complex (MAC) disease remains important. Prophylaxis against PCP is essential for all patients with symptomatic HIV disease, including those with $CD4^+$ cell counts of less than 200/μL. Prophylaxis against MAC is recommended after the $CD4^+$ cell count decreases to fewer than 50/μL. Prophylaxis against PCP and MAC disease can be continued as long as drug toxicities or problematic drug-drug interactions do not occur.

An alternative and equivalent strategy to continued prophylaxis is discontinuing primary opportunistic infection prophylaxis if substantial immune reconstitution has occurred in response to antiretroviral therapy.[6] Prophylaxis against PCP can be discontinued when $CD4^+$ cell counts have been more than 200/μL for 3 to 6 months. Similarly, MAC prophylaxis can be discontinued if the $CD4^+$ cell count has been more than 100/μL for 3 to 6 months.[7] If substantial viral loads (more than 10,000 copies/mL by bDNA assay) are present, this strategy might not be as effective. Although clinical studies generally have used a 6-month time frame to assess the adequacy of this strategy, discontinuing prophylaxis after 3 months appears safe as long as careful observation is possible. The strategy used for PCP prophylaxis will be satisfactory for toxoplasmosis prophylaxis in most instances. Discontinuing secondary PCP prophylaxis (ie, maintenance therapy after PCP has occurred) after 3 to 6 months of immune recovery of a $CD4^+$ cell count to 200 /μL appeared safe in preliminary results from some studies and is a reasonable approach, especially if trimethoprim-sulfamethoxazole toxicity occurs. Discontinuing maintenance therapy (secondary prophylaxis) for cytomegalovirus appears safe in patients who have maintained $CD4^+$ cell counts of more than 100–150/μL for more than 3 to 6 months in response to antiretroviral therapy. Because maintenance therapy against cytomegalovirus can be associated with drug toxicity, this strategy is preferred.

Tuberculosis coinfection with HIV requires special management concerns.[8,9] Tuberculosis prophylaxis is essential for persons with a positive tuberculin skin test (greater than 5 mm in HIV-infected persons), for persons with a previously positive tuberculin skin test without previous chemoprophylaxis, and for those who have had recent contact with active tuberculosis. Prophylaxis regimens are isoniazid for 9 months or isoniazid plus pyrazinamide or rifampin (or rifabutin) for 2 months. Treatment of active tuberculosis in HIV-infected persons and prophylaxis against possible multidrug-resistant tuberculosis usually require consultation with tuberculosis experts.

The Table

Table 1 gives our recommendations for treating specific diseases and the major symptoms of HIV disease and 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.

Sources of Information

The most helpful and up-to-date sources of information can now be found on the Internet. Especially useful Web sites are listed in Table 2. A selected bibliography highlights some additional articles of clinical interest.[10–20]

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 on weekdays at 1–800-933–3413. Our National Clinicians' Post-Exposure Prophylaxis Hotline (PEPline) at 1–888-HIV- 4911 provides 24-hour advice and support regarding occupational exposures to HIV and other blood-borne pathogens. 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.

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