Treatment of AIDS and HIV-Related Conditions: 2001

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Managing human immunodeficiency virus (HIV) disease and the acquired immunodeficiency syndrome (AIDS) has become more standardized yet more complex during the past year. Antiretroviral treatment guidelines now represent a general consensus on basic treatment principles and options[1] as benefits and risks of therapy have become more evident. Clinical manifestations of HIV infection, prognosis, and quality of life are clearly improved for most patients receiving potent antiretroviral therapy, yet viral resistance and chronic and short-term drug toxicities remain major problems. The markedly decreased incidence of opportunistic infections among treated patients has made unusual infections less common in daily HIV management. The role of resistance assays in HIV care is still being assessed, but they offer great possibilities for improving our ability to find satisfactory antiretroviral regimens when others have failed. Finally, for the patient and the primary care clinician, the universal challenges of maintaining adherence to complicated medication regimens and avoiding toxicities and drug-drug interactions remain enormous obstacles.

Excellent HIV care requires applying the principles of primary care, family care, and chronic care management with knowledge and experience in managing HIV infection.[2] Multidisciplinary team collaboration among primary care clinicians, pharmacists, case workers, nurses, and AIDS experts can offer the best opportunity to provide comprehensive care.

This Current Report—HIV updates our annual treatment guidelines.[3] These 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 telephone calls to our National HIV Telephone Consultation Service (Warmline). Because HIV 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[1] and for prevention of opportunistic infections,[4] which are updated frequently on the Internet (Table 2). These and other federal guidelines are available at http://www.hivatis.org.

Initiating Antiretroviral Therapy

Concerns about development of antiretroviral drug resistance and long-term antiretroviral drug toxicity have tempered the enthusiasm for early treatment of asymptomatic persons. The strategy that promoted early aggressive therapy to maximally reduce viral load at all costs has given way to a more cautionary approach. Current recommendations[1] for initiating antiretroviral therapy include the following concepts: initiating (and continuing) therapy should always be based on the willingness, readiness, and capability of the HIV-infected person to adhere to a rigorous and presumably lifelong treatment program; all patients with symptomatic HIV disease should be offered antiretroviral therapy; asymptomatic persons with a $CD4^+$ lymphocyte count less than 350/μL or HIV RNA levels greater than 30,000 copies/mL (bDNA assay) or 55,000 copies/mL (RT-PCR assay) should be offered antiretroviral therapy; and patients with $CD4^+$ cell counts fewer than 200/μL should receive antiretroviral therapy whenever possible. Persons who wish to have antiretroviral therapy

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Table 1. Treatment Regimens for HIV Disease.

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Skin/Mucocutaneous p. 292 | **Esophageal p. 297** | **Central Nervous System p. 303**
Ophthalmologic p. 294 | **Gastrointestinal p. 298**

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL/SYSTEMIC			
Antiretroviral (therapy)			
Combination antiretroviral (ARV) therapy is always recommended. Preferred regimens include two nucleoside reverse transcriptase inhibitors (NRTIs) along with either 1 or 2 protease inhibitors (PIs) or with the nonnucleoside reverse transcriptase inhibitor (nNRTI) efavirenz. Preferred NRTI combinations are zidovudine plus lamivudine or didanosine, and stavudine plus lamivudine or didanosine. Preferred PI therapy is with nelfinavir or indinavir, or with dual PI combination therapy with ritonavir plus indinavir, saquinavir, or lopinavir. Alternative NRTI combinations are didanosine plus lamivudine, and zidovudine plus zalcitabine. Alternative agents that can be used with 2 NRTIs include abacavir, amprenavir, delavirdine, nevirapine, ritonavir, saquinavir, and nelfinavir plus saquinavir. Cross-resistance among PIs is common, as is cross-resistance among nNRTIs. Zidovudine and stavudine should not be used in combination. Indinavir and saquinavir should not be used in combination. Other drug combinations might be necessary; resistance testing and expert consultation can be helpful. See text for further discussion			
Nucleoside reverse transcriptase inhibitors (NRTIs)		*NRTI drug class effects:* Nausea, vomiting; aminotransferase elevations (alanine transaminase [ALT], aspartate transaminase [AST]); lactic acidosis with hepatic steatosis; mitochondrial toxicity; lipoatrophy	
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 combinations: zidovudine 300 mg plus lamivudine 150 mg (Combivir) given as one tablet po bid; and zidovudine 300 mg plus lamivudine 150 mg plus abacavir 300 mg (Trizivir), given as one tablet po bid. Take with or without food	Until efficacy wanes or toxicity occurs	See NRTI drug class effects, above. Malaise, headache, 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. 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. Avoid concomitant use with ribavirin	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 NRTI 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 buffered tablets, or 200 mg po bid as 2 100-mg chewable tablets or 250-mg po bid powder for patients > 60 kg; 125 mg (tablets) or 167 mg (powder) po bid for patients < 60 kg. Available as enteric-coated capsules (Videx EC) given as 400-mg EC capsule po qd (> 60 kg) or 250-mg EC capsule po qd (< 60 kg). Dosage reduction (ie, 200 mg/d) in renal failure. Take on an empty stomach	Until efficacy wanes or toxicity occurs	See NRTI drug class effects, above. Pancreatitis; painful peripheral neuropathy (dosage related, reversible); abdominal cramps, diarrhea related to antacid in formulation; rash; hyperglycemia; hyperuricemia; headache, insomnia, seizures; elevated triglyceride and amylase levels; thrombocytopenia; retinal atrophy *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, lopinavir, delavirdine, ritonavir, tetracyclines, quinolone antibiotics). Oral and intravenous ganciclovir might increase didanosine toxicity. Consider increasing didanosine dosage with methadone use	Monitor for signs of neuropathy. Two buffered 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, lopinavir, ritonavir, tetracyclines, delavirdine, quinolone antibiotics) whose absorption is impaired by buffered products Enteric-coated capsules might cause less diarrhea and fewer drug interactions Didanosine plus stavudine combination should not be given to pregnant women because of increased risk of fatal lactic acidosis

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL/SYSTEMIC (cont.)			
Antiretroviral (therapy) (cont.)			
Nucleoside reverse transcriptase inhibitors (NRTIs) (cont.)			
Zalcitabine (ddC, Hivid) 0.75 mg po tid; 0.375 mg po tid for patients < 30 kg. Dosage reduction in renal failure. Take with or without food	Until efficacy wanes or toxicity occurs	See NRTI drug class effects, above. Painful peripheral neuropathy (dosage related, reversible); rash; stomatitis, aphthous ulcers; pancreatitis; esophageal ulceration; seizures; cardiomyopathy *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) 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	See NRTI drug class effects, above. Painful peripheral neuropathy; anemia, macrocytosis; psychological disturbances, insomnia, anxiety, panic attacks *Drug interactions* Avoid concomitant use with zidovudine or drugs that can cause neurotoxicity or pancreatic toxicity	Lower dosages (20 mg po bid) might have a lower incidence of peripheral neuropathy and equivalent efficacy Do not use in combination with zidovudine because of antagonistic antiviral activity Didanosine plus stavudine combination should not be given to pregnant women because of increased risk of fatal lactic acidosis
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 combinations: zidovudine 300 mg plus lamivudine 150 mg (Combivir) given as one tablet po bid; and zidovudine 300 mg plus lamivudine 150 mg plus abacavir 300 mg (Trizivir), given as one tablet po bid. Take with or without food	Until efficacy wanes or toxicity occurs	See NRTI drug class effects, above. Headache, fatigue, insomnia; peripheral neuropathy, muscle aches; rash; rare neutropenia, thrombocytopenia; paronychia	Provides some efficacy against hepatitis B. Once-daily dosing (300 mg po qd) under investigation
Abacavir (Ziagen) 300 mg po bid. Available as liquid solution. Available also as fixed-dose combinations: zidovudine 300 mg plus lamivudine 150 mg (Combivir) given as one tablet po bid; and zidovudine 300 mg plus lamivudine 150 mg plus abacavir 300 mg (Trizivir), given as one tablet po bid. Take with or without food	Until efficacy wanes or toxicity occurs	See NRTI drug class effects, above. Headache, malaise; abdominal pain, diarrhea, rash. Hypersensitivity reaction (2%–5%, usually in first 8 weeks): rash, flu-like symptoms, fever, malaise, fatigue, dyspnea, cough, pharyngitis, abdominal cramping, anorexia, nausea, vomiting, diarrhea, elevations in transaminases and CPK levels	Symptoms and signs of hypersensitivity reaction can be progressive; will resolve if drug stopped. Do not rechallenge, as anaphylactic reactions and deaths reported

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL/SYSTEMIC (cont.)			
Antiretroviral (therapy) (cont.)			
Protease inhibitors (PIs)		*PI drug class effects:* Nausea, vomiting; aminotransferase elevations, hepatitis; hypertriglyceridemia, hypercholesterolemia, abnormal fat accumulation, hyperglycemia, insulin resistance; osteopenia, osteoporosis *PI drug class interactions:* Avoid concomitant use with rifampin (except ritonavir), St. John's wort, garlic supplements, ergotamine, midazolam (Versed), and triazolam (Halcion); can use lorazepam (Ativan) and temazepam (Restoril). Decreased PI levels and increased phenobarbital, phenytoin, and carbamazepine levels when used in combination; dosage adjustments probably required. Avoid simvastatin (Zocor) or lovastatin (Mevacor) because of rhabdomyolysis; can use pravastatin (Pravachol), fluvastatin (Lescol), low-dose atorvastatin (Lipitor), or cerivastatin (Baycol). Limit sildenafil (Viagra) dosage to 25 mg q 48 h	
Nelfinavir (Viracept) 750 mg po tid or 1250 mg po bid. Available as powder for liquid formulation. Take with food. See dual PI combinations below; note dosage differences	Until efficacy wanes or toxicity occurs	See PI drug class effects, above. Diarrhea *Drug interactions* See PI drug class interactions, above. Moderate P-450 enzyme inhibitor. Decrease rifabutin dosage to 150 mg po qd or 300 mg po 2–3 times weekly and increase nelfinavir dosage to 1 g po tid	Resistant strains might be sensitive to other PIs Diarrhea is self-limiting; can be controlled with loperamide, calcium carbonate, oat bran, psyllium, or pancreatic enzymes
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	See PI drug class effects, above. Nephrolithiasis, crystalluria, interstitial nephritis; diarrhea, abdominal pain; asymptomatic hyperbilirubinemia; rash; insomnia, headache, dizziness, metallic taste; alopecia, dry skin; thrombocytopenia *Drug interactions* See PI drug class interactions above. Moderate P-450 enzyme inhibitor. 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	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	See PI drug class effects, above. Diarrhea, anorexia in more than 50% of patients; fatigue, weakness; headache, dizziness, circumoral paresthesias; hyperuricemia, increased creatine phosphokinase; taste disturbances *Drug interactions* See PI drug class interactions above. Potent hepatic P-450 enzyme inhibitor. Dosages of desipramine and other antidepressants, narcotics, and oral contraceptives might need adjustment	Not generally used as sole PI Capsules must be refrigerated; solution should not be refrigerated Hepatotoxicity might be greater with ritonavir than with other protease inhibitors High alcohol content of liquid formulation

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL/SYSTEMIC (cont.)			
Antiretroviral (therapy) (cont.)			
Protease inhibitors (PIs) (cont.)			
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	See PI drug class effects above. Headache, confusion; fever *Drug interactions* See PI drug class interactions, above. 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	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
Amprenavir (Agenerase) 1200 mg po bid. Take with or without food; avoid high fat meal. Available as liquid formulation. See dual PI combinations below; note dosage differences	Until efficacy wanes or toxicity occurs	See PI drug class effects above. Diarrhea; oral paresthesias, headache; rash, Stevens-Johnson syndrome *Drug interactions* See PI drug class interactions, above. Moderate P-450 enzyme inhibitor	Use with caution in patients with sulfa allergy. Contains vitamin E; avoid concomitant vitamin E coadministration Increase amprenavir dosage to 1200 mg po tid when used as sole PI with efavirenz Amprenavir solution contains propylene glycol, which is contraindicated in pregnancy and should be used with caution in hepatic or renal failure or in combination with metronidazole or disulfiram
Dual protease inhibitor combinations (Dual PIs)			
Ritonavir 200 mg po bid plus Indinavir 800 mg po bid	Until efficacy wanes or toxicity occurs	See PI class effects, drug interactions, and individual agents	Other bid dosing regimens that might be equivalent: ritonavir 100 mg plus indinavir 800 mg; ritonavir 200 mg plus indinavir 600 mg
Ritonavir 400 mg po bid plus Indinavir 400 mg po bid	Until efficacy wanes or toxicity occurs	See PI drug class effects, drug interactions, and individual agents	Might cause less nephrolithiasis
Ritonavir 400 mg po bid plus Saquinavir soft-gel capsules 400 mg po bid	Until efficacy wanes or toxicity occurs	See PI drug class effects, drug interactions, and 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 PI drug class effects, drug interactions, and individual agents	Data limited
Ritonavir 400 mg po bid plus Nelfinavir 500–750 mg po bid	Until efficacy wanes or toxicity occurs	See PI drug class effects, drug interactions, and individual agents	Data limited

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL/SYSTEMIC (cont.)			
Antiretroviral (therapy) (cont.)			
Dual protease inhibitor combinations (Dual PIs) (cont.)			
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 PI drug class effects, drug interactions, and individual agents	Data limited
Ritonavir 200 mg po bid plus Amprenavir 600 mg po bid	Until efficacy wanes or toxicity occurs	See PI drug class effects, drug interactions, and 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
Lopinavir 400 mg plus ritonavir 100 mg combination (Kaletra); given as 3 fixed-dose capsules po bid with food. Available as liquid formulation. Increase dosage to 4 capsules po bid if administered with efavirenz or nevirapine	Until efficacy wanes or toxicity occurs	See PI drug class effects, drug interactions, and individual agents. Diarrhea; skin rash; headache, weakness; edema *Drug interactions* See ritonavir, above	Refrigerate capsules; stable at room temperature for 2 months only Better tolerated than ritonavir alone. Ritonavir-resistant strains can be sensitive to lopinavir-ritonavir combination
Nonnucleoside reverse transcriptase inhibitors (nNRTIs)			
Efavirenz (Sustiva) 600 mg po qhs with or without food; 200 mg po tid if insomnia or nightmares occurs	Until efficacy wanes or toxicity occurs	Dizziness, anxiety, inability to concentrate, lightheadedness, headache, dysphoria, nightmares; nausea; rash (less than other nNRTIs); aminotransferase elevations, hepatitis. Avoid in pregnancy *Drug interactions* Mixed P-450 enzyme inducer and inhibitor. Avoid use with either saquinavir or amprenavir when used as sole PIs. 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 lopinavir-ritonavir to 4 capsules po bid. Reduces methadone levels; dosage adjustment 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 Avoid coadministration with St. John's wort and garlic tablets, as they can reduce efavirenz levels

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL/SYSTEMIC (cont.)			
Antiretroviral (therapy) (cont.)			
Nonnucleoside reverse transcriptase inhibitors (nNRTIs) (cont.)			
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. Black box warning about rare fulminant hepatotoxicity; risk increased with concurrent chronic hepatitis and concomitant hepatotoxic drugs. Nausea, vomiting, diarrhea; fatigue, fever, headaches; rare hematologic toxicity *Drug interactions* P-450 enzyme inducer; avoid concomitant use with saquinavir as sole PI, rifampin, and rifabutin. Decreases methadone and estrogen levels; dosage adjustment necessary. Increase lopinavir-ritonavir to 4 capsules po bid. Increase indinavir to 1 g po q 8 h	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. Dose escalation can minimize occurrence of rash; prophylactic antihistamines and corticosteroids remain controversial 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 P-450 enzyme inhibitor. Avoid concomitant use of rifampin, rifabutin, phenytoin, carbamazepine, simvastatin, lovastatin, alprazolam, midazolam, triazolam, ergotamine, St. John's wort, and garlic supplements; can use lorazepam and temazepam. 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 and saquinavir dosage to 600 mg po tid 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			
Tenofovir disoproxil fumerate 300 mg po qd	Until efficacy wanes or toxicity occurs	Creatine phosphokinase elevation; aminotransferase elevation. Other toxicities not yet reported by manufacturer	Nucleotide analog. Role unclear; might offer benefit in salvage therapy. Active against HBV. Approval expected in 2001. Available through expanded access at 1-800-276-0231
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 (preferred) or 1,250 mg po bid or indinavir 800 mg po q 8 h	4 weeks	Nevirapine should not be used; fulminant hepatic failure has occurred from nevirapine use in occupational postexposure prophylaxis 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. Can substitute other antiretroviral agents when source patient has received extensive treatment with ARV drugs. Add nelfinavir, indinavir, or other PI for high-risk exposures and when source patient suspected to have ARV resistance. Can call 1-888-HIV-4911 for additional assistance

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL/SYSTEMIC (cont.)			
Antiretroviral (therapy) (cont.)			
Pregnancy			
Combination ARV therapy recommended according to ARV guidelines. When possible, use zidovudine-containing antiretroviral regimen during pregnancy, plus intrapartum zidovudine until delivery	Until end of pregnancy	See above adverse effects and drug interactions Adverse effects on fetus not clear. Anemia, neutropenia; possible mitochondrial toxicity with neurologic abnormalities (infant). Viral resistance to lamivudine is commonly induced in infants; clinical implications unknown	Prenatal and intrapartum therapy with zidovudine or zidovudine plus lamivudine, along with postnatal treatment of infant, decreases HIV transmission Discussion of risks and benefits is essential. Consider cesarean section
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. Deep venous thrombosis; 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 $< 50/\mu L$			Can discontinue MAC prophylaxis in persons whose $CD4^+$ cell count increases to $> 100/\mu L$ for more than 3–6 months in response to antiretroviral therapy
Clarithromycin (Biaxin) 500 mg po bid OR	Indefinitely	Clarithromycin and azithromycin side effects include nausea, vomiting, dyspepsia, diarrhea, hearing loss, aminotransferase elevations	Clarithromycin might provide prophylaxis against *Cryptosporidium*
		Drug interactions	
Azithromycin (Zithromax) 1200 mg po once weekly or 500 mg po qd	Indefinitely	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	

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GENERAL/SYSTEMIC (cont.)			
***Mycobacterium avium* complex (MAC) (cont.)**			
Primary prophylaxis (cont.)			
OR			
Rifabutin (Mycobutin) 300 mg po qd	Indefinitely	Nausea (can be reduced by administering 150 mg po bid). Rash. Uveitis with dosages greater than 300 mg po qd and in patients receiving concomitant clarithromycin, fluconazole, delavirdine, 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 antiretroviral drugs. See individual agents, 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 q	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 (cont.)			
***Mycobacterium avium* complex (MAC) (cont.)**			
For serious illness or failure to respond within 1 month, can add one or two of the following:			
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			
Rifabutin (variable dosage) or Rifampin 600 mg po qd plus Pyrazinamide 20 mg/kg po qd	2 months	See individual drug toxicities *Drug interactions* Rifabutin dosage adjustment with PIs and nNRTIs; See individual agents, above. PIs, except ritonavir, should not be administered concurrently with rifampin	When short-course prophylaxis is administered with or without directly observed therapy (DOT), consultation with tuberculosis experts is recommended. 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
Cryptococcosis		See CENTRAL NERVOUS SYSTEM, *Cryptococcus neoformans*	
SKIN/MUCOCUTANEOUS			
Kaposi sarcoma			
Observation, local treatment (radiation therapy, cryotherapy, excision, or intralesional vinblastine), systemic chemotherapy, or interferon-α			Treatment not required unless lesions are symptomatic or cosmetically bothersome. Effective antiretroviral therapy can improve systemic and localized Kaposi sarcoma

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
SKIN/MUCOCUTANEOUS (cont.)			
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	10 days	Nausea, vomiting, diarrhea; headache, dizziness, fatigue, insomnia. Hemolytic uremic syndrome (if > 3 g/d)	
OR			
Famciclovir (Famvir) 250 mg po tid	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		Chronic maintenance therapy might be necessary for repeated episodes
Disseminated, extensive, or persistent herpes simplex			
Acyclovir 5 mg/kg per 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 per 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	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 q po tid	7–10 days		

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
SKIN/MUCOCUTANEOUS (cont.)			
Acyclovir-resistant herpes infections			
Foscarnet 40 mg/kg per 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 Keratoconjunctivitis requires more frequent (as often as 2 hours, maximum 9 drops a day) trifluridine application
Cidofovir (See OPHTHALMOLOGIC, CMV, below)	Same	See OPHTHALMOLOGIC, CMV, below	Cidofovir might be effective
Bacillary angiomatosis			
Erythromycin 500 mg po qid, clarithromycin 500–1000 mg po qd, or azithromycin 1 g po qd	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
OR			
Doxycycline 100 mg po bid	2 months		
OPHTHALMOLOGIC			
Cytomegalovirus (CMV)			
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, vomiting; confusion, dizziness, headache. Discontinue zidovudine during induction to minimize additive hematologic toxicity (neutropenia). To avoid hematologic toxicity, substitute didanosine, abacavir, 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 (absolute neutrophil count [ANC] < 500/μL) on two consecutive measurements. High risk of catheter-related sepsis
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, hypokalemia, hypophosphatemia, hypomagnesemia, 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 or 2000 mL oral fluids before each foscarnet administration can minimize nephrotoxicity. Creatinine clearance (CrCl) should be measured in cachectic patients and in patients with renal insufficiency to ensure proper use of administration nomogram. Give calcium carbonate 500 mg po tid and magnesium supplementation to prevent deficiencies. High risk of catheter-related sepsis
OR			

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
OPHTHALMOLOGIC (cont.)			
Cytomegalovirus (CMV) (cont.)			
Acute retinitis (cont.)			
Induction (cont.)			
Valganciclovir (Valcyte) 900 mg po bid with food. Dosage reduction in renal failure	21-day induction	Granulocytopenia, anemia, thrombocytopenia; diarrhea, nausea, vomiting, abdominal pain; fever; headache, insomnia, peripheral neuropathy, paresthesias; retinal detachment	Oral prodrug of ganciclovir. Comparable efficacy to intravenous ganciclovir in one study
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
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 $\geq$ 1.5/mg/dL, CrCl $\leq$ 55 mL/min, 2+ proteinuria)	14-day induction period	Life-threatening nephrotoxicity; fever; nausea, diarrhea; rash; uveitis, iritis, sight-threatening 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 ANC consistently $<$ 500/μL
OR			
Ganciclovir implant (Vitasert) q 6–9 months or intravitreal fomivirsen injection (Vitravene) on day 1, 15, and 30, then monthly thereafter	Indefinitely	Surgical complications, including retinal detachment, intravitreal hemorrhage, and endophthalmitis; cataracts. Ganciclovir implantation can cause temporary reduction in visual acuity after surgery	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. Intravitreal foscarnet can also be effective for resistant CMV
plus			
Ganciclovir (Cytovene) 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			Can discontinue secondary CMV prophylaxis in persons with adequate vision and non-sight-threatening lesion whose $CD4^+$ count increases to $>$ 100–150/μL for 3–6 months in response to antiretroviral therapy
Valganciclovir 900 mg po qd with food	Indefinitely	See above	
OR			

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
OPHTHALMOLOGIC (cont.)			
Cytomegalovirus (CMV) (cont.)			
Maintenance (secondary prophylaxis) (cont.)			
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; ocular hypotonia can lead to visual loss	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. Dissolve slowly in mouth	1–2 weeks or until resolved; maintenance (with lowest effective dosage) might be required for severe or frequent recurrences	Minimal toxicity. Unpleasant taste, nausea, vomiting; aminotransferase elevations	Troches have high sugar content and often require frequent administration. Suppositories can be more convenient
OR			
Nystatin (Mycostatin) 100,000 U/mL, swish and swallow 5 mL po q 6 h or one 500,000-U tablet dissolved slowly in mouth q 6 h	Same	Large oral doses can produce diarrhea, nausea, vomiting	Generally less effective than ketoconazole, fluconazole, and clotrimazole. Can be effective in fluconazole-resistant candidal infection
OR			

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
ORAL CAVITY (cont.)			
Candida Albicans (cont.)			
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 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
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			
Itraconazole (Sporanox) 200 mg po bid	Same as above	Nausea, vomiting; hypokalemia; hypertension; aminotransferase elevations; adrenal insufficiency; rhabdomyolysis. *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
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

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
ESOPHAGEAL (cont.)			
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			
Hepatitis C			
Interferon plus Ribavirin	Individualized	Acute flu-like syndrome 2–4 hours after treatment (fever, chills, headache, lethargy, arthralgias, myalgias); irritability, fatigue, depression, headache, anorexia, nausea, rash, alopecia; thrombocytopenia, leukopenia, hemolytic anemia, bacterial infections	Treatment with ribavirin plus interferon or pegylated interferon can improve hepatitis C. Treatment decisions need to be individualized because of substantial drug toxicities and the lack of predictable clinical benefit
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 mcg/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. Other 5-hydroxytryptamine (5HT) antagonists available
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 10 mg IM q 4–6 h. Dosage reduction in renal failure	As needed	Same as above	Increased risk of extrapyramidal reactions
Diarrhea			
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

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
GASTROINTESTINAL (cont.)			
Diarrhea (cont.)			
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 per 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 mcg q 1–2 wk until maximum of 500 mcg 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 or 1 g po bid	10–14 days or indefinitely	Nausea, vomiting, diarrhea; rare ototoxicity and nephrotoxicity (similar to other aminoglycosides[B]) only if absorbed through ulcerative bowel lesions	No evidence of efficacy. Addition of azithromycin 600 mg po qd might increase effectiveness
Isospora belli* and *Cyclospora cayetanensis			
Trimethoprim-sulfamethoxazole (TMP-SMX, Septra, Bactrim) 1 DS (double-strength) tablet po bid or qid if no response	7 days	See PULMONARY, PCP	Usually effective. For persons who respond to initial therapy continue TMP-SMX DS 1 tablet or ciprofloxacin 500 mg po 3 times weekly for 10 weeks. Ciprofloxacin 500 mg po bid for 7 days is an alternative
OR			
Ciprofloxacin (Cipro) 500 mg po bid			
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 $< 200/\mu L$) symptomatic HIV disease, or oral candidiasis			Can discontinue PCP primary prophylaxis in persons whose $CD4^+$ cell count increases to $>200/\mu L$ 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	See TMP-SMX below	TMP-SMX considered most effective for prophylaxis. TMP-SMX provides additional prophylaxis against toxoplasmosis and common bacterial infections

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
PULMONARY (cont.)			
***Pneumocystis carinii* pneumonia (PCP) (cont.)**			
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	Patients allergic to sulfa might tolerate dapsone; some cross-sensitivity. See dapsone, below	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) 1,500 mg po qd or 750 mg po bid, with or without pyrimethamine 25–75 mg po q wk	Indefinitely	Headaches; nausea, diarrhea, aminotransferase elevations; rash, drug fever; neutropenia, anemia; transient conjunctivitis; erythema multiforme. See atovaquone, below	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			
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 $> 150/\mu L$. 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	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	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 Note: Patients with substantial hypoxemia require concomitant corticosteroids (see below)	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; antihistamine might be helpful
		Hematologic: neutropenia, leukopenia, thrombocytopenia, anemia	If ANC $< 500/\mu L$ or if platelet count $< 30{,}000/\mu L$ 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 effects of TMP	TMP decreases creatinine tubular secretion and can elevate serum creatinine levels. Discontinue TMP-SMX if serum creatinine > 3.0 mg/dL

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
PULMONARY (cont.)			
***Pneumocystis carinii* pneumonia (PCP) (cont.)**			
Acute PCP (cont.)			
		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
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 or 450 mg po q 6 h	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

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
PULMONARY (cont.)			
Alternatives to TMP-SMX for acute PCP (cont.)			
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 *Drug interactions* Drug interactions with rifampin and rifabutin can render dapsone ineffective	Effective in mild-to-moderate PCP only. Check G6PD before starting dapsone. Check methemoglobin levels if symptomatic or discrepancy between oxygen saturation and simultaneous arterial PaO_2. Treat methemoglobinemia > 20% (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
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			
Atovaquone suspension (750 mg/5 mL) 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 $PaO_2 \geq 70$ mm Hg			
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 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 mm Hg. Begin corticosteroids concurrent with PCP treatment or if PaO_2 decreases to ≤ 70 mm Hg 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

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
CENTRAL NERVOUS SYSTEM			
Toxoplasma gondii			
Prophylaxis			
PCP prophylaxis regimens except aerosolized pentamidine provide protection against toxoplasmosis. Prophylaxis recommended for persons with immunoglobulin G (IgG) antibody to *Toxoplasma* and $CD4^+$ count $< 100/\mu L$	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. 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. Patients requiring concurrent treatment for acute PCP can receive pyrimethamine plus TMP/SMX instead of pyrimethamine plus sulfadiazine
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 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		

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
CENTRAL NERVOUS SYSTEM (cont.)			
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
Acute meningitis or acute disseminated cryptococcosis			
Amphotericin B 0.7–1.0 mg/kg/d IV with or without 5-flucytosine 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			
Fluconazole 400–800 mg po qd. Dosage reduction in renal failure. Higher dosages (eg, 800–1,200 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 (CNS) 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
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	

Continued

Table 1. Continued

System, Problem, and Drug Regimen	Duration	Adverse Effects/Drug Interactions	Comments
CENTRAL NERVOUS SYSTEM (cont.)			
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	Serologic and clinical follow-up required to assess adequacy of neurosyphilis 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 CNS 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			
Gabapentin (Neurontin) 300–400 mg po tid via dose escalation; dosage reduction in renal failure	Indefinitely	Thrombocytopenia; somnolence, dizziness, ataxia, nystagmus, fatigue, headache; nausea, vomiting, diarrhea	Can be helpful when other agents fail. Maximum dosage is 3,600 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
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

initiated when their $CD4^+$ cell count levels are greater than 350 /μL or when they have detectable viral loads at any level should be offered antiretroviral therapy if they understand the risks and benefits of therapy and are committed and able to adhere to the difficult medication regimens. The new guidelines are in agreement with those who favor the more conservative approach to antiretroviral therapy.[3,5,6] In addition, patients with the acute retroviral syndrome and possibly patients within 6 months of seroconversion should receive antiretroviral therapy whenever possible. The acute retroviral syndrome can include fever, myalgias, sore throat, headache, rash, oral or genital ulcers, and adenopathy.

Antiretroviral regimens can be difficult to follow even for the most well-intentioned and motivated patient. The primary care clinician and the patient must acknowledge these inherent difficulties and develop realistic expectations, as suboptimal antiretroviral therapy can lead to irreversible drug resistance. It might be better to withhold antiretroviral therapy for patients who cannot maintain adherence to treatment regimens, thus avoiding the risk of developing resistance.

Some reduction in viral load should be apparent within 4 to 6 weeks of initiating therapy. Ideally, the viral load will decrease to undetectable levels (less than 50 copies/mL) within 4 to 6 months. Effective therapy usually shows a viral

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

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, as well as 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.ucsf.edu/hivcntr
National HIV Telephone Consultation Service (Warmline) and National Clinicians' Post-Exposure Prophylaxis Hotline (PEPline) information. Based in the National HIV/AIDS Clinicians' Consultation Center at San Francisco General Hospital
Clinical trials
www.actis.org
Official AIDS Clinical Trials Information Service (ACTIS) Web site for information on clinical trials. Additional information available by calling ACTIS at 1-800-TRIALSA; or can be found on the National Institutes of Health Web site, www.niaid.nih.gov

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

load (HIV RNA) decrease of at least 1 log. A minimally significant viral load change is a 0.5-log (3-fold) increase or decrease. Patients who obtain substantial decreases in viral loads, but not to undetectable levels, can still obtain clinical benefit from antiretroviral therapy. A sustained rise in $CD4^+$ cell count of 100 /μL or more usually accompanies effective therapy. Divergent results in viral load and $CD4^+$ counts can also occur.

Recommended Antiretroviral Drug Combinations

Potent antiretroviral drug combinations, also termed highly active antiretroviral therapy (HAART), include two nucleoside reverse transcriptase inhibitors (NRTIs) with the addition of either one or two protease inhibitors (PIs) or the nonnucleoside reverse transcriptase inhibitor (nNRTI) efavirenz. The preferred NRTI combinations are zidovudine plus lamivudine, zidovudine plus didanosine, stavudine plus lamivudine, and stavudine plus didanosine. The recommended PIs are nelfinavir, indinavir, and ritonavir plus either indinavir, saquinavir, or lopinavir. Ritonavir is extremely effective in raising the blood levels of other PIs. Because of concerns about toxicities and the potential for developing resistance to the PI class of drugs, some experts prefer efavirenz (in combination with two NRTIs) to preserve the PI class of drugs for subsequent regimens. Alternative drug combinations are available but can lack the potency or have more toxicities than the preferred combinations listed above. If the NRTI drugs must be changed, alternative NRTIs are didanosine plus lamivudine and zidovudine plus zalcitabine. If the PI or efavirenz component of therapy needs to be changed, the most suitable alternative is probably to change to the other class (eg, change from PI to efavirenz or to dual PI, or change from efavirenz to PI therapy.

Another suitable alternative is to change to (two NRTIs plus) abacavir if the viral load is less than 100,000 copies/mL.[7] Other less suitable alternatives to the PIs-efavirenz options listed above include amprenavir; ritonavir, saquinavir, nevirapine; delavirdine; and nelfinavir plus saquinavir. Table 1 lists other alternative combinations.

Antiretroviral Therapy Failure and Resistance Testing

Antiretroviral therapy can fail because of poor adherence, acquired drug resistance, poor drug absorption, drug-drug interactions, or lack of drug potency. New opportunistic infections and other clinical illnesses, rising viral load (usually a 3-fold increase or more), or a falling $CD4^+$ cell count usually indicate failed therapy. Virologic failure as indicated by rising viral loads is not always accompanied by either decreasing $CD4^+$ counts or clinical progression. Many patients retain clinical benefit even after the reemergence of high viral load.[8]

Resistance testing can be helpful in making decisions when changing therapies. The test should be obtained while the patient is taking the failing regimen. Three kinds of resistance tests are available: genotypic, phenotypic, and virtual phenotypic, which compares the patient's genotypic results with phenotypic results from patients with similar genotypic patterns. Some words of caution are in order about all these tests: none is well standardized; laboratory variability is substantial; the results can be difficult to interpret, sometimes because of complexity and at other times because of oversimplification; only the predominant viral population (not minor strains) is tested; and the correlation between resistance testing results and clinical drug effectiveness has not been established. Resistance testing cannot establish which drugs will be effective, but it can help assess whether certain drugs or classes of drugs might be ineffective.

Multiple drug resistance is often discovered on resistance testing when regimens are failing. New regimen selection often requires combinations of agents from different antiretroviral classes and use of dual PI therapy. Consultation with an expert AIDS clinician is often required.

Complications of Antiretroviral Therapy

Table 1 lists the major complications of drugs used in HIV disease.[9,10] The NRTI drug class is associated with lipoatrophy, as well as with lactic acidosis, hepatomegaly, and steatosis. The lactic acidosis syndrome, which usually begins with lactic acidemia and nonspecific gastrointestinal symptoms, can progress to severe or fatal lactic acidosis. All NRTI drugs should be discontinued. Combinations of didanosine and stavudine appear to be more problematic; cautious rechallenge using other NRTIs has been successful.

Hyperglycemia and diabetes mellitus are strongly associated with PI use. The lipodystrophy syndrome, including central obesity, peripheral fat wasting, visceral and dorsocervical (buffalo hump) fat deposition, and sometimes lipid abnormalities, is associated with PI and NRTI use but can occur in the absence of antiretroviral therapy. The clinical importance of the various lipid abnormalities has not been fully assessed.

With improvement in the immune system, paradoxical responses can occur. These include flare-ups of latent opportunistic infections, such as cytomegalovirus (CMV) uveitis, or viral hepatitis (B or C), herpes zoster, fungal and mycobacterial diseases, and even Kaposi sarcoma and lymphomas.[11] These clinical flares should not prompt discontinuation of antiretroviral therapy.

Opportunistic Infections

Effective combination antiretroviral therapy has reduced opportunistic infections and malignancies markedly during the past few years.[12] Table 1 has been revised, omitting some opportunistic infections and malignancies, such as treatment of histoplasmosis, coccidioidomycosis, and eosinophilic folliculitis. Treatment recommendations for these conditions can be found in our previous review.[3] Primary prophylaxis against *Pneumocystis carinii* pneumonia (PCP) and *Mycobacterium avium* complex (MAC) disease can be discontinued if substantial immune reconstitution has occurred in response to antiretroviral therapy. Prophylaxis against PCP can be discontinued when $CD4^+$ cell counts have been 200/μL or higher for a period of 3 to 6 months. Similarly, MAC prophylaxis can be discontinued if the $CD4^+$ cell count has been 100/μL or higher for 3 to 6 months.[13,14] Discontinuing secondary PCP prophylaxis (ie, maintenance therapy after PCP has occurred) after 3 to 6 months of immune recovery of $CD4^+$ cell count to 200 /μL appears safe as well.[15,16] Discontinuing CMV maintenance therapy (secondary prophylaxis) appears safe in patients who have maintained $CD4^+$ counts greater than 100 to 150/μL for more than 3 to 6 months in response to antiretroviral therapy. Primary prophylaxis against toxoplasmosis is rarely necessary, as most PCP prophylaxis regimens, except aerosolized pentamidine, provide toxoplasmosis prophylaxis.

Tuberculosis coinfection with HIV presents special management concerns.[17,18] Therapy with

rifabutin, rather than rifampin, is required with coadministration of PIs and nNRTIs. Tuberculosis prophylaxis is essential for persons with a positive tuberculin skin test (>5 mm in HIV-infected persons), for persons with a previously positive tuberculin skin test without prior chemoprophylaxis, and for those who have had recent contact with active tuberculosis. Treatment of active tuberculosis in HIV-infected persons and prophylaxis against possible multidrug-resistant tuberculosis usually require consultation with tuberculosis experts.

Hepatitis C and HIV coinfection is common and problematic.[19] Progressive hepatitis C can add substantially to morbidity and mortality. Therapy with interferon and ribavirin can be effective in some patients, but it can also be associated with unfavorable side effects. Selecting which patients might benefit from combination interferon-ribavirin therapy should be individualized in concert with expert consultation.

Table 1 gives our recommendations for treating specific diseases and the major symptoms of HIV infection 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.[20–26] 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 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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