

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 anti-retroviral treatment, where the disappointing results of the Concorde zidovudine trial^{2,3} have not only resulted in a reevaluation of early anti-retroviral 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/μL; can be offered to patients with CD4+ counts as high as 500 cells/μL. 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/μL; 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 |

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Table 1. Continued.

| System & Problem | Drug Regimen | Duration | Common Adverse Effects | Comments |
|--|---|--|--|--|
| GENERAL (cont.) | | | | |
| Mycobacterium avium 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 plus Rifampin 600 mg po qd plus Pyrazinamide (PZA) 15–30 mg/kg po qd (2 g po qd maximum) plus Ethambutol 15 mg/kg po qd (2.5 g po qd maximum) or Streptomycin 15 mg/kg IM qd (1 g IM qd maximum) | At least 9 months, and 6 months beyond culture conversion | Aminotransferase elevations and hepatitis; neuropathy; sedation and mental status changes See <i>M. avium</i> complex Aminotransferase elevations, abdominal pain; rash; arthralgia; hyperuricemia See <i>M. avium</i> complex | 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 |
| | <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 |

Continued

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; anemia, granulocytopenia; aminotransferase elevations; phlebitis, penile ulcerations | Administered by infusion pump via central line. Infusion of 500 mL–1L 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 | | | | |
| Candida albicans | 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 |

Continued

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 |

Continued

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 |

Continued

Table 1. *Continued.*

| System & Problem | Drug Regimen | Duration | Common Adverse Effects | Comments |
|---|--|----------------------------|--|---|
| GASTRO-INTESTINAL (cont.) | | | | |
| Cryptosporidium | 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 |
| Isospora belli | 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 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 |
| PULMONARY | | | | |
| Pneumocystis carinii pneumonia (PCP) | <i>Acute Pneumocystis carinii pneumonia</i> | | | |
| | 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 Rashes: maculopapular, exfoliative, Stevens-Johnson syndrome Hematological: neutropenia, leukopenia, thrombocytopenia, anemia | 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 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 If ANC < 500 cells/ μ L or if platelet count < $30 \times 10^9/L$ 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 ($\text{Na}^+ < 115$ 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 | | | | |

Continued

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 plus Leucovorin calcium (folinic acid) 20 mg/m ² IV or po q 6 h | 21 days 24 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 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 | |

Continued

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., Respirgard 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 plus Primaquine 15 mg po qd | Indefinitely | See above See above | Efficacy and proper dosages for PCP prophylaxis unknown |
| | 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 plus Pyrimethamine 25–75 mg po qd–qod plus Leucovorin calcium (folinic acid) 10–25 mg po qd | 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 |

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 |

Continued

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 | 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 acetazolamide (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 | | |

Continued

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 (Mexitol) 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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