Current Report — HIV

Treatment Of AIDS And HIV-Related Conditions: 1992

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Management of human immunodeficiency virus (HIV) disease is now an essential part of primary care. Several advances in treatment have occurred in the 10 months since the publication of our previous treatment recommendations in *JABFP*.[1] Recognizing that practitioners' clinical experience with acquired immunodeficiency syndrome (AIDS) and HIV disease varies considerably and that HIV therapeutics is a rapidly changing area in medicine, the "Current Report — HIV" provides information to guide the primary care provider in HIV management.[1-9]

Treatment Regimens for HIV Disease

The treatment recommendations in Table 1 are based on the medical literature and our clinical experience at San Francisco General Hospital. Although there is a diversity of approaches among AIDS experts, our recommendations are intended as a basic guide to the most common therapeutic problems. The emphasis is on the safe use of drugs proved to be effective against HIV and opportunistic infections.

We have been selective in the topics covered in this update. Certain HIV-related conditions, such as generalized lymphadenopathy, oral hairy leukoplakia, and thrombocytopenia without bleeding, require evaluation to exclude treatable problems, but these conditions do not require specific treatment and are, therefore, not included in the table. Similarly, we have not included common problems, such as pneumonia, sinusitis, vaginitis, and diarrhea caused by the usual bacterial pathogens, which are treated in the standard fashion. Recommendations for treatment of HIV-infected children are not included because they have been discussed in other reviews.[10,11]

In the primary care of patients infected with HIV, proven treatments should not be neglected so unproven agents can be tried. Early diagnosis, prophylaxis against *Pneumocystis carinii* pneumonia (PCP), antiretroviral therapy, treatment of opportunistic infections, and attention to psychosocial aspects of care should be the foremost concern of the primary care provider. Because of the severe morbidity and mortality associated with AIDS, the use of unproven drugs is understandable. For example, trichosanthin (Compound Q, GLQ223), ditiocarb (ditrocarb), and ribavirin are just a few of the agents available through compassionate-use protocols and from buyers' clubs. Although widely used, many of these drugs have not been sufficiently evaluated for efficacy and toxicity; therefore, they are not recommended in this article. It is important for the primary care provider, the patient, and the family to remember that these treatments might be harmful and prevent the use of other beneficial drugs. Treatment with experimental drugs is best reserved for formal clinical trials, which should be performed in conjunction with comprehensive primary care.

Antiretroviral Therapy

The optimal time to initiate antiviral therapy to slow the progression of HIV disease remains uncertain.[6,12] Treatment can begin with CD4+ (T-helper) lymphocyte counts as high as 500 cells/mm^3. Zidovudine (AZT [Retrovir™]) has been

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the mainstay of antiretroviral treatment since the late 1980s.[13-17] The approval of didanosine (ddI, 2′,3′-dideoxyinosine [Videx™])[18,19] and the expected approval of dideoxycytidine (ddC) expand our treatment options. Scientific data on didanosine and dideoxycytidine are unfortunately limited to changes in surrogate laboratory markers noted during Phase I and Phase I/II studies and to uncontrolled data submitted by practitioners in expanded access and open-label studies. Comparative clinical end-point studies are not available. How these drugs ultimately fit into HIV management in the next few years will be determined more by practice trends than by science.

Currently, we recommend initial treatment with zidovudine alone, although there is support for initial combined therapy with zidovudine plus didanosine or dideoxycytidine.[20] Additional toxicity, however, is likely when combination therapy is used. Concurrent administration of lower dosages of two antiretroviral agents (e.g., less than 300 mg of zidovudine daily) intended to avoid toxicity might not be efficacious and is not recommended. Didanosine is indicated for patients who either do not tolerate or who have failed initial zidovudine therapy. The clinical and laboratory indicators signifying "failed therapy" are difficult to define precisely in this chronic progressive disease. Persistently falling CD4+ lymphocyte counts, new or progressive opportunistic infections and malignancies, or persistent generalized symptoms and signs, such as fevers, weight loss, and inanition, can be interpreted as "failed therapy." Another indication for didanosine usage (although not approved by the Food and Drug Administration) is the patient's desire to try this alternative antiretroviral agent. Alternating zidovudine with didanosine (e.g., alternating months) has been suggested and constitutes another reasonable approach.

Opportunistic Infections

New recommendations for treating cytomegalovirus (CMV), herpes simplex and zoster, *Mycobacterium avium-intracellularae* complex (MAC), and *P. carinii* infections are included in the table. Foscarnet (Foscavir™) is an alternative agent for cytomegalovirus disease[21,22] and for acyclovir-resistant herpes infections.[23] Foscarnet appears as effective as ganciclovir (Cytovene™) in treating cytomegalovirus retinitis. Because it does not cause neutropenia, as does ganciclovir, foscarnet might be better tolerated by patients taking zidovudine, which also can cause neutropenia. Whether treatment with foscarnet plus zidovudine increases survival of patients with CMV retinitis more than treatment with ganciclovir plus didanosine or zidovudine is not clear. The nephrotoxicity of foscarnet and the necessity of giving it daily by an infusion pump limit its usefulness.

A new multidrug regimen against MAC disease is recommended. The finding of acid-fast bacilli can indicate infection by *Mycobacterium tuberculosis*, MAC, or other mycobacteria. Antimicrobial treatment of symptomatic MAC disease can relieve symptoms and possibly prolong life.[24,26] Standard treatment of *M. tuberculosis* disease is usually effective.[27-29]

Trimethoprim-sulfamethoxazole (TMP-SMX) is now recommended as first-line treatment against acute *P. carinii* pneumonia, as prophylaxis against PCP in patients with CD4+ lymphocyte counts less than 200 cells/mm^3 (primary prophylaxis), and as suppressive therapy for patients with previous episodes of acute PCP (secondary prophylaxis). TMP-SMX appears more effective than other agents. Moderate degrees of drug toxicity can be tolerated in high-dose acute PCP treatment. The lower dosages now recommended for prophylaxis and suppression are usually well tolerated. Because pulse oximetry can be misleading, we recommend arterial blood gas measurements in evaluating acute pulmonary disease. The response to treatment of acute PCP is variable. Oxygen therapy, antibiotic treatment of concurrent bacterial pneumonia, and other supportive measures can produce initial improvement. Some patients, however, will have clinical deterioration within a few days following initiation of treatment. The ongoing inflammatory pulmonary process exacerbated by the lysis of *P. carinii* organisms in the first days of treatment, along with large amounts of intravenous fluids, can produce pulmonary edema. Therefore, fluid overload should not be overlooked in patients with worsening respiratory status or apparent failure to respond to TMP-SMX. Diuretics may be necessary. Corticosteroids are now indicated in patients with acute PCP and substantial hypoxemia (PaO_2 less than 70 mmHg).[30]

Table 1. Treatment Regimens for HIV Disease.

System & Organism	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 can be offered to patients with CD4+ cell counts as high as 500 cells/mm³. Toxicity is less with 300–600 mg daily than the 1200–1500 mg dosages used previously Transfusions or erythropoietin may be necessary for anemia. Discontinue drug if Hgb < 6.0 g/dL. Decrease dosage or interrupt for absolute neutrophil count (ANC) < 500 cells/mm³. Careful monitoring required when used with other myelosuppressive drugs
	OR			
	Didanosine (ddI) (Videx™) 200 mg po bid for patients 50–75 kg; 125 mg po bid for < 50 kg; 300 mg po bid for > 75 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	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 tablets. Two tablets must be given per dose to provide adequate buffer for absorption. Administer 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			
	Dideoxycytidine (ddC) 0.375–0.75 mg po tid	Indefinitely	Painful peripheral neuropathy (with higher dosages, reversible); mucocutaneous eruptions; seizures	Investigational. Available by expanded access program. Does not appear to be as effective as zidovudine. Can be used in patients who fail or are intolerant to zidovudine. Neurotoxicity can improve with ddC "rest periods." Alternating regimens of ddC and zidovudine may be less toxic
	HIV-related dementia, thrombocytopenia, psoriasis			
	Zidovudine 1200 mg po qd in divided doses	Indefinitely	See above	Lower dosages (300–600 mg po qd) may be effective but have not been assessed in these conditions. Zidovudine efficacy in AIDS dementia is variable

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Table 1. ***Continued.***

System & Organism	Drug Regimen	Duration	Common Adverse Effects	Comments
GENERAL (cont.)				
	Postexposure prophylaxis			
	Zidovudine 200 mg po q 4 hr while awake (1000 mg po qd)	4–6 weeks	See above. Safety of zidovudine in pregnancy has not been established	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). Counseling required
***Mycobacterium avium* complex (MAC)**	*Use four of the following drugs in combination*			
	Rifampin 10 mg/kg po qd (600 mg po qd maximum) PLUS Ethambutol 15 mg/kg po qd (1 gm po qd maximum) PLUS Clarithromycin (Biaxin™) 500 mg po qid or 1 gm po bid PLUS Clofazimine (Lamprene™) 100 mg po qd PLUS 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, clofazimine, and ethambutol are best given at bedtime to minimize gastrointestinal side effects. Drug toxicity may be difficult to differentiate from MAC-induced multisystem toxicity. 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 Toxicity may limit treatment to fewer than four drugs. Rifampin, ethambutol, and clarithromycin should be used whenever tolerated. Azithromycin (Zithromax ™) 500 mg po qd also appears effective and can substitute for clarithromycin
	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 & Organism	Drug Regimen	Duration	Common Adverse Effects	Comments
OPHTHALMOLOGIC				
Cytomegalovirus (CMV)	Ganciclovir (Cytovene™)			
	Induction: 5 mg/kg IV q 12 hr or 2.5 mg/kg IV q 8 hr; dosage modification in renal failure	10–14 days for acute retinal infection; 21 days usually required for extraocular infection	Neutropenia, leukopenia, renal failure, hepatic failure, anemia, phlebitis, rash, thrombocytopenia, nausea. Severe neutropenia (ANC < 500 cells/mm³). Discontinue zidovudine during induction to minimize additive hematologic toxicity. Can substitute didanosine for zidovudine, or change to foscarnet, when hematologic toxicity occurs	CMV retinitis can be arrested or improved with IV ganciclovir therapy. Intravitreal ganciclovir appears effective if IV causes unacceptable toxicity. Lifelong suppressive therapy required to prevent recurrence. Ganciclovir can also be effective in CMV esophagitis, colitis, and proctitis; not usually effective in CMV pneumonitis. Consider granulocyte colony-stimulating factor (G-CSF) 300 μg SQ M-W-F for 1 wk for ganciclovir-induced neutropenia (ANC < 500 cells/mm³) or discontinue ganciclovir until ANC > 500 cells/mm³
	Maintenance: 5 mg/kg IV as 1-hr infusion 5–7 times/wk; dosage modification in renal failure	Indefinitely		
	OR			
	Foscarnet (Foscavir™)			
	Induction: 60 mg/kg/dose IV q 8 hr for 2 weeks as 2-hr infusion; discontinuation or dosage modification required in renal failure	14–21 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 determined in cachectic patients and in patients with renal insufficiency to assure 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		
SKIN/MUCOCUTANEOUS				
Kaposi's 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

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Table 1. *Continued.*

System & Organism	Drug Regimen	Duration	Common Adverse Effects	Comments
SKIN/MUCO-CUTANEOUS				
Kaposi's sarcoma (cont.)	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	12-week induction; chronic maintenance	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 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:* 200–800 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 when repeated episodes occur
Herpes zoster (shingles)	Intravenous acyclovir (see below) or acyclovir 800 mg po 5 times/d	7–10 days	Same	Intravenous therapy preferred. Oral therapy not generally recommended because higher acyclovir levels are required for efficacy (oral bioavailability = 25%)
Disseminated, extensive, or persistent herpes simplex	Acyclovir *Acute:* 5 mg/kg/dose IV q 8 hr; dosage modification in renal failure	10–14 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 & Organism	Drug Regimen	Duration	Common Adverse Effects	Comments
SKIN/MUCO-CUTANEOUS (cont.)				
Disseminated, extensive, or persistent herpes zoster	Acyclovir 10–15 mg/kg/dose IV q 8 hr; dosage modification in renal failure	10–14 days		
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 under CMV	See under CMV
ORAL CAVITY				
Candida albicans	Ketoconazole (Nizoral™)			
	Acute: 400 mg po qd	Until resolved; maintenance usually required with lowest effective dosage	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			Need gastric acidity to be effective; avoid antacids and H_2 antagonists
				Ketoconazole or clotrimazole initially for oral thrush. Ketoconazole recommended for clotrimazole/nystatin failure and/or esophageal candidiasis
	OR			
	Clotrimazole (Mycelex™) troches 10 mg dissolved slowly in mouth 5 times/d	Same	Unpleasant taste, nausea, vomiting; minimal toxicity. Abnormal liver function tests	Improvement seen within 2–3 days
	OR			
	Nystatin (Mycostatin™) 100,000 U/mL, swish & swallow 5 mL po q 6 hr; or vaginal tabs 500 mg 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™) 50–100 mg po qd. Higher dosages may be necessary	Same	See under *Cryptococcus neoformans*	More expensive than other agents. Very effective in oral candidiasis unresponsive to above oral agents
	OR			
	Amphotericin B 0.3–0.4 mg/kg IV qd	10 days or until resolution	See under *Cryptococcus neoformans*	Candidal esophagitis unresponsive to oral agents requires low-dose amphotericin B
Periodontal disease	Hydrogen peroxide gargles for 30 sec bid	Indefinitely		Less expensive than chlorhexidine

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Table 1. *Continued.*

System & Organism	Drug Regimen	Duration	Common Adverse Effects	Comments
ORAL CAVITY				
Periodontal disease (cont.)	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 (above)	14–21 days; maintenance with lowest effective dosage may be required	See above	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
Cytomegalovirus	Ganciclovir; see OPHTHALMOLOGIC (above)	14–21 days; maintenance may be required	See above	Diagnose by endoscopic appearance plus biopsy showing CMV inclusion bodies and positive culture
Herpes simplex	IV acyclovir; see SKIN/MUCOCUTANEOUS (above)	10–14 days; maintenance required	See above	Diagnose by endoscopic appearance plus positive culture
GASTROINTESTINAL				
HIV enteropathy	*Symptomatic treatment*			
	Loperamide (Imodium™) 4 mg po initially then 2 mg q 6 hr around the clock and prn (maximum of 16 mg qd, 8 tablets)	As needed	Abdominal cramps, nausea, vomiting	Around-the-clock regimen more effective than prn. Treat to 2–3 bowel movements/d
	OR			
	Diphenoxylate atropine (Lomotil™) 1–2 tablets po 3–6 times daily for 24–48 hr; then one tablet tid and prn to control diarrhea (maximum 20 mg qd, 8 tablets)	As needed	Ileus	Same
	OR			
	Tincture of opium 0.3–0.9 cc tid-qid and prn	As needed	Ileus. Altered mental status. Adverse effects common to narcotic analgesics	Same
	OR			
	Octreotide (Sandostatin™) 100–500 μg SQ tid, increase by 100–200 μg q 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 & Organism	Drug Regimen	Duration	Common Adverse Effects	Comments
GASTRO-INTESTINAL				
HIV enteropathy (cont.)	OR			
	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
Cryptosporidium	See *Symptomatic treatment* (above)	Indefinitely	See above	No drug effectively eradicates cryptosporidium
	Spiramycin (Rovamycin™) 1 g po qid	Unknown	Rare adverse effects: nausea, vomiting, epigastric pain	Investigational; available from FDA. Treatment is not very effective (< 20%) and has been associated with high rate of *Clostridium difficile* infection
Isospora belli	Trimethoprim-sulfamethoxazole (TMP-SMX) 1 DS (double-strength) tablet po qid	21 days	See TMP-SMX under pulmonary	Usually effective
PULMONARY				
***Pneumocystis carinii* (PCP)**	*Acute Pneumocystis carinii* pneumonia			
	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	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
			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/mm³ or if platelet count < 30 × 10⁹/L and bleeding occurs, consider alternative treatment. Leucovorin calcium (folinic acid) 10–20 mg po qd may prevent hematologic toxicity
			Gastrointestinal: nausea, vomiting, toxic hepatitis	Pretreatment with lorazepam, prochlorperazine, meclopropamide, or 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

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Table 1. *Continued.*

System & Organism	Drug Regimen	Duration	Common Adverse Effects	Comments
PULMONARY ***Pneumocystis carinii*** **(PCP) (cont.)**			Renal: increased BUN and creatinine	TMP can decrease creatinine tubular secretion and falsely elevate serum creatinine levels. Discontinue TMP-SMX if serum creatinine > 256 μmol/L (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 may 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
			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 may occur
			Renal: increased BUN and creatinine; hyperkalemia	Discontinue pentamidine if creatinine > 256 μmol/L (3.0 mg/dL). Can resume administration if creatinine < 177 μmol/L (2mg/dL). Concomitant nephrotoxic agents and dehydration can increase risk of pentamidine nephrotoxicity
			Rarely: neutropenia, thrombocytopenia; hypocalcemia, hypomagnesemia; hepatitis, pancreatitis; cardiac arrhythmias	

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Table 1. ***Continued.***

System & Organism	Drug Regimen	Duration	Common Adverse Effects	Comments
PULMONARY ***Pneumocystis carinii*** **(PCP)** **(cont.)**	OR			
	Dapsone 100 mg po qd plus TMP 15 mg/kg/d po in 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	Proved effective in mild PCP only. Check glucose-6-phosphate dehydrogenase (G6PD) before starting dapsone. Check methemoglobin levels weekly. Treat methemoglobin 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 ($pO_2 > 60$ mmHg). Patients allergic to TMP-SMX may tolerate dapsone-TMX without recurrent toxicity
	OR			
	Clindamycin 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, methemoglobinemia; diarrhea, nausea, abdominal cramps	Check G6PD before initiating primaquine therapy. Check methemoglobin levels weekly. Consider in patients with mild PCP, intolerant of or unresponsive to first line therapy or to dapsone-TMP. Lower dosage of primaquine (15 mg po qd) may be effective
	OR			
	566C80 750 mg po tid	Treat for 21 days	Rash, drug fever; headaches; nausea, diarrhea, increased liver enzymes; neutropenia, anemia	Available by Treatment IND (Investigational New Drug) or Open-Label Protocol for patients who fail or are intolerant to TMP-SMX, pentamidine, or dapsone-TMP
	Adjunctive therapy for acute PCP with PaO_2 ≤ 70 mmHg			
	Prednisone (po) or methylprednisolone (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

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Table 1. ***Continued.***

System & Organism	Drug Regimen	Duration	Common Adverse Effects	Comments
PULMONARY				
***Pneumocystis carinii* (PCP) (cont.)**	*Prophylaxis or suppression of PCP for patients with CD4+ < 200 cells/mm³ or prior episode of PCP*			
	TMP-SMX 1 DS tablet po qd or bid. 1 DS tablet 3 times/ wk (e.g., M-W-F) may be effective	Indefinitely	See TMP-SMX above	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 above	Probably as effective as 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 due to low pentamidine serum concentrations. Bronchospasm and coughing are common, especially in smokers. Pretreatment with inhaled bronchodilator (e.g., albuterol) may help	Inhaled pentamidine appears effective for prophylaxis of pulmonary PCP but does not prevent extrapulmonary recurrences. 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
	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

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Table 1. ***Continued.***

System & Organism	Drug Regimen	Duration	Common Adverse Effects	Comments
CENTRAL NERVOUS SYSTEM				
Toxoplasma gondii	Sulfadiazine 1 g po q 6 hr PLUS Pyrimethamine 75–100 mg po loading dose, then 25–75 mg po qd PLUS Leucovorin calcium (folinic acid) 10–25 mg po qd	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. Leucovorin may delay onset of bone marrow toxicity. Sulfadiazine probably provides effective prophylaxis or suppression against PCP
	If sulfa allergy Pyrimethamine 25–100 mg po qd PLUS Clindamycin (Cleocin™) 600–900 mg po or IV qid	Same	Same Nausea, vomiting, diarrhea, abdominal cramps	Same
Cryptococcus neoformans	*Acute meningitis or disseminated cryptococcosis* Amphotericin B 0.5–0.8 mg/kg/d IV over 4–6 hr with or without 5-flucytosine 150 mg/kg po qd in 4 divided doses OR Amphotericin B with or without 5-flucytosine (as above) followed by fluconazole 400 mg po qd	6 weeks or total of 1.5–2 g 6–8 weeks total; amphotericin B for first 2–4 weeks or until clinically improved	Renal failure, hypokalemia, hypomagnesemia, fever, chills, anemia, thrombophlebitis. Granulocytopenia from flucytosine	Pretreatment with diphenhydramine, acetaminophen, or meperidine may decrease 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

Continued

Table 1. ***Continued.***

System & Organism	Drug Regimen	Duration	Common Adverse Effects	Comments
CENTRAL NERVOUS SYSTEM				
Cryptococcus neoformans **(con't)**	OR			
	Fluconazole *Acute:* 400–800 mg po qd	8–12 weeks	Nausea, vomiting, dizziness; diarrhea, hepatitis; rare cutaneous reactions. Increased phenytoin and 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: 200–400 mg po qd	Indefinitely		
	OR			
	Amphotericin 0.5–0.8 mg/kg/d 3–5 times/wk	Indefinitely	See above	
CNS 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			

Conclusion

For HIV-infected persons and their families, a primary care approach, with attention to multisystem illness as well as family, social, and cultural issues, can provide guidance and support necessary for the overall care of this complex and serious chronic disease. A selected bibliography supplements the material in Table 1. Included are additional articles with management and therapeutic implications.[31-48] Further clinical guidance and extensive bibliographies can be found in other articles, texts,[49-51] and computer-based information systems.[52]

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