Current Report—HIV

Treatment Of AIDS And HIV-Related Conditions — 1993

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Important changes have occurred in the treatment of human immunodeficiency virus (HIV) disease, including the acquired immunodeficiency syndrome (AIDS). This "Current Report — HIV" updates our previous treatment recommendations[1] and acts as a guide for the primary care of HIV disease. These recommendations are based on the medical literature and our clinical experience at San Francisco General Hospital. Most treatment options are listed in order of our preference as well as clinical efficacy (Table 1). When multiple treatment options have comparable efficacy, those regimens listed first are least likely to result in drug toxicity, are easiest to administer, are most cost effective, or are supported by the most clinical experience.

Strategies of Care

The need to make critical decisions about such issues as choice of antiretroviral therapy, frequency of hematologic monitoring, benefits of prophylactic therapies, use of invasive diagnostic testing, and approach to terminal care occurs regularly. When studies do not provide compelling results about the best clinical approach, strong opinions prevail. Because there is a wide range of acceptable strategies, decisions about the above issues should reflect an approach with which the patient, family, and physician are most comfortable.

Submitted 5 March 1993.

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Supported in part by the Western AIDS Education and Training Center, Grant No. 1-D35 PE 00108-01, with the Bureau of Health Professions, Health Resources and Services Administration, Department of Health and Human Services.

Factors influencing strategies of care have been discussed previously in this series.[2] Some patients and their families request the most aggressive approaches possible, including any (noninvasive or invasive) testing and treatment options that offer a possibility of benefit. They can select treatments that include the early use of multiple medications, including combination antiretroviral drugs, antifungal and antimycobacterial prophylaxes, and unapproved medications available through nontraditional channels. Other patients consider such medications as being potentially harmful or know of patients who have done poorly while receiving these therapies. They may wish to delay or avoid additional testing or medications if possible. Most patients, however, follow their primary care provider's advice and receive standard evaluation and treatment. For patients whose most important concerns include food, shelter, substance use, and family and social problems, decision making about complicated medication regimens may not be appropriate until these more pressing and immediate life issues improve.

Physicians also must balance other important variables in guiding their patients. Because information on HIV disease changes rapidly, physicians are constantly reassessing the medical literature and the advice of local, regional, and national experts in the field. This information is incorporated into each physician's personal feeling and approach. Some physicians believe that it is wrong to withhold any potentially helpful therapies and feel obligated to intervene at the earliest point possible. An aggressive approach to treatment can seem most important. Other physicians prefer to withhold potentially toxic drugs whose efficacy diminishes over time until treatment is absolutely necessary. Because of the diversity of patient-generated and provider-generated variables, developing a strategy for care

becomes a matter of negotiation and renegotiation between the provider and patient.

It is understandable that most patients and many of their providers find the use of unproven drugs appealing. The physician should create a climate in which the patient can share the information that he or she is taking an unapproved drug without fear of disapproval. This information is key to understanding the development of unexpected drug toxicity or interactions. Unless clear toxicities occur, it is probably not the role of the primary care provider to proscribe their use altogether. However, the primary care provider should remind the patient and family that unproven treatments might be harmful as well as potentially helpful and might complicate the use of effective therapies. Treatment with experimental drugs is best reserved for formal clinical trials in conjunction with comprehensive primary care.

Antiretroviral Therapy

The optimal time to initiate antiretroviral therapy is uncertain. Most providers begin antiretroviral therapy after the CD4+ lymphocyte count decreases to fewer than 500 cells/μL on two separate occasions. We recommend a relatively conservative approach: antiretroviral therapy is *offered* when the CD4+ cell count falls to fewer than 500 cells/μL, antiretroviral therapy is *encouraged* when CD4+ cell counts are fewer than 400 cells/μL, and every attempt is made to try to ensure that all patients receive antiretroviral therapy well before the CD4+ cell count falls to fewer than 200 cells/μL. Because of concern about drug toxicities, we generally recommend initiating monotherapy with zidovudine at the standard 500 to 600 mg/d dosage. Patients unable to tolerate zidovudine therapy should be offered didanosine or, possibly, zalcitabine monotherapy. Many providers prescribe combination therapy (zidovudine plus didanosine or zidovudine plus zalcitabine) or alternate drugs (e.g., alternate month administration of zidovudine with didanosine). Available data neither support nor discourage these approaches. Further long-term studies are needed to compare regimens. Because didanosine and zalcitabine have similar toxicity profiles they should not be given together.

Deciding when antiretroviral treatment has failed is difficult. We recommend considering changing or combining drug therapy when new or recurrent opportunistic infections or malignancies occur; when disabling clinical symptoms, such as weight loss, diarrhea, or unexplained fevers, continue; or when the CD4+ lymphocyte count decreases by 50 percent or more within a 1- or 2-year period or to fewer than 50 CD4+ cells/μL. In deciding whether to change or add drugs, the patient's overall clinical course, ability to tolerate individual drug toxicities, and personal choices are more important than these arbitrary laboratory markers of disease progression.

Prophylaxis against Opportunistic Infections

All patients with CD4+ lymphocyte counts fewer than 200 cells/μL, patients with previous *Pneumocystis carinii* pneumonia (PCP), and patients with severe constitutional symptoms should receive prophylaxis against PCP. The drug of choice is trimethoprim-sulfamethoxazole. Second-line therapy is dapsone. For patients unable to tolerate these drugs, inhaled pentamidine, clindamycin plus primaquine, and atovaquone can be considered.

Many providers begin primary prophylaxis against potential opportunistic infections when immunodeficiency becomes severe (e.g., CD4+ cell count fewer than 100 cells/μL). Fluconazole prophylaxis against candidal esophagitis and cryptococcal meningitis is used by many, although neither the proper time to initiate prophylaxis nor the relative risks and benefits are clear. We do not recommend routine fluconazole prophylaxis. Prophylaxis against toxoplasmic encephalitis is probably inappropriate because this condition occurs in a small percentage of patients. Trimethoprim-sulfamethoxazole prophylaxis (against PCP) appears to provide some prophylactic benefit against toxoplasmic encephalitis. Prophylaxis against herpes simplex infections is not routinely warranted unless frequent recurrences occur. Rifabutin has been approved for prophylaxis against *Mycobacterium avium-intracellulare* complex (MAC) disease, but no survival benefits have been demonstrated in patients receiving rifabutin prophylaxis. In addition, there is concern about drug interactions and hepatotoxicity with rifabutin. Clarithromycin has also received attention as prophylaxis against MAC. Until the risks and benefits of prophylaxis against MAC have been established, we do not recommend routine prophylaxis.

Table 1. Treatment Regimens for HIV Disease.

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
GENERAL				
Antiretroviral (Anti-HIV)	*Asymptomatic and symptomatic patients*			
	Zidovudine (AZT, Retrovir) 500–600 mg po daily (e.g., 100 mg 5 times daily, 200 mg tid); 300–400 mg daily in divided doses for patients unable to tolerate higher dosages	Indefinitely	Malaise, headache, seizures, nausea, myalgias, insomnia; anemia, granulocytopenia, thrombocytopenia; long-term effects unknown. Toxic myopathy 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	Zidovudine is the usual first choice antiretroviral agent. For indications, see text Transfusions or erythropoietin (if endogenous erythropoietin level < 500 IU/L) may be necessary for anemia. Discontinue drug if Hgb < 6.0 g/dL. Decrease dosage or interrupt for absolute neutrophil count (ANC) < 500 cells/μL. Careful monitoring required when used with other myelosuppressive drugs
	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); rash; nausea, abdominal cramps, diarrhea; hyperglycemia; hyperuricemia; hepatitis; headache, insomnia, seizures; elevated triglyceride and amylase levels; thrombocytopenia; retinal atrophy	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, does not dissolve readily in water; tablets may need to be crushed manually. Packets containing powdered drug available from manufacturer by special order
	OR			
	Zalcitabine (ddC, HIVID) 0.75 mg po tid; 0.375 mg po tid for patients < 30 kg; dosage modification in renal failure	Indefinitely	Painful peripheral neuropathy (dosage related, reversible); rash; stomatitis; esophageal ulceration; seizures; hepatitis	Approved in combination with zidovudine. Not as effective as zidovudine for monotherapy. Can be used as monotherapy in patients who fail or are intolerant to zidovudine. Neurotoxicity can improve with zalcitabine "rest periods." Alternating regimens of zalcitabine and zidovudine can be less toxic
	OR			
	Stavudine (d4T)	Indefinitely	Painful peripheral neuropathy; hepatotoxicity; anemia, macrocytosis	Investigational; available by parallel track from manufacturer

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Table 1. ***Continued.***

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
GENERAL Antiretroviral (Anti-HIV) (cont.)	OR			
	Combination therapy	Indefinitely	See text	See text
	Postexposure prophylaxis			
	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). Safety of zidovudine in pregnancy has not been established. Counseling required
Weight loss	Megestrol (Megace) 40–80 mg po tid	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
***Mycobacterium avium* complex (MAC)**	Rifampin (Rimactane, Rifadin) 10 mg/kg po qd (600 mg po qd maximum) or rifabutin (Mycobutin) 300–600 mg po qd plus Ethambutol (Myambutol) 15 mg/kg po qd (1 g po qd maximum); dosage modification in renal failure plus one of the following Clarithromycin (Biaxin) 1 g po bid or Clofazimine (Lamprene) 100 m po qd or Ciprofloxacin (Cipro) 500–750 mg po bid	Indefinitely, if tolerated (minimum of 12 weeks)	Anorexia, hepatitis. Multisystem toxicity including renal, ocular (if ethambutol > 25 mg/kg/d). See toxicity for individual agents. Rifampin, rifabutin, clofazimine, and ethambutol are best given at bedtime to minimize gastrointestinal side effects. Drug toxicity may be difficult to differentiate from MAC-induced multisystem disease. Discoloration of body secretions with rifampin and clofazimine requires patient education. Clarithromycin side-effects similar to erythromycin	Treatment indicated for patients with signs, symptoms, and laboratory abnormalities consistent with MAC disease who can tolerate multidrug regimen. Long-term survival may be improved Rifampin or rifabutin, ethambutol, and clarithromycin should be used whenever tolerated. Azithromycin (Zithromax) also appears effective and can substitute for clarithromycin Rifabutin 100–300 mg po qd or clarithromycin 500 mg po qd-bid can be offered as primary prophylaxis for patients with advanced immunodeficiency (CD4 < 100 cells/μL). Survival benefits not demonstrated
	For severely ill patients add			
	Amikacin 7.5 mg/kg IM/IV qd	2–8 weeks	Nephrotoxicity, ototoxicity	Monitor drug levels
	When M. tuberculosis is suspected add			
	Isoniazid (INH) 300 mg po qd			

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Table 1. ***Continued.***

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
OPHTHALMOLOGIC				
Cytomegalovirus (CMV)	Ganciclovir (Cytovene) *Induction:* 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; renal failure, hepatic failure, anemia, phlebitis, rash, thrombocytopenia, nausea. Discontinue zidovudine during induction to minimize additive hematologic toxicity (neutropenia). To avoid hematologic toxicity can substitute didanosine or zalcitabine for zidovudine, or change to foscarnet plus zidovudine	CMV retinitis can be arrested or improved with IV ganciclovir therapy. 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 Start granulocyte colony-stimulating factor (G-CSF, filgastrim, Neupogen) 300 μg SQ three times weekly for ganciclovir-induced neutropenia (ANC < 500 cells/μL) on two consecutive measurements
	Maintenance: 5 mg/kg IV as 1-hr infusion 5–7 times/wk; dosage modification in renal failure	Indefinitely		Lifelong suppressive therapy required to prevent recurrence of retinitis. Daily administration is optimal. Administer G-CSF or change to foscarnet for ANC consistently < 500 cells/μL Combination therapy with ganciclovir plus foscarnet not routinely recommended. Can be used after resistance to both drugs demonstrated
	OR			
	Foscarnet (Foscavir) *Induction:* 60 mg/kg/dose IV q 8 hr as 2-hr infusion; 90 mg/kg/dose for severe retinitis or disease close to macula; 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; phlebitis, penile ulcerations	Administered by infusion pump via central line. Maintain hydration and avoid concurrent use of nephrotoxic agents when possible. Twenty-four–hr creatinine clearance should be measured in cachectic patients and in patients with renal insufficiency to ensure proper use of administration nomogram
	Maintenance: 90–120 mg/kg IV qd as 2-hr infusion; discontinuation or dosage modification required in renal failure	Indefinitely; infusions 7 times/wk		

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Table 1. ***Continued.***

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
SKIN/MUCO-CUTANEOUS				
Kaposi sarcoma	Observation			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 due to 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; hepatic dysfunction	Toxicities greater in patients taking zidovudine. Dosages greater than 10 mU/d necessary for efficacy
Seborrheic dermatitis	*Acute:* Hydrocortisone cream (HC) 2.5% plus ketoconazole cream 2% bid; severe cases may require ketoconazole 200–400 mg po qd for 3–4 weeks	Until resolved	See ORAL CAVITY, *Candida albicans*, ketoconazole	Commonly involves face, eyebrows, retroauricular areas, nasolabial folds, and scalp. Addition of antifungal cream enhances therapeutic response and reduces the frequency of steroid application
	Maintenance: HC cream 1% and ketoconazole cream 2% bid	Indefinitely		
Mucocutaneous herpes simplex (localized)	Acyclovir (Zovirax) *Acute:* 200–400 mg po 5 times/d	7–10 days	Oral: nausea, vomiting, diarrhea, dizziness	Topical acyclovir ineffective for most episodes
	Maintenance: 200–400 mg po 3–5 times/d	Indefinitely		Chronic maintenance therapy may be necessary for repeated episodes
Disseminated, extensive or persistent herpes simplex	Acyclovir *Acute:* 5 mg/kg/dose IV q 8 hr; dosage modification in renal failure	7–14 days	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
	Maintenance: 200–400 mg po 3–5 times/d	Indefinitely		

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Table 1. *Continued.*

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
SKIN/MUCO-CUTANEOUS (cont.)				
Herpes zoster (shingles)	Intravenous acyclovir (see below) or acyclovir 800 mg po 5 times/d	7–10 days	Same as below	Intravenous therapy preferred. Oral therapy not generally recommended because higher acyclovir levels are required for efficacy (oral bioavailability = 25%)
Disseminated, extensive, or persistent herpes zoster	Acyclovir 10 mg/kg/dose IV q 8 hr; dosage modification in renal failure	7–14 days		Alternate drugs are foscarnet and vidarabine
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
ORAL CAVITY				
Candida albicans	Ketoconazole (Nizoral)			
	Acute: 400 mg po qd	1–2 weeks or until resolved	Nausea; hepatocellular toxicity; anaphylaxis, urticaria. Higher doses can suppress testosterone levels	Improvement seen within 2–3 days
	Maintenance: 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
	OR			
	Clotrimazole (Mycelex) troches 10 mg dissolved slowly in mouth 5 times/d	Same	Minimal toxicity. Unpleasant taste, nausea, vomiting; abnormal liver function tests	Improvement seen within 2–3 days
	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			
	Fluconazole (Diflucan)			
	Acute: 50–100 mg po qd; higher dosages may be necessary	Same	See CENTRAL NERVOUS SYSTEM, *Cryptococcus neoformans*	More expensive than other agents. Effective in oral candidiasis unresponsive to above oral agents. Fluconazole-resistant organisms reported
	Maintenance: 100–150 mg po once weekly	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

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Table 1. ***Continued.***

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
ORAL CAVITY				
Candida albicans **(cont.)**	OR			
	Amphotericin B (Fungizone) 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, *Cryptococcus neoformans*	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				
Candida albicans	Fluconazole 200–400 mg po qd; ketoconazole, amphotericin; see ORAL CAVITY, *Candida albicans*	14–21 days; maintenance with lowest effective dosage may be required	See CENTRAL NERVOUS SYSTEM, *Cryptococcus neoformans*	Empiric treatment for patients with dysphagia or odynophagia who have oral thrush. Endoscopy with biopsy and cultures appropriate for patients who fail to respond within 1 week. Ketoconazole effective in most patients
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
GASTROINTESTINAL				
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; rare hepatotoxicity; 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

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Table 1. ***Continued.***

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
GASTRO-INTESTINAL Nausea and vomiting (cont.)	Lorazepam (Ativan) 0.5–2 mg po bid-tid	As needed	Similar to benzodiazepines; antegrade amnesia	Can be given by sublingual route
	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. IV preparation (2 mg/mL) can be reconstituted for oral administration in cherry or other fruit syrup. Stable for 1 week
	Dronabinol (tetrahydrocannabinol, THC, Marinol) 2.5–10 mg po q 8–12 hr	As needed	Restlessness, irritability, insomnia, dizziness, loss of coordination; psychotomimetic effects; tachycardia	Effective in drug-induced nausea
Diarrhea	*Symptomatic treatment*			
	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
	OR			
	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
	OR			
	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
	OR			
	Tincture of opium 10 mg morphine/mL, 0.3–1.0 mL po qid and prn (maximum 1 mL/dose or 6 mL/d)	As needed	Same	Same as above. Tincture of opium contains 25 times more morphine than paregoric
	OR			
	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

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Table 1. ***Continued.***

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
GASTRO-INTESTINAL (cont.)				
Cryptosporidium	See Diarrhea, *Symptomatic treatment*	Indefinitely	See Diarrhea	No drug effectively eradicates cryptosporidium
	Paromomycin (Humatin) 750 mg po tid	10–14 days	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, *Pneumocystis carinii* 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)**	*Acute* Pneumocystis carinii *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) may be effective and less toxic	Treat for 21 days	Adverse effects commonly appear between 7–14 days in more than 50% patients	TMP-SMX is the drug of choice for PCP and should be used unless severe reactions (e.g., anaphylaxis) are of concern Hospitalization recommended initially to monitor clinical course and drug toxicities. 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 desensitization. Severe toxicity (i.e., Stevens-Johnson syndrome) requires drug discontinuation
			Hematological: neutropenia, thrombocytopenia, anemia	If ANC < 500 cells/μL or if platelet count < 30 × 10^9/L and bleeding occurs, consider alternative treatment. Leucovorin calcium (folinic acid) 10–20 mg po qd may prevent hematologic toxicity

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Table 1. ***Continued.***

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
PULMONARY ***Pneumocystis carinii*** **pneumonia (PCP) (cont.)**			Gastrointestinal: nausea, vomiting, toxic hepatitis	Pretreatment with lorazepam, prochlorperazine, metoclopramide, or dronabinol (tetrahydrocannabinol, THC, Marinol) to reduce nausea. Refractory nausea may respond to ondansetron (Zofran). Nausea may be less with oral TMP-SMX. Hepatic enzyme increase to 4–5 times normal requires treatment change
			Renal: increased BUN and creatinine; hyperkalemia	TMP can decrease creatinine tubular secretion and falsely elevate serum creatinine levels. Discontinue TMP-SMX if serum creatinine >3.0 mg/dL. Concomitant nephrotoxic agents and dehydration can 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 ($Na^+ < 115$ 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
	Alternatives to TMP-SMX for acute PCP			
	Pentamidine isethionate (Pentam) 4 mg/kg/d as 1–2 hr IV infusion once daily	Treat for 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; hypoglycemia, hyperglycemia	Early or delayed hypoglycemia (can occur after discontinuation of therapy). 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

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Table 1. ***Continued.***

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
PULMONARY ***Pneumocystis carinii*** **pneumonia (PCP) (cont.)**			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 can increase risk of pentamidine nephrotoxicity
			Other: neutropenia, thrombocytopenia; hypocalcemia, hypomagnesemia; hepatitis; cardiac arrhythmias (rare)	
	OR			
	Dapsone 100 mg po qd plus TMP 15 mg/kg/d po in 3–4 divided doses	Treat for 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 glucose-6-phosphate dehydrogenase (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 may be less toxic than TMP-SMX and just as effective in mild illness (PaO_2 > 60 mmHg). Patients allergic to TMP-SMX may tolerate dapsone-TMP without recurrent toxicity
	OR			
	Clindamycin (Cleocin) 600 mg IV or po qid plus Primaquine 30 mg base po qd	Treat for 21 days	Maculopapular rash (day 10–12), fever; leukopenia, hemolytic anemia; diarrhea, nausea, vomiting, abdominal cramps, *Clostridium difficile* colitis. Methemoglobinemia from primaquine	Check G6PD before initiating primaquine therapy. Check methemoglobin levels when clinically indicated (see Dapsone). Consider in patients with mild-to-moderate PCP, intolerant of or unresponsive to first-line therapy or to dapsone-TMP. Lower dosage of primaquine (15 mg po qd) can be effective
	OR			
	Atovaquone (Mepron) 750 mg po tid with food	Treat for 21 days	Rash, drug fever; headaches; nausea, diarrhea, increased liver enzymes; neutropenia, anemia; transient conjunctivitis; erythema multiforme	For patients who fail or are intolerant to TMP-SMX, pentamidine, dapsone-TMP, or clindamycin-primaquine Take with food to increase drug absorption

Continued

Table 1. *Continued.*

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
PULMONARY				
***Pneumocystis carinii* pneumonia (PCP) (cont.)**	*Adjunctive therapy for acute PCP with PaO_2 ≤ 70 mmHg*			
	Prednisone (po) or methylprednisolone (Solu-Medrol) IV: 40 mg bid for 5 days followed by 40 mg qd for 5 days, followed by 20 mg qd for 11 days (can be tapered to zero over last 11 days also)	Treat for 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 patients with PaO_2 ≤ 70 mmHg. Begin corticosteroids concurrent with PCP treatment
	Prophylaxis or suppression of PCP for patients with CD4+ < 200 cells/μL, prior episode of PCP, or constitutional symptoms of HIV disease			
	TMP-SMX 1 DS tablet po qd or bid or 3 times/wk (e.g., M-W-F)	Indefinitely	See TMP-SMX	TMP-SMX considered most effective for prophylaxis or suppression. Once-daily administration may be easiest to remember. Three-day-per-week regimen may be best tolerated. Multiple TMP-SMX regimens have been used and all are effective. No efficacy comparisons exist between current dosing regimens
	Alternatives to TMP-SMX for prophylaxis or suppression			
	Dapsone 50–100 mg po daily	Indefinitely	See dapsone plus TMP	Probably less effective than TMP-SMX; may be less toxic
	OR			
	Inhaled pentamidine (Aeropent) 300 mg q 4 weeks or 150 mg q 2 weeks; requires specially designed nebulizer system, i.e., Respigard II, UltraVent	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	Inhaled pentamidine appears effective for prophylaxis of pulmonary PCP but does not prevent extrapulmonary disease. Efficacy for secondary prophylaxis uncertain. 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 *M. tuberculosis* infection because of risk of *M. tuberculosis* spread by aerosolization

Continued

Table 1. ***Continued.***

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
PULMONARY				
***Pneumocystis carinii* pneumonia (PCP) (cont.)**	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			
	OR			
	Atovaquone 750 mg po qd	Indefinitely	See above	Efficacy and proper dosages for PCP prophylaxis unknown
	OR			
	Pyrimethamine-sulfadoxine (Fansidar) 1 tablet po q week	Indefinitely	Stevens-Johnson syndrome, toxic epidermal necrolysis; leukopenia, bone marrow suppression; GI, CNS toxicity	No studies clearly demonstrate efficacy
CENTRAL NERVOUS SYSTEM				
Toxoplasma gondii	Sulfadiazine 1 g po q 6 hr	6–8 weeks for acute therapy; lifetime suppression with highest tolerated dosage	Rash, drug fever; bone marrow suppression, blood dyscrasias	Clinical response or regression of lesions on imaging studies is seen over 2–3 weeks. Maintenance required indefinitely to prevent relapse. Every other day administration of pyrimethamine and leucovorin may delay onset of bone marrow toxicity. Sulfadiazine probably provides effective prophylaxis or suppression against PCP
	plus			
	Pyrimethamine 75–100 mg po loading dose, then 25–50 mg po qd-qod			
	plus			
	Leucovorin calcium (folinic acid) 10–25 mg po qd			
	If sulfa allergy			
	Pyrimethamine 75–100 mg po loading dose, then 25–50 mg po qd-qod	Same	Same	Same
	plus one of the following in combination with pyrimethamine plus leucovorin			
	Clindamycin 600–900 mg po or IV qid	Same	Nausea, vomiting, diarrhea, abdominal cramps, pseudomembranous colitis	

Continued

Table 1. ***Continued.***

System & Problem	Drug Regimen	Duration	Common Adverse Effects	Comments
CENTRAL NERVOUS SYSTEM	or			
Toxoplasma gondii **(cont.)**	Clarithromycin 500 mg–1 g po bid	Same	See GENERAL, *Mycobacterium avium* complex	
	or			
	Azithromycin 500 mg po qd	Same	Similar to clarithromycin	
	OR			
	Atovaquone 750 mg po qid with meals	Same	See PULMONARY, *Pneumocystis carinii* pneumonia	
	OR			
	Pyrimethamine 75–100 mg po qd alone	Same	See above	Not as effective as above regimes
Cryptococcus neoformans	*Meningitis or disseminated cryptococcosis*			
	Acute: Amphotericin B 0.7–1.0 mg/kg/d IV with or without 5-flucytosine 150 mg/kg po qd in 4 divided doses for first 2–4 weeks or until clinically improved, followed by fluconazole 400 mg po qd	6–8 weeks; amphotericin total dosage not to exceed 2 g	Renal failure, hypokalemia, hypomagnesemia, fever, chills, anemia, thrombophlebitis Granulocytopenia from flucytosine	Pretreatment with diphenhydramine, acetaminophen, or IV meperidine can decrease amphotericin-induced fevers, chills, and rigors. Addition of heparin 500 U and hydrocortisone 50 mg to amphotericin IV solution can decrease phlebitis. 5-flucytosine not indicated if granulocytopenia or thrombocytopenia is present. Infusion of 500 mL–1L normal saline before administration of amphotericin B can minimize renal toxicity
	OR			
	Fluconazole 400–800 mg po qd	8–12 weeks	Nausea, vomiting, diarrhea; dizziness; hepatitis; rare cutaneous reactions; increased phenytoin (Dilantin) and warfarin (Coumadin) levels	Fluconazole penetrates CNS and most body tissues, including prostate. As effective as amphotericin B against mild or moderate disease; unknown whether equally effective against severe disease. Higher dosages may be necessary in moderate to severe disease
	Maintenance: Fluconazole 200–400 mg po qd	Indefinitely	Same	Higher dosages may 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 days	Usual penicillin adverse effects. Jarisch-Herxheimer reaction. Seizures from high-dose penicillin in renal failure	Intravenous penicillin preferred for adequate CNS penetration. Benzathine penicillin, ampicillin, doxycycline not recommended because efficacy not established. Ceftriaxone 1 g IV qd for 2 weeks can be considered for penicillin-allergic patients, although efficacy not proved
	OR			
	Procaine penicillin G 2.4 mU IM qd	10 days	Same. Probenecid rash	
	plus			
	Probenecid 500 mg po qid			
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
	OR			
	Phenytoin (diphenylhydantoin, Dilantin) 100 mg po tid	Indefinitely	Usual side effects	Generally ineffective
	OR			
	Carbamazepine (Tegretol) 100–300 mg po bid	Indefinitely	Leukopenia, bone marrow suppression, rare agranulocytosis; drowsiness, dizziness; hepatic dysfunction	Less desirable because of bone marrow effects
	OR			
	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
	OR			
	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

Conclusions

By using established treatments properly and avoiding unnecessary toxicity, the quality and length of life for patients with HIV disease and AIDS can be improved. The recommendations in Table 1 include new treatment recommendations for opportunistic infections and some of the common symptoms of HIV disease. A selected bibliography highlighting antiretroviral treatment,[2-16] management of opportunistic infections,[17-38] and other clinical aspects of HIV disease[39-51] supplements the information in Table 1.

We gratefully acknowledge the extraordinary and ongoing efforts of Mary Hanville, the staff of the HIV Telephone Consultation Service, and the faculty and staff at San Francisco General Hospital in making this work possible.

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