

Current Report — HIV Treatment Of AIDS And HIV-Related Conditions — 1994

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The Management of patients with human immunodeficiency virus (HIV) disease and the acquired immunodeficiency syndrome (AIDS) is an essential part of primary care. The current redirection of health care toward primary care emphasizes the importance family physicians will have in caring for this common disease. This *Current Report-HIV* updates our previous treatment recommendations,¹ which are based on the medical literature, as well as our clinical experience at San Francisco General Hospital.

Strategies of Care

The most important change in HIV therapeutics this year is the heightened awareness of the acceptability of different treatment approaches. This change is most obvious in the area of antiretroviral treatment, where the disappointing results of the Concorde zidovudine trial^{2,3} have not only resulted in a reevaluation of early antiretroviral intervention guidelines⁴ but have produced, as a side-effect, a reassessment by patients and providers of a wide range of clinical issues. The evidence upon which treatment decisions are made is now being weighed more carefully before treatment choices are exercised.

Discussions of therapeutic options among the patient, family, and provider now are recognized as paramount in clinical care, especially when studies do not provide compelling data about

optimal approaches or treatments. The absence of strong scientific data to direct clinical care produces dilemmas that can result in strong opinions. Both patients and providers can have a range of opinions about strategies of care.^{1,5} Some patients and their families might wish to use any possibly beneficial therapies and use them as early as possible. Others might chose to avoid drugs and other treatments unless they are clearly beneficial. The primary care physician needs to support these patient choices when clinically appropriate. When patients request direction for difficult choices, physicians must recognize that their recommendations are influenced not only by their understanding of the medical literature, the recommendations of experts, community standards, and, at times, the influence of pharmaceutical company representatives but also by their own personal attitudes about medical care. Some physicians encourage early and aggressive therapy, whereas others prefer to withhold treatments that do not yet have proven benefits. With this wide range of attitudes and strategies, excellent communication among patients, families, and providers is essential to arrive at an individualized treatment plan.

Recent Advances in Treatment

Table 1 lists the most common treatable problems in HIV therapeutics for adults. When multiple treatment options have comparable efficacy, regimens listed first are those that are supported by the most clinical experience, are least likely to result in drug toxicity, or are the most cost effective or easiest to administer. Most of the recent treatment changes reflect refinements in using well-established agents rather than the introduction of new drugs. Treatment with clarithromycin and ethambutol is now recommended for most cases of active *Mycobacterium avium* complex (MAC) disease.⁶⁻⁸ Clindamycin

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replaces sulfadiazine (which is not readily available) as an effective agent in combination with pyrimethamine in treating toxoplasmic encephalitis. Itraconazole has been found to be active against eosinophilic folliculitis, a problem that had been resistant to most therapies. Because of the emergence of multidrug-resistant tuberculosis, especially among HIV-coinfected persons, new recommendations now guide tuberculosis treatment.^{9,10} Trimetrexate is now available as one of the second-line agents in treating *Pneumocystis carinii* pneumonia (PCP). First-line treatment remains trimethoprim-sulfamethoxazole (TMP-SMX) therapy; adjuvant corticosteroid therapy is added to all anti-pneumocystis regimens when substantial hypoxemia ($\text{PaO}_2 \leq 70$ mmHg) is present.

The time to initiate antiretroviral therapy in asymptomatic patients is now clearly a matter of patient and provider choice.^{3-5,11} Antiretroviral therapy is recommended for all symptomatic persons and asymptomatic persons whose CD4+ lymphocyte counts have decreased to fewer than 200 cells/ μL . Some patients and providers will choose to initiate antiretroviral therapy when the CD4+ lymphocyte count decreases to fewer than 500 cells/ μL , or at some point between 500 and 200 cells/ μL . Although all these strategies are acceptable, providers and patients should know that many years can lapse between the arbitrary 500 cells/ μL CD4+ lymphocyte count threshold and the development of AIDS or other symptomatic disease. The benefits of antiretroviral therapy wane with time. Studies of multidrug antiretroviral therapy remain inconclusive, resulting in a wide range of opinions about whether monotherapy or multidrug therapy might be best. Monotherapy is generally recommended to avoid excessive toxicities.

The benefits of prophylaxis against PCP are now well established.¹² All persons with symptomatic HIV disease and those with asymptomatic infection with fewer than 200 CD4+ cells/ μL should receive PCP prophylaxis. Trimethoprim-sulfamethoxazole prophylaxis against PCP probably provides additional prophylaxis against central nervous system toxoplasmosis. Benefits of prophylaxis against other opportunistic infections, however, are not yet established. Data on rifabutin prophylaxis against MAC disease indicate a reduction in mycobacteremia but no survival benefits¹³ and do not provide con-

vincing evidence that prophylaxis benefits outweigh the risks of drug interactions and other toxicities in this late-stage AIDS complication. Many providers are not following recent national guidelines^{6,7} that recommend initiating rifabutin prophylaxis when the CD4+ lymphocyte count decreases to fewer than 100 cells/ μL . Instead, they are delaying prophylaxis until the CD4+ count is fewer than 50 cells/ μL , or they are observing patients closely and treating with standard therapy those patients who develop active MAC disease. Primary prophylaxis with fluconazole against cryptococcal disease and acyclovir prophylaxis against herpes infections have not been demonstrated to be necessary, so decisions about these therapies are more a matter of personal preference than of correct or incorrect care.

Drug Toxicity

Drug toxicity in HIV infected persons is common and can be severe.¹⁴⁻¹⁶ Drug-related rashes, neutropenia, anemia, thrombocytopenia, gastrointestinal side effects, and abnormalities of hepatic and renal function occur in most patients during the course of HIV disease. Because patients with advanced HIV disease tend to require multiple drugs, additive drug toxicities combined with serious underlying disease become particularly challenging. Unless the toxicities are serious, we attempt to continue necessary drugs while closely monitoring for toxicities. When serious or persistent toxicities occur, alternate approaches can usually be found. The presence of unexpected toxicity should remind the primary care provider to inquire about self-administration of nonapproved drugs, which might cause or contribute to toxicity.

Conclusions

Comprehensive care of persons with HIV disease involves antiretroviral treatment and PCP prophylaxis to delay or prevent disease, early identification and treatment of HIV-related opportunistic infections, careful attention to the psychosocial and family aspects of HIV disease, and a patient-physician-family partnership. The present lack of a cure for HIV disease should not deflect either the patient or the provider from the critically important task of managing these problems. The recommendations in Table 1 address pharmacotherapeutic

Table 1. Treatment Regimens for HIV Disease.

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
GENERAL				
Antiretroviral (Anti-HIV)	<i>Asymptomatic and symptomatic patients</i>			
	Zidovudine (AZT, Retrovir) 500–600 mg po daily (e.g., 200 mg tid, 100 mg 5 times daily); 300–400 mg daily in divided doses for patients unable to tolerate higher dosages and patients with end-stage renal disease	Indefinitely	Malaise, headache, seizures, nausea, insomnia, myalgias; anemia, granulocytopenia, thrombocytopenia. Lactic acidosis. Hepatomegaly with steatosis; aminotransferase elevations (alanine transaminase [ALT], aspartate transaminase [AST]). Toxic myopathy (with elevated creatine phosphokinase [CPK]) with long-term use. Blue to black discoloration of nails and skin in pigmented races. Drug interactions: prn acetaminophen (Tylenol) administration does not increase zidovudine toxicity	Ideal time to initiate antiretroviral treatment uncertain. Recommend treatment for all symptomatic patients and asymptomatic patients with repeated CD4+ lymphocyte counts < 200 cells/ μ L; can be offered to patients with CD4+ counts as high as 500 cells/ μ L. Zidovudine is the usual first-choice antiretroviral agent Transfusions or erythropoietin (if endogenous erythropoietin level < 500 IU/L) might be necessary for anemia. Discontinue drug if hemoglobin (Hgb) < 6.0 g/dL. Decrease dosage or interrupt for absolute neutrophil count (ANC) < 500 cells/ μ L; consider granulocyte colony-stimulating factor (G-CSF) (see OPHTHALMOLOGIC, CMV). Careful monitoring required when used with other myelosuppressive drugs (i.e., trimethoprim-sulfamethoxazole, ganciclovir). Change to alternate agent if unable to tolerate or marked progression of disease
OR				
	Didanosine (ddI, Videx) 200 mg po bid for patients > 60 kg; 125 mg po bid for < 60 kg	Indefinitely	Pancreatitis; painful peripheral neuropathy (dosage related, reversible); nausea, abdominal cramps, diarrhea related to antacid in formulation; rash; hyperglycemia; hyperuricemia; aminotransferase elevations; headache, insomnia, seizures; elevated triglyceride and amylase levels; thrombocytopenia; retinal atrophy. Concomitant administration of H ₂ antagonists, antacids, and omeprazole (Prilosec) can result in additional toxicity	Can be used in patients who fail or are intolerant to zidovudine. Avoid alcohol and other pancreatic toxins (e.g., systemic pentamidine). Available as 25-, 50-, 100-, and 150-mg chewable or crushable tablets. Two tablets must be given per dose to provide adequate buffer for absorption. Administer on empty stomach 2 hours apart from other drugs (e.g., ketoconazole, dapsone, tetracyclines, quinolone antibiotics) whose absorption is impaired by buffered products. Can be difficult to chew; tablets do not dissolve readily in water, can be crushed manually. Powdered formulation available from manufacturer by special order

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Table 1. *Continued.*

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
GENERAL Antiretroviral (Anti-HIV) (cont.)	OR			
	Zalcitabine (ddC, HIVID) 0.75 mg po tid; 0.375 mg po tid for patients < 30 kg	Indefinitely	Painful peripheral neuropathy (dosage related, reversible); rash; stomatitis, aphthous ulcers; pancreatitis; esophageal ulceration; seizures; aminotransferase elevations; cardiomyopathy	Can be used as monotherapy in patients who fail or are intolerant to zidovudine. Not as effective as zidovudine for monotherapy. Neurotoxicity can improve with zalcitabine "rest periods"
	OR			
	Stavudine (d4T)	Indefinitely	Painful peripheral neuropathy; aminotransferase elevations; anemia, macrocytosis	Investigational; available by compassionate use protocol for patients intolerant to zidovudine, didanosine, and zalcitabine
	OR			
	Combination therapy (zidovudine plus didanosine or zalcitabine)	Indefinitely	Additive toxicities can complicate management, especially for patients with late-stage disease and patients receiving multiple other medications	No clear evidence of added benefit from combination therapy or from sequential therapy (alternating regimens of zidovudine and didanosine or zalcitabine)
	<i>Postexposure prophylaxis</i>			
	Zidovudine 1200 mg po qd in divided doses for 3 days, followed by 1000 mg po qd in divided doses for 25 days	4 weeks	See above	Not known whether postexposure prophylaxis is effective. Failures have been reported. Administration within 1–2 hours of needlestick or other injury appears best (in animal models). Appears safe in pregnancy. One-month treatment with didanosine or zalcitabine alone or in combination with zidovudine recommended by some experts when index case is receiving zidovudine. Counseling required
Weight loss	Megestrol (Megace) 80 mg po tid. Higher dosages (800 mg po qd) might be necessary	Indefinitely	Nausea, vomiting; edema; depression. Progestin side effects	Megestrol can increase appetite and cause weight gain. Uncertain whether this weight gain improves health. Usually well tolerated. Available also as a suspension for patients requiring higher dosages
	Dronabinol (Tetrahydrocannabinol [THC], Marinol) 2.5 mg po bid 30 min–1 hr before meals	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. Not recommended for persons sensitive to marijuana effects

Continued

Table 1. *Continued.*

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
GENERAL (cont.)				
<i>Mycobacterium avium</i> complex (MAC)	<i>Acute:</i> Clarithromycin (Biaxin) 500 mg po bid. Higher dosages (maximum 1 g po bid) might be necessary	Indefinitely, if tolerated (minimum of 12 weeks)	Drug toxicity can be difficult to differentiate from MAC-induced multisystem disease. Rifampin, rifabutin, clofazimine, and ethambutol are best given at bedtime to minimize gastrointestinal side effects	Treatment indicated for patients with progressive signs, symptoms, and laboratory abnormalities consistent with MAC disease. Evaluate benefits and risks of multidrug regimen before treating asymptomatic disease (e.g., elevated alkaline phosphatase levels considered to be the result of MAC disease)
	plus		Clarithromycin side-effects include nausea, vomiting, hearing loss, aminotransferase elevations	At least two drugs (preferably clarithromycin and ethambutol) should be used. Azithromycin (Zithromax) 500 mg po qd also appears effective and can substitute for clarithromycin. A third or fourth drug can be added for serious illness
	Ethambutol (Myambutol) 15 mg/kg po qd (1 g po qd maximum); dosage modification in renal failure		Optic neuritis (if > 25 mg/kg/d); hyperuricemia	When both <i>Mycobacterium tuberculosis</i> and MAC infections are suspected, add isoniazid, rifampin, and pyrazinamide to ethambutol and clarithromycin. See <i>M. tuberculosis</i>
	plus one or two of the following for serious illness or failure to respond within 1 month			
	Clofazimine (Lamprene) 100 mg po qd		Nausea, vomiting. Reversible pink to brown-black discoloration of skin, eyes, body secretions. Retinal degeneration	
	Ciprofloxacin (Cipro) 500–750 mg po qd		Nausea, vomiting, abdominal pain. Anxiety, insomnia, euphoria; tremor; hallucinations; seizures	
	Rifampin (Rimactane, Rifadin) or rifabutin (Mycobutin) 450–600 mg po qd		Red-orange discoloration of body secretions and fluids. Elevated bilirubin and alkaline phosphatase levels, hepatitis; anorexia; flu-like syndrome; thrombocytopenia	Rifampin is a potent hepatic P-450 enzyme inducer; higher dosages of methadone, zidovudine, clarithromycin, and fluconazole might be required. See Rifabutin
<i>For severely ill patients add</i>				
	Amikacin 7.5–10 mg/kg IM/IV qd	2–8 weeks	Nephrotoxicity, ototoxicity	Monitor drug levels in patients with renal failure

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Table 1. *Continued.*

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
GENERAL				
<i>Mycobacterium avium</i> complex (MAC) (cont.)	<i>Prophylaxis:</i> Rifabutin 300 mg po qd or 150 mg po bid	Indefinitely	Nausea (can be reduced by administering 150 mg po bid). Rash. Rare neutropenia, thrombocytopenia, anemia; flu-like syndrome with fever, myalgias, headache; elevated bilirubin and alkaline phosphatase levels, hepatitis	Survival benefits not demonstrated. Rifabutin can be offered as primary prophylaxis for patients with advanced immunodeficiency (CD4+ < 50 or 100 cells/ μ L). Patients who are unable to tolerate or do not wish to receive MAC prophylaxis can be monitored for signs and symptoms of active disease. Clarithromycin 500 mg po qd-bid can substitute for rifabutin
			Rifabutin increases metabolism of methadone, zidovudine, and clarithromycin; higher dosage might be required	Exclude <i>M. tuberculosis</i> infection before initiating MAC prophylaxis
<i>Mycobacterium tuberculosis</i>	<i>Active tuberculosis</i>			
	Isoniazid (INH) 300 mg po qd	At least 9 months, and 6 months beyond culture conversion	Aminotransferase elevations and hepatitis; neuropathy; sedation and mental status changes	Begin with 4-drug therapy because of the possibility of multidrug resistant <i>M. tuberculosis</i> infection. After 2 months can continue INH and rifampin only, depending upon susceptibility testing results. Directly observed therapy (DOT) can permit more flexible (e.g., 3 times/week) treatment schedules. Consultation with tuberculosis experts and coordination with tuberculosis control agencies often required
	plus			
	Rifampin 600 mg po qd		See <i>M. avium</i> complex	
	plus			
	Pyrazinamide (PZA) 15–30 mg/kg po qd (2 g po qd maximum)		Aminotransferase elevations, abdominal pain; rash; arthralgia; hyperuricemia	
	plus			
	Ethambutol 15 mg/kg po qd (2.5 g po qd maximum)		See <i>M. avium</i> complex	
	or			
	Streptomycin 15 mg/kg IM qd (1 g IM qd maximum)		Hearing loss; nephrotoxicity; nystagmus, ataxia	
	<i>Prophylaxis</i>			
	Isoniazid 300 mg po qd	12 months	See above	INH prophylaxis for all HIV-infected persons with $\geq$ 5-mm intermediate strength tuberculin skin test induration and those with strong history of tuberculosis exposure, regardless of skin test reactivity

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Table 1. *Continued.*

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
GENERAL (cont.)				
Histoplasmosis	<i>Acute:</i> Amphotericin B (Fungizone) 0.7–1.0 mg/kg IV qd	Until 15 mg/kg total dosage has been administered	See CENTRAL NERVOUS SYSTEM, <i>Cryptococcus neoformans</i>	Amphotericin B recommended initially; oral therapy does not appear as effective. Itraconazole 200 mg po bid or fluconazole 400 mg po bid might be effective. Ketoconazole not indicated
	<i>Maintenance:</i> Itraconazole (Sporanox) 200 mg po qd OR Amphotericin B 50 mg IV q week, twice weekly, or every other week	Indefinitely	See SKIN/MUCOCUTANEOUS, eosinophilic folliculitis	Fluconazole 400 mg po qd might be effective Optimal frequency of administration not determined
SKIN/MUCOCUTANEOUS				
Kaposi sarcoma	Observation	Indefinitely		Treatment not required unless lesions are symptomatic or cosmetically bothersome
	OR			
	Local treatment (radiation therapy, cryotherapy, excision, or intralesional vinblastine)	Until lesions and symptoms are resolved or controlled	Mucositis in head and neck regions from radiation therapy	Treatment effective for cosmetic purposes, relief of symptoms, and to help reduce edema caused by lymphatic obstruction
	OR			
	Systemic chemotherapy with vinblastine and vincristine, vincristine alone, or combination of doxorubicin, bleomycin, and vincristine	Same	Usual chemotherapeutic agent side effects	Multidrug therapy can help control disease but does not alter prognosis. Consultation by oncologist or AIDS specialist usually required
	OR			
	Interferon-alpha 5 mU/d SQ, increase by 5 mU/d every 2 weeks as tolerated to a maximum of 35 mU/d	Indefinitely	Fatigue, myalgia, asthenia; neutropenia, thrombocytopenia; aminotransferase elevations	Hematologic toxicities increased in patients taking zidovudine. Dosages greater than 10 mU/d necessary for efficacy
Seborrheic dermatitis	<i>Acute:</i> Hydrocortisone (HC) cream 2.5% plus ketoconazole cream 2% bid; severe cases can require ketoconazole 200–400 mg po qd for 3–4 weeks	Until resolved	See ORAL CAVITY, <i>Candida albicans</i> , ketoconazole	Commonly involves face, eyebrows, retroauricular areas, nasolabial folds, and scalp. Addition of antifungal cream enhances therapeutic response and reduces the frequency of steroid application
	<i>Maintenance:</i> HC cream 1% and ketoconazole cream 2% bid	Indefinitely		

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Table 1. *Continued.*

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
SKIN/MUCOCUTANEOUS (cont.)				
Mucocutaneous herpes simplex	Acyclovir (Zovirax) <i>Acute:</i> 200–400 mg po 5 times/d	7–10 days	Oral: nausea, vomiting, diarrhea, dizziness	Topical acyclovir ineffective for most episodes
	<i>Maintenance:</i> 200–400 mg po 3–5 times/d	Indefinitely		Chronic maintenance therapy can be necessary for repeated episodes
Disseminated, extensive or persistent herpes simplex	Acyclovir <i>Acute:</i> 5 mg/kg/dose IV q 8 hr; dosage modification in renal failure	7–14 days or until lesions resolve	Intravenous: lethargy, tremors, confusion, hallucinations; phlebitis; increased serum creatinine, reversible crystalline nephropathy	Severe herpes infections (e.g., esophagitis, colitis, encephalitis) require intravenous acyclovir. Maintain good urine output and hydration to prevent acyclovir crystallization
	<i>Maintenance:</i> 200–400 mg po 3–5 times/d	Indefinitely		
Herpes zoster (shingles, disseminated, or persistent zoster)	Acyclovir 10 mg/kg/dose IV q 8 hr; or acyclovir 800 mg po 5 times/d; dosage modification in renal failure for intravenous acyclovir	7–10 days or until lesions resolve		Intravenous therapy preferred. Oral therapy not generally recommended because higher acyclovir levels are required for efficacy (oral bioavailability = 25%). Alternate drugs are foscarnet and vidarabine. Trifluridine (Viroptic) applied to skin covered with polymyxin B-bacitracin (Polysporin) ointment q 8 hr. Keratoconjunctivitis requires more frequent trifluridine application, as often as q 2 hr
Acyclovir-resistant herpes infections	Foscarnet 40 mg/kg/dose IV q 8 hr; dosage modification in renal failure	10–14 days or until lesions clear	See OPHTHALMOLOGIC, CMV	See OPHTHALMOLOGIC, CMV. Trifluridine might be effective. See SKIN/MUCOCUTANEOUS, herpes zoster
Bacillary angiomatosis	Erythromycin 500 mg po qid	2 months	Nausea, vomiting; aminotransferase elevations. Jarisch-Herxheimer reaction with systemic disease. Hearing loss	Skin lesions can resolve in 1–3 weeks, but 2 months' treatment needed. Systemic disease (i.e., hepatic, splenic, central nervous system, bone, or other organ involvement) or cutaneous recurrences require treatment for 4 months or indefinitely. Azithromycin 1 g po qd and possibly clarithromycin 500 mg–1 g po qd can be used as alternatives, but less information about efficacy is available
	OR Doxycycline (Minocycline) 100 mg po bid	2 months		

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Table 1. *Continued.*

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
SKIN/MUCO-CUTANEOUS (cont.)				
Eosinophilic folliculitis	Itraconazole 200 mg po once daily	2 weeks	Nausea, vomiting. Hypokalemia; hypertension; aminotransferase elevations; adrenal insufficiency; rhabdomyolysis. Teratogenic	Take with food. If no response in 2 weeks, increase dosage to 200 mg po bid for 2 additional weeks. Response rate 60%. If no response after 4 weeks, discontinue itraconazole and continue symptomatic treatment with topical corticosteroids and antihistamines
	plus High-potency fluorinated corticosteroid cream bid			
	plus Antihistamine (Diphenhydramine [Benadryl] 25–50 mg po qid, hydroxyzine [Atarax, Vistaril] 25–50 mg po qid, doxepin [Sinequan] 25–100 mg po qd)		Potent hepatic enzyme inducers such as isoniazid, rifampin, and phenytoin increase metabolism of itraconazole; higher itraconazole dosages can be required	Avoid terfenadine (Seldane), astemizole (Hismanal), or loratadine (Claritin) in combination with azole antibiotics because of increased risk of torsades de pointes and ventricular tachyarrhythmias
OPHTHALMOLOGIC				
Cytomegalovirus (CMV)	Ganciclovir (Cytovene) <i>Induction:</i> 5 mg/kg IV q 12 hr; dosage modification in renal failure	14 days for acute retinal infection; 14–21 days usually required for extraocular infection	Neutropenia, leukopenia, anemia, thrombocytopenia (avoid if platelet count < 30,000/ μ L); aminotransferase elevations; renal failure; phlebitis; rash; nausea. Discontinue zidovudine during induction to minimize additive hematologic toxicity (neutropenia). To avoid hematologic toxicity, substitute didanosine or zalcitabine for zidovudine, or change to foscarnet plus zidovudine	CMV retinitis can be arrested or improved with IV ganciclovir therapy. Oral ganciclovir might be effective; not available at this time. Intravitreal ganciclovir appears effective if IV causes unacceptable toxicity. Ganciclovir can also be effective in CMV esophagitis, colitis, and proctitis; not usually effective in CMV lung infection
	<i>Maintenance:</i> 5 mg/kg IV as 1-hr infusion 7 times/wk or 6 mg/kg IV 5 times/wk; dosage modification in renal failure	Indefinitely		Start G-CSF (filgrastim, Neupogen) 150–300 μ g SQ three times weekly for ganciclovir-induced neutropenia (ANC < 500 cells/ μ L) on two consecutive measurements Lifelong suppressive therapy required to prevent recurrence of retinitis. Daily administration is optimal. Administer G-CSF or change to foscarnet if ANC consistently < 500 cells/ μ L Combination therapy with ganciclovir plus foscarnet not routinely recommended. Can be used after resistance to both drugs demonstrated

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Table 1. *Continued.*

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
OPHTHALMO-LOGIC Cytomegalovirus (CMV) (cont.)	OR			
	Foscarnet (Foscavir) <i>Induction:</i> 60 mg/kg/dose IV q 8 hr or 90 mg/kg/dose IV q 12 hr as 2-hr infusion; discontinuation or dosage modification required in renal failure	14-day induction	Nephrotoxicity common; tremors, headaches, occasional seizures, muscle spasms; hypocalcemia, hypercalcemia, hypophosphatemia, hyperphosphatemia; anemia, granulocytopenia; aminotransferase elevations; phlebitis, penile ulcerations	Administered by infusion pump via central line. Infusion of 500 mL–1 L normal saline before each foscarnet administration can minimize nephrotoxicity. Avoid concurrent use of nephrotoxic agents when possible. Twenty-four-hour creatinine clearance should be measured in cachectic patients and in patients with renal insufficiency to ensure proper use of administration nomogram
	<i>Maintenance:</i> 90–120 mg/kg IV qd as 2-hr infusion; discontinuation or dosage modification required in renal failure	Indefinitely; infusions 7 times/wk		Maintenance with 120 mg/kg/d might be more effective but also more toxic
	OR			
	Foscarnet plus Ganciclovir	Indefinitely		Continue maintenance dosage of current drug (foscarnet or ganciclovir); provide standard induction with alternate drug, followed by maintenance with both drugs
ORAL CAVITY <i>Candida albicans</i>	Ketoconazole (Nizoral) <i>Acute:</i> 400 mg po qd	1–2 weeks or until resolved	Nausea, vomiting; aminotransferase elevations; anaphylaxis, urticaria. Higher dosages can suppress testosterone levels, gynecomastia; adrenal suppression	Improvement within 2–3 days
	<i>Maintenance:</i> 200 mg po qd-bid for 7 consecutive days per month or qd if necessary	Maintenance usually required with lowest effective dosage		Need gastric acidity to be effective; avoid antacids, H ₂ antagonists, and didanosine. Higher dosages might be necessary if taking rifampin
	OR			
	Fluconazole (Diflucan) <i>Acute:</i> 100–200 mg po qd; higher dosages might be necessary	Same	See CENTRAL NERVOUS SYSTEM, <i>Cryptococcus neoformans</i>	More expensive than other agents. Effective in oral candidiasis unresponsive to above oral agents. Fluconazole-resistant organisms reported
	<i>Maintenance:</i> 100–200 mg po once weekly or 50–100 mg po qd	Same		Increased frequency of administration (e.g., qd or 3 times weekly) or higher dosages (e.g., 200 mg po qd for 3 consecutive days once per month) can be required
	OR			
	Clotrimazole (Mycexel) troches 10 mg dissolved slowly in mouth 5 times/d	Same	Minimal toxicity. Unpleasant taste, nausea, vomiting; aminotransferase elevations	Improvement within 2–3 days

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Table 1. *Continued.*

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
ORAL CAVITY <i>Candida albicans</i> (cont.)	OR			
	Nystatin (Mycostatin) 100,000 U/mL, swish and swallow 5 mL po q 6 hr or one 500,000-unit tablet dissolved slowly in mouth q 6 hr	Same	Large oral doses can produce diarrhea, nausea, vomiting	Generally less effective than ketoconazole, fluconazole, and clotrimazole
	OR			
	Amphotericin B mouthwash 0.1 mg/mL, swish and swallow 5 mL qid	Same	Unpalatable; nausea, vomiting	Not absorbed. No systemic effects. Must be prepared from IV solution
	OR			
	Amphotericin B 0.3–0.4 mg/kg IV qd	10 days or until resolution	See CENTRAL NERVOUS SYSTEM, <i>Cryptococcus neoformans</i>	Candidal esophagitis unresponsive to oral agents requires low-dose IV amphotericin B
Periodontal disease	Hydrogen peroxide gargles for 30 sec bid	Indefinitely		Less expensive than chlorhexidine
	OR			
	Chlorhexidine gluconate (Peridex) oral rinse 15 mL swished in mouth for 30 sec bid	Indefinitely	Staining of teeth	
ESOPHAGEAL <i>Candida albicans</i>	Fluconazole 200–400 mg po qd; higher dosages might be required	14–21 days; maintenance with lowest effective dosage	See CENTRAL NERVOUS SYSTEM, <i>Cryptococcus neoformans</i>	Empiric treatment for patients with dysphagia or odynophagia who have oral thrush. Endoscopy with biopsy and cultures appropriate for patients who fail to respond within 1 week. Ketoconazole less expensive than fluconazole and effective in most patients. Fluconazole effective in more patients than ketoconazole; can be reserved for ketoconazole-resistant esophageal candidiasis
	OR			
	Ketoconazole 200 mg po bid; amphotericin; see ORAL CAVITY, <i>Candida albicans</i>			
Cytomegalovirus	Ganciclovir; foscarnet; see OPHTHALMOLOGIC, CMV	14–21 days	See OPHTHALMOLOGIC, CMV	Diagnose by endoscopic appearance plus biopsy showing CMV inclusion bodies and positive culture. Long-term suppressive therapy not routinely indicated. Consider only after multiple recurrences. Beware of drug resistance
Herpes simplex	IV acyclovir; see SKIN/MUCOCUTANEOUS, disseminated, extensive, or persistent herpes simplex	10–14 days; maintenance required	See SKIN/MUCOCUTANEOUS, herpes simplex	Diagnose by endoscopic appearance plus positive culture

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Table 1. *Continued.*

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
GASTRO-INTESTINAL				
Nausea and vomiting	Prochlorperazine (Compazine) 2.5–10 mg IV or 5–10 mg po or IM q 6 hr or 25 mg pr q 12 hr	As needed	Fatigue, drowsiness, dizziness, depression; extrapyramidal reactions; dystonic reactions; aminotransferase elevations; constipation	Nausea is most often caused by drugs; pretreatment or concurrent treatment can permit administration of necessary drugs. Central nervous system, biliary tract, pancreatic, or other gastrointestinal disease must be considered
	Metoclopramide (Reglan) 10 mg po qid or 1 mg/kg IV q 3 hr or 10 mg IM q 4–6 hr. Dosage adjustment in renal failure	As needed	Same as above	Same as above
	Lorazepam (Ativan) 0.5–2 mg po or SL tid-qid	As needed	Similar to benzodiazepines; antegrade amnesia	Effective for anticipatory nausea
	Ondansetron (Zofran) 0.15 mg/kg IV infusion over 15 min q 6 hr or 4–10 mg po q 6 hr	As needed	Constipation, diarrhea, abdominal pain; fever, chills; headache; sedation	Reserved for intractable nausea and vomiting unresponsive to other agents
	Dronabinol 2.5–10 mg po q 8–12 hr	As needed	See GENERAL, weight loss	Effective in drug-induced nausea
Diarrhea	<i>Symptomatic treatment</i>			
	Loperamide (Imodium) 4 mg po initially then 2 mg q 6 hr 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 mg po 3–6 times daily for 24–48 hr; then 2.5–5 mg tid and prn to control diarrhea (maximum 20 mg qd)	As needed	Ileus; nausea, vomiting, abdominal discomfort; anticholinergic side effects secondary to atropine	Same as above. 2.5 mg diphenoxylate-atropine is equivalent to 5 mL paregoric
	Paregoric 0.4 mg morphine/mL, 5–10 mL qd-qid	As needed	Ileus; altered mental status; adverse effects common to narcotic analgesics	Same as above
	Tincture of opium 10 mg morphine/mL, 0.3–1.0 mL po qid and prn (maximum 1 mL/dose or 6 mL/d)	As needed	Ileus; altered mental status, hallucinations. Adverse effects common to narcotic analgesics	Tincture of opium contains 25 times more morphine than paregoric
	Octreotide (Sandostatin) 100 µg SQ tid, increase by 100–200 µg q 1–2 weeks until maximum of 500 µg SQ tid or until 50% decrease of stool output	Indefinitely	Nausea, pain at injection site	Not approved by FDA. Short-term efficacy demonstrated. Long-term safety and efficacy unknown. Malabsorption not improved

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Table 1. *Continued.*

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
GASTRO-INTESTINAL (cont.)				
<i>Cryptosporidium</i>	See Diarrhea, <i>Symptomatic treatment</i>	Indefinitely	See Diarrhea	No drug effectively eradicates <i>Cryptosporidium</i>
	Paromomycin (Humatin) 750 mg po tid	10–14 days or indefinitely	Nausea, vomiting, diarrhea; rare ototoxicity and nephrotoxicity (similar to other aminoglycosides) only if absorbed through ulcerative bowel lesions	Nonabsorbable aminoglycoside. Effective in some patients
<i>Iso spor a belli</i>	Trimethoprim-sulfamethoxazole (TMP-SMX) 1 DS (double-strength) tablet po qid	21 days	See PULMONARY, <i>Pneumocystis carinii</i> pneumonia	Usually effective
Cytomegalovirus	Ganciclovir; foscarnet; see OPTHALMOLOGIC, CMV	14–21 days	See OPTHALMOLOGIC, CMV	Diagnose by endoscopic appearance plus biopsy showing CMV inclusion bodies and positive culture. Long-term suppressive therapy not routinely indicated. Consider only after multiple recurrences. Beware of drug resistance
PULMONARY				
<i>Pneumocystis carinii</i> pneumonia (PCP)	<i>Acute Pneumocystis carinii</i> pneumonia			
	Trimethoprim-sulfamethoxazole (TMP-SMX, Septra, Bactrim) 15 mg TMP per kg daily given in 3–4 divided doses po or over 1–2 hr IV infusion; lower dosages (12 mg TMP per kg daily) can be effective and less toxic	21 days	Adverse effects commonly appear between 7 and 14 days in more than 50% of patients	TMP-SMX is the drug of choice and should be used unless severe reactions (e.g., anaphylaxis, severe rashes, Stevens-Johnson syndrome) are of concern. Oral and intravenous routes equally effective, but IV recommended for first episode PCP because acute deterioration and drug toxicity can be unpredictable. Can provide prophylaxis against toxoplasmosis
			Rashes: maculopapular, exfoliative, Stevens-Johnson syndrome	Mild rash does not necessitate stopping or changing treatment: institute antihistamine or consider oral desensitization. Severe toxicity (i.e., Stevens-Johnson syndrome, anaphylaxis) requires drug discontinuation
			Hematological: neutropenia, leukopenia, thrombocytopenia, anemia	If ANC < 500 cells/ μ L or if platelet count < 30×10^9 /L and bleeding occurs, consider alternative treatment. Leucovorin calcium (folinic acid) 10–20 mg po qd might prevent hematologic toxicity

Continued

Table 1. *Continued.*

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
PULMONARY				
<i>Pneumocystis carinii</i> pneumonia (PCP) (cont.)			Gastrointestinal: nausea, vomiting, aminotransferase elevations	Pretreatment with lorazepam, prochlorperazine, metoclopramide, or dronabinol to reduce nausea. See GASTROINTESTINAL, Nausea and vomiting. Refractory nausea can respond to ondansetron. Nausea can be less with oral TMP-SMX. Aminotransferase elevations 4–5 times normal requires treatment change
			Renal: increased blood urea nitrogen (BUN) and creatinine; hyperkalemia secondary to hypoaldosterone effects of TMP	TMP decreases creatinine tubular secretion and can falsely elevate serum creatinine levels. Discontinue TMP-SMX if serum creatinine >3.0 mg/dL. Concomitant nephrotoxic agents and dehydration increase risk of nephrotoxicity
			Hyponatremia	Can be caused by large volume of 5% dextrose in water (D5W) needed for IV administration; can dilute each 80 mg TMP in 75 mL D5W or change to oral TMP-SMX. For severe hyponatremia ($\text{Na}^+ < 115 \text{ mEq/dL}$) TMP-SMX can be diluted in normal saline. However, the TMP-SMX-saline solution must be administered within 1 hour of preparation to avoid precipitation of the TMP-SMX
			Drug fever	Drug fever can herald onset of neutropenia, rash, hepatitis, and bone marrow toxicity
	<i>Alternatives to TMP-SMX for acute PCP</i>			
	Pentamidine isethionate (Pentam) 4 mg/kg/d as 1–2-hr IV infusion once daily; 3 mg/kg/d might also be effective	21 days		IM injections are not recommended (painful, sterile abscess; greater risk of hypotension); inhaled pentamidine not effective in acute PCP
			Orthostatic hypotension can be severe and occur with initial infusion	Slow IV infusion over 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. Avoid concomitant pancreatic toxins such as didanosine, zalcitabine, and alcohol
			Renal: increased BUN and creatinine; hyperkalemia	Discontinue pentamidine if creatinine > 3.0 mg/dL. Can resume administration if creatinine < 2 mg/dL. Concomitant nephrotoxic agents and dehydration increase risk of pentamidine nephrotoxicity

Continued

Table 1. Continued.

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
PULMONARY				
<i>Pneumocystis carinii</i> pneumonia (PCP) (cont.)			Other: neutropenia, thrombocytopenia; hypocalcemia, hypomagnesemia; aminotransferase elevations; cardiac arrhythmias (rare) with prolongation of QT interval and T-wave flattening	
	OR			
	Clindamycin (Cleocin) 600 mg IV or po tid–qid	21 days	Maculopapular rash (day 10–12), fever, diarrhea, nausea, vomiting, abdominal cramps, <i>Clostridium difficile</i> colitis, aminotransferase elevations	Consider in patients with mild-to-moderate PCP, intolerant of or unresponsive to TMP-SMX
	plus			
	Primaquine 30-mg base po qd		Methemoglobinemia from primaquine, hemolysis in glucose-6-phosphate dehydrogenase (G6PD)-deficient patients, leukopenia	Check G6PD before initiating primaquine therapy. Check methemoglobin levels when clinically indicated (see Dapsone). Lower dosage of primaquine (15 mg po qd) can be effective
	OR			
	Dapsone 100 mg po qd plus either TMP 15 mg/kg/d po in 3–4 divided doses or pyrimethamine 25–75 mg po qd	21 days	See toxicities for TMP-SMX. Methemoglobinemia, dose-related hemolysis, bone marrow suppression; rash; fever; nausea, abdominal pain; hyperkalemia; proteinuria, papillary necrosis. Drug interactions with didanosine, rifampin, and rifabutin can render dapsone ineffective	Proved effective in mild-to-moderate PCP only. Check G6PD before starting dapsone. Check methemoglobin levels if suggested by discrepancy between oxygen saturation and simultaneous arterial PaO ₂ . Pulse oximetry is inaccurate in presence of methemoglobinemia. Treat methemoglobinemia (> 20%) with methylene blue 2 mg/kg (1% solution) IV once. Data suggest dapsone-trimethoprim is less toxic than TMP-SMX and just as effective in mild-to-moderate illness. Patients allergic to TMP-SMX might tolerate dapsone-TMP without toxicity
	OR			
	Atovaquone (Mepron) 750 mg po tid with food	21 days	Rash, drug fever; headaches; nausea, diarrhea, aminotransferase elevations; neutropenia, anemia; transient conjunctivitis; erythema multiforme	Higher therapeutic failure rate than TMP-SMX. For patients who fail or are intolerant to TMP-SMX, pentamidine, dapsone-TMP, or clindamycin-primaquine. Take with high-fat diet to increase drug absorption. Patients with enteropathy might not absorb a sufficient amount of atovaquone to treat adequately
	plus			
	Pyrimethamine 25–75 mg po qd			

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Table 1. Continued.

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
PULMONARY <i>Pneumocystis carinii</i> pneumonia (PCP) (cont.)	OR			
	Trimetrexate (Neutrexin) 45 mg/m ² IV qd	21 days	Granulocytopenia; fever, rash; aminotransferase elevations	Can be effective in some patients intolerant to or refractory to TMP-SMX therapy. Additions of dapsone might be beneficial
	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
	<i>Adjunctive corticosteroid therapy for acute PCP with PaO₂ ≤ 70 mmHg</i>			
	Prednisone po or methylprednisolone (Solu-Medrol) IV: 40 mg bid for 5 days followed by 40 mg qd for 5 days, followed by 20 mg qd for 11 days (can be tapered to zero over last 11 days also)	21 days	Hyperglycemia, electrolyte imbalance. Exacerbation of thrush and herpes infections. Higher dosages can increase frequency of other opportunistic infections	Corticosteroids indicated in conjunction with antipneumocystis therapy in all patients with PaO ₂ ≤ 70 mmHg. Begin corticosteroids concurrent with PCP treatment or if PaO ₂ decreases to ≤ 70 mmHg within 72 hours of initiating PCP treatment
<i>Prophylaxis or suppression of PCP for patients with CD4+ < 200 cells/μL, prior episode of PCP, or constitutional symptoms of HIV disease</i>				
	TMP-SMX 1 DS tablet po qd or qod or 3 times/wk (e.g., M-W-F) or 1 tablet po bid	Indefinitely	See TMP-SMX	TMP-SMX considered most effective for prophylaxis or suppression. Once-daily administration is easiest to remember. Three-day-per-week regimen might be best tolerated. Multiple TMP-SMX regimens have been used and all appear effective. TMP-SMX provides additional prophylaxis against toxoplasmosis
<i>Alternatives to TMP-SMX for prophylaxis or suppression</i>				
	Dapsone 50–100 mg po daily or 200 mg po q week with or without TMP 15 mg/kg/d or pyrimethamine 75 mg po qd	Indefinitely	See dapsone plus TMP	Probably less effective than TMP-SMX; might be less toxic, but some cross-sensitivity with TMP-SMX likely

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Table 1. Continued.

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
PULMONARY				
<i>Pneumocystis carinii</i> pneumonia (PCP) (cont.)	OR			
	Inhaled pentamidine (Aeropent) 300 mg q 4 weeks or 150 mg q 2 weeks; requires specially designed nebulizer system, e.g., Respigard II	Indefinitely	Adverse systemic effects are minimal because of low pentamidine serum concentrations. Bronchospasm and coughing are common, especially in smokers. Pretreatment with inhaled bronchodilator (e.g., albuterol) can help. Rare pancreatitis, hypoglycemia; rare nephrotoxicity. Increased risk of spontaneous pneumothorax	Effective for prophylaxis against primary PCP. Does not prevent extrapulmonary disease. Efficacy for secondary prophylaxis inferior to TMP-SMX. Upper lobe recurrences probably due to poor drug distribution when inhaled in upright position. Monthly IM or IV injections of pentamidine 4 mg/kg can be considered if other options are not available. Inhaled pentamidine should not be used in patients with possible <i>M. tuberculosis</i> infection because of risk of <i>M. tuberculosis</i> spread by aerosolization
	OR			
	Clindamycin 450–600 mg po bid–tid	Indefinitely	See above	Efficacy and proper dosages for PCP prophylaxis unknown
	plus			
	Primaquine 15 mg po qd		See above	
	OR			
	Atovaquone 750 mg po qd–bid with or without pyrimethamine 25–75 mg po qd	Indefinitely	See above	Efficacy and proper dosages for PCP prophylaxis unknown
	OR			
	Pyrimethamine-sulfadoxine (Fansidar) 1 tablet po q 2 weeks	Indefinitely	Stevens-Johnson syndrome, toxic epidermal necrolysis; leukopenia, bone marrow suppression; GI, CNS toxicity	No studies clearly demonstrate efficacy
CENTRAL NERVOUS SYSTEM				
<i>Toxoplasma gondii</i>	Clindamycin 600–900 mg po or IV qid	6–8 weeks for acute therapy; lifetime suppression with highest tolerated dosage	Nausea, vomiting, diarrhea, abdominal cramps, pseudo-membranous colitis; blood dyscrasias	Clinical response or regression of lesions on imaging studies is seen for 2–3 weeks. Maintenance required indefinitely to prevent relapse. Every other day administration of pyrimethamine and leucovorin might delay onset of bone marrow toxicity
	plus			
	Pyrimethamine 25–75 mg po qd–qod			
	plus			
	Leucovorin calcium (folinic acid) 10–25 mg po qd			

Continued

Table 1. *Continued.*

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
CENTRAL NERVOUS SYSTEM Toxoplasma gondii (cont.)	<i>Intolerant to or failing to respond to above</i>			
	Pyrimethamine 25–75 mg po qd-qod plus leucovorin 10–25 mg po qd plus one of the following	Same	Same	Same
	Sulfadiazine 1 g po q 6 hr or	Same	Rash, drug fever; bone marrow suppression, leukopenia, thrombocytopenia	Available by IND through CDC. Sulfadiazine probably provides effective prophylaxis and suppression against PCP
	Clarithromycin 500 mg–1 g po bid or	Same	See GENERAL, <i>Mycobacterium avium</i> complex	
	Azithromycin (Zithromax) 500 mg–1 g po qd or	Same	Similar to clarithromycin	
	Atovaquone 750 mg po qid with meals OR	Same	See PULMONARY, <i>Pneumocystis carinii</i> pneumonia	Appears less effective than other agents
	Pyrimethamine alone 75–100 mg po qd OR	Same	See above	Not as effective as above regimens
	Doxycycline 100 mg po tid-qid	Same	Tetracycline side effects	Not proven effective

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Table 1. *Continued.*

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
CENTRAL NERVOUS SYSTEM (cont.)				
<i>Cryptococcus neoformans</i>	<i>Meningitis or disseminated cryptococcosis</i>			
	<i>Acute:</i> 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 or until clinically improved, followed by fluconazole 400 mg po qd or itraconazole 200 mg po bid	6–8 weeks; amphotericin total dosage not to exceed 2 g	Renal failure, hypokalemia, hypomagnesemia; fever, chills; anemia, thrombophlebitis Granulocytopenia; nausea, vomiting, diarrhea, aminotransferase elevations; rash from flucytosine	Pretreatment with diphenhydramine, acetaminophen, or IV meperidine can decrease amphotericin-induced fevers, chills, and rigors. Administer for 4–6 hr in D5W. Addition of heparin 500 U and hydrocortisone 50 mg to amphotericin IV solution can decrease phlebitis. Infusion of 500 mL–1L normal saline before administration of amphotericin B can minimize renal toxicity. 5-flucytosine not indicated if granulocytopenia or thrombocytopenia is present. Maintain 5-flucytosine levels between 50–100 µg/dL. Markedly increased intracranial pressure might require acetazolamine (Diamox) 250–500 mg po or IV qid or cerebrospinal fluid drainage or possibly corticosteroids
	OR			
	Fluconazole 400–800 mg po qd	8–12 weeks	Nausea, vomiting, diarrhea; dizziness; aminotransferase elevations; rare cutaneous reactions; increased phenytoin (Dilantin) and warfarin (Coumadin) levels	As effective as amphotericin B against mild or moderate disease; unknown whether equally effective against severe disease. Higher dosages might be necessary in moderate to severe disease or in patients taking rifampin. Fluconazole penetrates CNS and most body tissues, including prostate
	<i>Maintenance:</i> Fluconazole 200–400 mg po qd	Indefinitely	Same	Higher dosages might be necessary for recurrent disease
	OR			
	Amphotericin 0.5–0.8 mg/kg/d 3–5 times q wk	Indefinitely	Same	

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Table 1. *Continued.*

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
CENTRAL NERVOUS SYSTEM (cont.)				
Syphilis	Aqueous crystalline penicillin G 2–4 mU IV q 4 hr (total 12–24 mU/d)	10–14 days	Usual penicillin adverse effects; Jarisch-Herxheimer reaction; seizures from high-dose penicillin in renal failure	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. Persons reporting allergy to penicillin might require penicillin desensitization before treatment. Ceftriaxone 1 g IV qd for 2 weeks can be considered for penicillin-allergic patients, although efficacy not proved; consultation with an expert advised. Administer Benzathine penicillin G 2.4 mU IM once after completion of neurosyphilis treatment
	OR			
	Procaine penicillin G 2.4 mU IM qd plus Probenecid 500 mg po qid	10–14 days	Same. Probenecid rash	
Peripheral neuropathy	Amitriptyline (Elavil) or desipramine (Norpramin) 25–150 mg po hs	Indefinitely	Usual tricyclic side-effects; drowsiness; orthostatic hypotension; anticholinergic symptoms	Pain relief occurs sooner than antidepressant effects. Desipramine causes less sedation and fewer anticholinergic effects. Other tricyclic drugs might be equally effective
	Phenytoin (diphenylhydantoin, Dilantin) 100 mg po tid	Indefinitely	Usual side effects and drug-drug interactions	Generally ineffective
	Carbamazepine (Tegretol) 100–300 mg po bid	Indefinitely	Leukopenia, bone marrow suppression, rare agranulocytosis; rash; drowsiness, dizziness; aminotransferase elevations	Less desirable because of bone marrow effects. Need to monitor carbamazepine levels to avoid toxicity
	Mexiletine (Mexitil) 50–150 mg po bid–tid	Indefinitely	Nausea, vomiting, epigastric pain; dizziness, tremor; bradycardia; rare seizures, leukopenia, agranulocytosis	Less desirable because of side effects
	Capsaicin (Axsain, Zostrix-HP) 0.075% topical cream qid	Indefinitely	Minor burning sensation, skin irritation, erythema	Pain relief delayed 2–4 weeks. No systemic effects

problems common in HIV disease. A selected bibliography highlighting the most important management and therapeutic problems, such as antiretroviral therapy,^{2-5,11,17-28} dermatologic problems,^{15,16,29,30} infectious diseases (caused by *M. avium* complex,^{6-8,13,31,32} *M. tuberculosis*,^{9,10,33-38} fungi,^{39,44} cytomegalovirus,⁴⁵⁻⁴⁷ herpesvirus,⁴⁸ cryptosporidia,⁴⁹ *Pneumocystis carinii*,^{12,50-57} and other pulmonary pathogens,⁵⁸ *Cryptococcus neoformans*,⁵⁹⁻⁶¹ *Toxoplasma gondii*,⁶²⁻⁶⁵ and *Treponema pallidum*⁶⁶⁻⁷⁰), noninfectious problems,⁷¹⁻⁷⁴ health care maintenance,^{75,76} as well as general references,^{70,77-83} supplements the information in Table 1. Information about clinical trials is available through the Centers for Disease Control AIDS Clinical Trials Information Service (telephone 1-800-TRIALS-A) and from local and regional research units.

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References

1. Goldschmidt RH, Dong BJ. Treatment of AIDS and HIV-related conditions: 1993. J Am Board Fam Pract 1993; 6:297-315.
2. Aboulker J, Swart AM. Preliminary analysis of the Concorde trial. Concorde Coordinating Committee. Lancet 1993; 341:889-90 [letter].
3. Goldschmidt RH. The Concorde zidovudine trial and antiretroviral strategies for asymptomatic patients. J Am Board Fam Pract 1993; 6:604-6.
4. Sande MA, Carpenter CC, Cobbs CG, Holmes KK, Sanford JP. Antiretroviral therapy for adult HIV-infected patients. JAMA 1993; 270:2583-9.
5. Goldschmidt RH, Legg JJ, Brossier KA. Antiretroviral strategies. J Am Board Fam Pract 1993; 6:75-9.
6. Masur H. Recommendations on prophylaxis and therapy for disseminated *Mycobacterium avium* complex disease in patients infected with the human immunodeficiency virus. Public Health Service Task Force on Prophylaxis and Therapy for *Mycobacterium Avium* Complex. N Engl J Med 1993; 329:898-904.
7. Recommendations on prophylaxis and therapy for disseminated *Mycobacterium avium* complex for adults and adolescents infected with human immunodeficiency virus. U.S. Public Health Service Task Force on Prophylaxis and Therapy for *Mycobacterium Avium* Complex. MMWR 1993; 42(RR-9):14-20.
8. Goldschmidt RH, Dong BJ. Rifabutin prophylaxis against *Mycobacterium avium* complex disease. J Am Board Fam Pract 1994; 7:58-61.
9. Initial drug therapy for tuberculosis in the era of multidrug resistance: recommendations of the Advisory Council for the Elimination of Tuberculosis. MMWR 1993; 42 (RR-7):1-8.
10. Iseman MD. Treatment of multidrug-resistant tuberculosis. N Engl J Med 1993; 329:784-91.
11. Bartlett JG. Zidovudine now or later? N Engl J Med 1993; 329:351-2.
12. Hoover DR, Saah AJ, Bacellar H, Phair J, Detels R, Anderson R, et al. Clinical manifestations of AIDS in the era of pneumocystis prophylaxis. N Engl J Med 1993; 329:1922-6.
13. Nightingale SD, Cameron DW, Gordin FM, Sullam PM, Cohn DL, Chaisson RE, et al. Two controlled trials of rifabutin prophylaxis against *Mycobacterium avium* complex infection in AIDS. N Engl J Med 1993; 329:828-33.
14. Lee BL, Safrin S. Interactions and toxicities of drugs used in patients with AIDS. Clin Infect Dis 1992; 14:773-9.
15. Bayard PJ, Berger TG, Jacobson MA. Drug hypersensitivity reactions and human immunodeficiency virus disease. J Acquir Immune Defic Syndr 1992; 5:1237-57.
16. Coopman SA, Johnson RA, Platt R, Stern RS. Cutaneous disease and drug reactions in HIV infection. N Engl J Med 1993; 328:1670-4.
17. Volberding PA, Lagakos SW, Koch MA, Pettinelli C, Myers MW, Booth DK, et al. Zidovudine in asymptomatic human immunodeficiency virus infection: a controlled trial in persons with fewer than 500 CD4-positive cells per cubic millimeter. N Engl J Med 1990; 322:941-9.
18. Fischl MA, Parker CB, Pettinelli C, Wulfsohn M, Hirsch MS, Collier AC, et al. A randomized controlled trial of a reduced daily dose of zidovudine in patients with the acquired immunodeficiency syndrome. N Engl J Med 1990; 323:1009-14.
19. Fischl MA, Richman DD, Grieco MH, Gottlieb MS, Volberding PA, Laskin OL, et al. The efficacy of azidothymidine (AZT) in the treatment of patients with AIDS and AIDS-related complex. A double-blind, placebo-controlled trial. N Engl J Med 1987; 317:185-91.
20. Hamilton JD, Hartigan PM, Simberkoff MS, Day PL, Diamond GR, Dickinson GM, et al. A controlled trial of early versus late treatment with zidovudine in symptomatic human immunodeficiency virus infection. Results of the Veterans Affairs Cooperative Study. N Engl J Med 1992; 326: 437-43.
21. Graham NM, Zeger SL, Park LP, Phair JP, Detels R, Vermund SH, et al. Effect of zidovudine and *Pneumocystis carinii* pneumonia prophylaxis on progression of HIV-1 infection to AIDS. The Multicenter AIDS Cohort Study. Lancet 1991; 338: 265-9.

22. Graham NM, Zeger SL, Park LP, Vermund SH, Detels R, Rinaldo CR, et al. The effects of survival of early treatment of human immunodeficiency virus infection. *N Engl J Med* 1992; 326:1037-42.
23. Moore RD, Hidalgo J, Sugland BW, Chaisson RE. Zidovudine and the natural history of the acquired immunodeficiency syndrome. *N Engl J Med* 1991; 324:1412-6.
24. Lambert JS, Seidlin M, Reichman RC, Plank CS, Lavery M, Morse GD, et al. 2',3'-dideoxyinosine (ddI) in patients with the acquired immunodeficiency syndrome or AIDS-related complex. A phase I trial. *N Engl J Med* 1990; 322:1333-40.
25. Drusano GL, Yuen GJ, Lambert JS, Seidlin M, Dolin R, Valentine FT. Relationship between dideoxyinosine exposure, CD4 counts, and p24 antigen levels in human immunodeficiency virus infection. A phase I trial. *Ann Intern Med* 1992; 116:562-6.
26. Cooley TP, Kunches LM, Saunders CA, Ritter JK, Perkins CJ, McLaren C, et al. Once-daily administration of 2',3'-dideoxyinosine (ddI) in patients with the acquired immunodeficiency syndrome or AIDS-related complex. Results of a phase I trial. *N Engl J Med* 1990; 322:1340-5.
27. Kahn JO, Lagakos SW, Richman DD, Cross A, Pettinelli C, Liou SH, et al. A controlled trial comparing continued zidovudine with didanosine in human immunodeficiency virus infection. The NIAID AIDS Clinical Trials Group. *N Engl J Med* 1992; 327:581-7.
28. Meng TC, Fischl MA, Boock AM, Spector SA, Bennett D, Bassiakos Y, et al. Combination therapy with zidovudine and dideoxycytidine in patients with advanced human immunodeficiency virus infection. A phase I/II study. *Ann Intern Med* 1992; 116:13-20.
29. Koehler JE, Tapper JW. Bacillary angiomatosis and bacillary peliosis in patients infected with human immunodeficiency virus. *Clin Infect Dis* 1993; 17:612-24.
30. Berger TG, Obuch ML, Goldschmidt RH. Dermatologic manifestations of HIV infection. *Am Fam Physician* 1990; 41:1729-42.
31. Horsburgh CR Jr. *Mycobacterium avium* complex infection in the acquired immunodeficiency syndrome. *N Engl J Med* 1991; 324:1332-8.
32. Horsburgh CR Jr, Havlik JA, Ellis DA, Kennedy E, Fann SA, Dubois RE, et al. Survival of patients with acquired immune deficiency syndrome and disseminated *Mycobacterium avium* complex infection with and without antimycobacterial chemotherapy. *Am Rev Respir Dis* 1991; 144:557-9.
33. Small PM, Schechter GF, Goodman PC, Sande MA, Chaisson RE, Hopewell PC. Treatment of tuberculosis in patients with advanced human immunodeficiency virus infection. *N Engl J Med* 1991; 324:289-94.
34. Barnes PF, Bloch AB, Davidson PT, Snider DE Jr. Tuberculosis in patients with human immunodeficiency virus infection. *N Engl J Med* 1991; 324:1644-50.
35. Centers for Disease Control. Tuberculosis and human immunodeficiency virus infection: recommendations of the Advisory Committee for the Elimination of Tuberculosis (ACET). *MMWR* 1989; 38:236-8, 243-50.
36. Centers for Disease Control. The use of preventive therapy for tuberculosis infection in the United States. Recommendations of the Advisory Committee for Elimination of Tuberculosis. *MMWR* 1990; 39(RR-8):9-12.
37. Centers for Disease Control. Prevention and control of tuberculosis in U.S. communities with at-risk minority populations. Recommendations of the Advisory Council for the Elimination of Tuberculosis. *MMWR* 1992; 41(RR-5):1-11.
38. Centers for Disease Control. Prevention and control of tuberculosis among homeless persons. Recommendations of the Advisory Council for the Elimination of Tuberculosis. *MMWR* 1992; 41(RR-5):13-23.
39. Antifungal chemotherapy in patients with acquired immunodeficiency syndrome. British Society for Antimicrobial Chemotherapy Working Party. *Lancet* 1992; 340:648-51.
40. Diamond RD. The growing problem of mycoses in patients infected with the human immunodeficiency virus. *Rev Infect Dis* 1991; 13:480-6.
41. Wheat LJ, Connolly-Stringfield PA, Baker RL, Curfman MF, Eads ME, Israel KS, et al. Disseminated histoplasmosis in the acquired immune deficiency syndrome: clinical findings, diagnosis and treatment, and review of the literature. *Medicine* 1990; 69:361-74.
42. Sarosi GA, Johnson PC. Disseminated histoplasmosis in patients infected with human immunodeficiency virus. *Clin Infect Dis* 1992; 14(Suppl 1): S60-7.
43. Wheat J, Hafner R, Wulfsohn M, Spencer P, Squires K, Powderly W, et al. Prevention of relapse of histoplasmosis with itraconazole in patients with the acquired immunodeficiency syndrome. The National Institute of Allergy and Infectious Diseases Clinical Trials and Mycoses Study Group Collaborators. *Ann Intern Med* 1993; 118:610-6.
44. Sharkey-Mathis PK, Velez J, Fetchick R, Graybill JR. Histoplasmosis in the acquired immunodeficiency syndrome (AIDS): treatment with itraconazole and fluconazole. *J Acquir Immune Defic Syndr* 1993; 6:809-19.
45. Drew WL. Cytomegalovirus infection in patients with AIDS. *Clin Infect Dis* 1992; 14:608-15.
46. Mortality in patients with the acquired immunodeficiency syndrome treated with either foscarnet or ganciclovir for cytomegalovirus retinitis. Studies of Ocular Complications of AIDS Research Group, in collaboration with the AIDS Clinical Trials Group. *N Engl J Med* 1992; 326:213-20.
47. Dieterich DT, Poles MA, Lew EA, Mendez PE, Murphy R, Addessi A, et al. Concurrent use of ganciclovir and foscarnet to treat cytomegalovirus

- infection in AIDS patients. *J Infect Dis* 1993; 167: 1184-8.
48. Safrin S, Crumpacker C, Chatis P, Davis R, Hafner R, Rush J, et al. A controlled trial comparing foscarnet with vidarabine for acyclovir-resistant mucocutaneous herpes simplex in the acquired immunodeficiency syndrome. The AIDS Clinical Trials Group. *N Engl J Med* 1991; 325:551-5.
49. Fichtenbaum CJ, Ritchie DJ, Powderly WG. Use of paromomycin for treatment of cryptosporidiosis in patients with AIDS. *Clin Infect Dis* 1993; 16: 298-300.
50. Masur H. Prevention and treatment of pneumocystis pneumonia. *N Engl J Med* 1992; 327:1853-60.
51. Consensus statement on the use of corticosteroids as adjunctive therapy for *Pneumocystis carinii* pneumonia in the acquired immunodeficiency syndrome. The National Institutes of Health University of California Expert Panel for Corticosteroids as Adjunctive Therapy for *Pneumocystis carinii* Pneumonia. *N Engl J Med* 1990; 323:1500-4.
52. Hardy WD, Feinberg J, Finkelstein DM, Power ME, He W, Kaczka C, et al. A controlled trial of trimethoprim-sulfamethoxazole or aerosolized pentamidine for secondary prophylaxis of *Pneumocystis carinii* pneumonia in patients with the acquired immunodeficiency syndrome: AIDS Clinical Trials Group Protocol 021. *N Engl J Med* 1992; 327: 1842-8.
53. Schneider MM, Hoepelman AI, Schattenkerk JK, Nielsen TL, van der Graff Y, Frissen JP, et al. A controlled trial of aerosolized pentamidine or trimethoprim-sulfamethoxazole as primary prophylaxis against *Pneumocystis carinii* pneumonia in patients with human immunodeficiency virus infection. *N Engl J Med* 1992; 327:1836-41.
54. Girard PM, Landman R, Gaudebout C, Olivares R, Saimot AG, Jelazko P. Dapsone-pyrimethamine compared with aerosolized pentamidine as primary prophylaxis against *Pneumocystis carinii* pneumonia and toxoplasmosis in HIV infection. The PRIO Study Group. *N Engl J Med* 1993; 328:1514-20.
55. Falloon J, Kovacs J, Hughes W, O'Neill D, Polis M, Davey RT Jr, et al. A preliminary evaluation of 566C80 for the treatment of *Pneumocystis carinii* pneumonia in patients with the acquired immunodeficiency syndrome. *N Engl J Med* 1991; 325:1534-8.
56. Allegra CJ, Chabner BA, Tuazon CU, Ogata-Arakaki D, Baird B, Drake JC, et al. Trimetrexate for the treatment of *Pneumocystis carinii* pneumonia in patients with the acquired immunodeficiency syndrome. *N Engl J Med* 1987;317:978-85.
57. White MW, Haddad ZH, Brunner E, Sainz C. Desensitization to trimethoprim sulfamethoxazole in patients with acquired immune deficiency syndrome and *Pneumocystis carinii* pneumonia. *Ann Allergy* 1989; 62:177-9.
58. Murray JF, Mills J. Pulmonary infectious complications of human immunodeficiency virus infection. *Am Rev Respir Dis* 1990; 141:1356-72, 1582-98.
59. Powderly WG. Cryptococcal meningitis and AIDS. *Clin Infect Dis* 1993; 17:837-42.
60. Saag MS, Powderly WG, Cloud GA, Robinson P, Grieco MH, Sharkey PK, et al. Comparison of amphotericin B with fluconazole in the treatment of acute AIDS-associated cryptococcal meningitis. *N Engl J Med* 1992; 326:83-9.
61. Powderly WG, Saag MS, Cloud GA, Robinson P, Meyer RD, Jacobson JM, et al. A controlled trial of fluconazole or amphotericin B to prevent relapse of cryptococcal meningitis in patients with the acquired immunodeficiency syndrome. *N Engl J Med* 1992; 326:793-8.
62. Luft BJ, Remington JS. Toxoplasmic encephalitis in AIDS. *Clin Infect Dis* 1992; 15:211-22.
63. Dannemann B, McCutchan JA, Israelski D, Antoniskis D, Leport C, Luft B, et al. Treatment of toxoplasmic encephalitis in patients with AIDS. A randomized trial comparing pyrimethamine plus clindamycin to pyrimethamine plus sulfadiazine. *Ann Intern Med* 1992; 116:33-43.
64. Luft BJ, Hafner R, Korzun AH, Leport C, Antoniskis D, Bosler EM, et al. Toxoplasmic encephalitis in patients with the acquired immunodeficiency syndrome. Members of the ACTG 077p/ANRS 009 Study Team. *N Engl J Med* 1993; 329:995-1000.
65. Porter SB, Sande MA. Toxoplasmosis of the central nervous system in the acquired immunodeficiency syndrome. *N Engl J Med* 1992; 327:1643-8.
66. Lukehart SA, Hook EW 3d, Baker-Zander SA, Collier AC, Critchlow CW, Handsfield HH. Invasion of the central nervous system by *Treponema pallidum*: implications for diagnosis and treatment. *Ann Intern Med* 1988; 109:855-62.
67. Hook EW 3d, Marra CM. Acquired syphilis in adults. *N Engl J Med* 1992; 326:1060-9.
68. Goldschmidt RH. Diagnosis and treatment of syphilis in HIV-infected patients. *J Am Board Fam Pract* 1989; 2:154-5.
69. Centers for Disease Control. Recommendations for diagnosing and treating syphilis in HIV-infected patients. *MMWR* 1988; 37:600-2, 607-8. Reprinted in: *JAMA* 1988; 260:2488-9.
70. Centers for Disease Control and Prevention. 1993 Sexually transmitted diseases treatment guidelines. *MMWR* 1993; 42(RR-14):1-102.
71. Lieschke GJ, Burgess AW. Granulocyte colony-stimulating factor and granulocyte-macrophage colony-stimulating factor. *N Engl J Med* 1992; 327:28-35, 99-106.
72. Cello JP, Grendell JH, Basuk P, Simon D, Weiss L, Wittner M, et al. Effect of octreotide on refractory AIDS-associated diarrhea: a prospective, multicenter clinical trial. *Ann Intern Med* 1991; 115:705-10.
73. Cello, JP. Acquired immunodeficiency syndrome cholangiopathy: spectrum of disease. *Am J Med* 1989; 86:539-46.
74. Grunfeld C, Feingold KR. Metabolic disturbances and wasting in the acquired immunodeficiency syndrome. *N Engl J Med* 1992; 327:329-37.

75. Jewett JF, Hecht FM. Preventive health care for adults with HIV infection. *JAMA* 1993; 269:1144-53.
76. Goldschmidt RH. Laboratory testing for the presence of HIV infection and the progression of HIV disease. *J Am Board Fam Pract* 1990; 3: 60-2.
77. Sande MA, Volberding PA, editors. *The medical management of AIDS*. Philadelphia: W.B. Saunders, 1992.
78. Goldschmidt RH, Legg JJ. Counseling patients about HIV test results. *J Am Board Fam Pract* 1991; 4:361-3.
79. Goldschmidt RH. Accidental exposure to infection by health care workers. *J Am Board Fam Pract* 1990; 3:129-130.
80. Centers for Disease Control. 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. *MMWR* 1992; 41(RR-17): 1-19.
81. Goldschmidt RH. The new AIDS surveillance case definition. *J Am Board Fam Pract* 1993; 6:189-90.
82. El-Sadr W, Oleske JM, Agins BD, Bauman KA, Brosgart CL, Brown GM, et al. Evaluation and management of early HIV infection. Clinical practice guideline No. 7. Rockville, MD: Agency for Health Care Policy and Research, Public Health Service, US Department of Health and Human Services, January 1994. AHCPR publication no. 94-0572.
83. American Medical Association. HIV early intervention: physician guidelines. 2nd ed. Chicago: American Medical Association, 1994.