Current Report — HIV

Treatment of AIDS and HIV-Related Conditions

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With about 1 million persons in the US infected with the human immunodeficiency virus (HIV), the inevitable impact of the epidemic on primary care was only a matter of time. That time has come. The majority of family physicians are now caring for patients infected with HIV.

Providing primary care for patients infected with HIV presents a great challenge. Our understanding of the immunology and pathology of and therapy for HIV infection continues to evolve rapidly. The number of possible opportunistic infections, malignancies, and other complications associated with HIV disease is enormous. Multidrug regimens for prophylaxis, acute care, and chronic suppression are usually required. Providing this complex medical treatment while remaining attentive to the social, psychological, and family components of care is the challenge we must meet.

Fortunately, the management of HIV infection has standardized in the last few years. This "Current Report—HIV" updates treatment recommendations outlined in our earlier review article in *JABFP*.[1] Subsequent articles in the series have addressed new developments in managing HIV infection.[2-9] A comprehensive review of the dermatologic manifestations of HIV infection supplements these articles.[10]

Treatment Recommendations for HIV Infection

The treatment recommendations in Table 1 are based on the medical literature and our experience at San Francisco General Hospital. Unapproved drugs, with the exception of some that are widely available for compassionate use, are not included. Although enthusiasm for new but unproven drugs is understandable with a disease such as AIDS, it is important for the primary provider, the patient, and the family to remember that most of these treatments might also be harmful. In the primary care of patients infected with HIV, proven treatments should not be neglected so unproven agents can be tried. Treatment with experimental drugs should be reserved for carefully designed clinical trials, which should be performed in conjunction with comprehensive primary care.

We have been selective in the topics covered in this update. Certain conditions that need evaluation to exclude treatable problems but do not require specific treatment are not discussed. These include oral hairy leukoplakia, generalized lymphadenopathy resulting from benign follicular hyperplasia, and thrombocytopenia without bleeding. Other problems, such as bacterial pneumonia, sinusitis, vaginitis, and diarrhea caused by the usual enteric pathogens, occur frequently in HIV-infected persons but are not discussed because they are treated in the standard fashion. Recommendations for the treatment of HIV-infected children are not included because they are discussed in other recent reviews.[11,12]

Early Intervention

The most important change in management in the past few years is early intervention for HIV-infected persons before the development of AIDS. Studies show that early intervention results in fewer opportunistic infections and a prolongation of life.

Early intervention starts with identifying HIV-infected asymptomatic persons. Periodic monitoring of laboratory markers of disease progression is then used to identify thresholds for medical intervention. The most commonly used laboratory marker is the CD4+ (T-helper) lym-

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phocyte count. Because low CD4+ counts do not always indicate advancing HIV disease, CD4+ test results must be verified with repeated measurements and interpreted cautiously.[5]

The first treatment threshold in early intervention occurs when the CD4+ count falls below 500 cells/mm^3. Although data are needed to establish the long-term efficacy of zidovudine and the optimal time to initiate antiretroviral treatment, most AIDS experts begin antiretroviral therapy with zidovudine shortly after this threshold is reached.[13-16] Zidovudine is given orally at a dosage of 500–600 mg daily. Treatment schedules of 100 mg five times daily while awake or 200 mg three times daily are the best established dosage requirements. A dosage of 100 mg three times daily can be used in patients unable to tolerate standard dosages.[17] Hematologic toxicity (anemia) occurs infrequently with daily zidovudine dosages of 600 mg or less. Although data are inconclusive, dementia and some other advanced AIDS conditions might respond better to higher zidovudine dosages.

The second threshold in early intervention is when the CD4+ count drops below 200 cells/mm^3. Prophylaxis against *Pneumocystis carinii* pneumonia (PCP) with trimethoprim-sulfamethoxazole, aerosolized pentamidine, or dapsone should be instituted at this point.[18-20]

Special Considerations

Nonspecific symptoms and signs, e.g., fever, anorexia, malaise, and wasting, occur frequently. Although HIV disease itself can cause these findings, specific infections (most commonly PCP) and malignancies should first be excluded. Other causes include bacterial (e.g., pneumococcal, salmonella) sepsis, cytomegalovirus infection, cryptococcosis, and disseminated infection by *Mycobacterium avium* complex (MAC). Although there is no evidence that treatment of MAC prolongs life, treatment can help alleviate clinical manifestations, such as fever, abdominal pain due to MAC infection of the liver, and wasting.[21]

Infection with *Mycobacterium tuberculosis* presents special problems in HIV-infected patients.[22] Because immunosuppression impairs cell-mediated immunity, the tuberculin skin test is considered positive in HIV-infected persons when there is 5-mm induration. Prophylaxis is indicated for patients who have a positive skin test without active disease. Conventional therapy of active tuberculosis appears effective.[23]

Symptomatic treatment is extremely important in HIV care. For example, proper symptomatic management of diarrhea is essential, regardless of whether a treatable pathogen can be identified. Treating fever and pain, however, can present problems. Although helpful, the injudicious use of nonsteroidal anti-inflammatory drugs (NSAIDs) can be associated with avoidable nephrotoxicity. Our experience has led us to be very cautious when prescribing these drugs. Many AIDS patients have other factors that contribute to NSAID nephrotoxicity. These factors include volume depletion caused by diarrhea, vomiting, fever, or poor oral intake; hypoalbuminemia; concomitant nephrotoxic drug administration; and HIV-induced renal and adrenal insufficiency.

Therapeutic interventions depend on the patient's overall condition. For example, acute pneumonia with hypoxemia, fever, moderate-to-severe respiratory symptoms, or a markedly abnormal chest radiograph should prompt immediate treatment for PCP, rather than awaiting the results of diagnostic tests. Likewise, empiric treatment for cerebral toxoplasmosis in patients who have abnormal findings on imaging studies that suggest toxoplasmosis is another example of the overriding need to treat. On the other hand, Kaposi's sarcoma lesions do not require treatment unless they are painful, bulky, cosmetically or psychologically bothersome, or cause lymphatic obstruction.

Pneumocystis carinii pneumonia remains the most common and treatable complication of HIV disease. Treatment of acute PCP with trimethoprim-sulfamethoxazole or intravenous pentamidine is usually successful.[24,25] Recently, it has been shown that the prompt use of corticosteroids for all patients with PCP whose PaO_2 is less than or equal to 70 mmHg improves outcome. Adjuvant therapy with corticosteroids is now indicated for patients with this degree of hypoxemia.[26]

Drug toxicity is very common in HIV-infected patients. Rashes, nephrotoxicity, bone marrow suppression, hepatotoxicity, nausea, and fever occur at some time in almost all patients. These reactions can be confused with manifestations of

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™) 300–600 mg po daily (e.g., 100 mg tid, 100 mg 4–5 times daily, 200 mg tid)	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. The optimal dosage and dosing interval are unknown. 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) < 750 cells/mm³. Discontinue drug for ANC < 500 cells/mm³. Careful monitoring required when used with other myelosuppressive drugs.
	OR			
	Dideoxyinosine (ddI) 167–375 mg po bid	Indefinitely	Pancreatitis; painful peripheral neuropathy (dose related, reversible); hyperuricemia; hepatitis; headache, insomnia, seizures; elevated triglyceride and amylase.	Investigational. Can be used in patients who fail or are intolerant to zidovudine. Available via expanded access through treatment IND (investigational new drug) or open label. Avoid alcohol and other pancreatic toxins (e.g., pentamidine). Administer with antacids to increase oral absorption.
	OR			
	Dideoxycytidine (ddC) 0.03–0.09 mg/kg/d po in three divided doses	Indefinitely	Painful peripheral neuropathy (with higher dosages, reversible); mucocutaneous eruptions; seizures.	Investigational. 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.
	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.

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Table 1. ***Continued.***

System & Organism	Drug Regimen	Duration	Common Adverse Effects	Comments
GENERAL				
***Mycobacterium avium* complex (MAC)**	Rifampin 10 mg/kg po qd (600 mg po qd maximum) PLUS Ethambutol 15 mg/kg po qd (1 gm po qd maximum) PLUS Ciprofloxacin (Cipro™) 750 mg po bid or Clofazimine 50–100 mg po qd PLUS Isoniazid (INH) 300 mg po qd if *M tuberculosis* is suspected PLUS	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. Drug toxicity may be difficult to differentiate from MAC-induced multisystem toxicity. Discoloration of body secretions with rifampin and clofazimine requires patient education.	Treatment indicated for patients with signs, symptoms, and laboratory abnormalities consistent with MAC disease who can tolerate multidrug regimen. No change in long-term prognosis.
	Amikacin 7.5 mg/kg IM/IV qd for severely ill patients or when fevers continue despite oral therapy	2–8 weeks	Nephrotoxicity, ototoxicity.	Monitor drug levels.
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. Dosage needs to be adjusted in severe neutropenia (ANC < 500 cells/mm³). Discontinue zidovudine to minimize additive hematologic toxicity.	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.
	Maintenance: 2.5–5 mg/kg IV as 1 hr infusion 5–7 times/week	Indefinitely	Discontinue therapy if ANC < 500 cells/mm³.	

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Table 1. ***Continued.***

System & Organism	Drug Regimen	Duration	Common Adverse Effects	Comments
OPHTHALMOLOGIC	OR			
Cytomegalovirus (CMV) (cont.)	Foscarnet *Induction:* 60 mg/kg/dose IV q 8 hr as 2-hr infusion; 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.	Investigational. Available via expanded access for patients with documented CMV infections who fail or are intolerant to ganciclovir. Maintain hydration and avoid concurrent use of nephrotoxic agents when possible.
	Maintenance: 60 mg/kg IV qd as 2 hr infusion	Indefinitely; infusions 5 times/week		
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.
	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 mil U/d SQ, increase by 5 mil U/d every 2 weeks as tolerated to a maximum of 35 mil U/d	12 week induction; chronic maintenance	Fatigue, myalgia, asthenia; neutropenia, thrombocytopenia; hepatic dysfunction.	Toxicities greater in patients taking zidovudine. Dosages > 10 mil U/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		

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Table 1. ***Continued.***

System & Organism	Drug Regimen	Duration	Common Adverse Effects	Comments
SKIN/MUCOCUTANEOUS				
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	IV: lethargy, tremors, confusion, hallucinations; phlebitis; increased serum creatinine, reversible crystalline nephropathy.	Severe herpes infections (e.g., esophagitis, colitis, encephalitis) require IV acyclovir. Maintain good urine output and hydration to prevent acyclovir crystallization.
	Maintenance: 200–400 mg po 3–5 times/d	Indefinitely		
Disseminated, extensive or persistent Herpes zoster	Acyclovir 10–15 mg/kg/dose IV q 8 hr; dosage modification in renal failure	10–14 days		
	OR			
	Foscarnet 60 mg/kg/dose IV q 8 hr; dosage modification in renal failure	10–14 days or until lesions clear	See under CMV.	Investigational. Available via expanded access for documented acyclovir resistant herpes simplex virus.
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 7 consecutive days per month or qd if necessary			Need acid media 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.

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Table 1. ***Continued.***

System & Organism	Drug Regimen	Duration	Common Adverse Effects	Comments
ORAL CAVITY	OR			
Candida albicans **(cont.)**	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	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.
	OR			
	Chlorhexidine gluconate (Peridex™) oral rinse 15 mL swished in mouth for 30 sec bid	Indefinitely	Staining of teeth.	
ESOPHAGEAL				
Candida albicans	Ketoconazole, fluconazole, 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 OPHTHALOMOLOGIC (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 per day.

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Table 1. ***Continued.***

System & Organism	Drug Regimen	Duration	Common Adverse Effects	Comments
GASTRO-INTESTINAL	OR			
HIV enteropathy (cont.)	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.
Cryptosporidium	See *Symptomatic treatment* (above)	Indefinitely	See above.	No drug effectively eradicates cryptosporidium.
	Spiramycin (Rovamycin™) 1 gm 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 incidence of *Clostridium difficile* infection.
	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.	Investigational.
Isospora belli	Trimethoprim-sulfamethoxazole (TMP-SMX) 1 double-strength (DS) tablet po qid	21 days	See TMP-SMX under pulmonary.	Usually effective.
PULMONARY				
***Pneumocystis carinii* (PCP)**	*Acute:PCP*			
	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 over 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.	Mild rash does not necessitate stopping or changing treatment: institute antihistamine. Severe toxicity (i.e., Stevens-Johnson syndrome) requires drug discontinuation.
			Hematological: neutropenia, thrombocytopenia, anemia.	If ANC is less than 500 cells/mm³ or if platelet count is less than 30 × 10⁹/L and bleeding occurs, consider alternative treatment.

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Table 1. ***Continued.***

System & Organism	Drug Regimen	Duration	Common Adverse Effects	Comments
PULMONARY ***Pneumocystis carinii*** **(PCP) (cont.)**			GI: nausea, vomiting, toxic hepatitis.	Pretreatment with lorazepam, prochlorperazine, meclopropamide, or tetrahydrocannabinol (THC, Marinol™) to reduce nausea. Nausea may be less with oral TMP-SMX. Hepatic enzyme increase to 4–5 times normal requires treatment change.
			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.	May be due to 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.
	OR			
	Pentamidine isethionate (Pentam™) 4 mg/kg 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 may decrease incidence of hypotension. Check blood pressure at end of infusion.
			Hypoglycemia; hyperglycemia.	Early or delayed hypoglycemia (may 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.	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.

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Table 1. ***Continued.***

System & Organism	Drug Regimen	Duration	Common Adverse Effects	Comments
PULMONARY				
Pneumocystis carinii **(PCP) (cont.)**			Rarely: neutropenia, thrombocytopenia; hypocalcemia, hypomagnesemia; hepatitis, pancreatitis; cardiac arrhythmias.	
	Alternative acute PCP therapy			
	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 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.
	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.
	Prophylaxis/suppression of PCP for patients with prior PCP or CD4+ < 200 cells/mm³			
	TMP-SMX 1 DS tablet po qd 3 times per week (e.g., M-W-F) or 1 DS po qd or bid	Indefinitely	See TMP-SMX above.	Three-day-per-week regimen may be best tolerated. Multiple TMP-SMX dosing regimens have been used and all are effective. No efficacy comparisons exist between current dosing regimens.

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Table 1. *Continued.*

System & Organism	Drug Regimen	Duration	Common Adverse Effects	Comments
PULMONARY	OR			
***Pneumocystis carinii* (PCP) (cont.)**	Inhaled pentamidine (Aeropent™) 300 mg q 4 weeks or 150 mg/kg 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 is 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/IV injections of pentamidine 4 mg/kg can be considered if other options are not available.
	OR			
	Dapsone 50–100 mg po daily	Indefinitely	See dapsone plus TMP above.	Probably as effective as TMP-SMX; may be less toxic.
	OR			
	Pyrimethamine-sulfadoxine (Fansidar™) 1 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. Drug toxicity can outweigh potential benefits of empiric therapy or limit chronic prophylaxis therapy. Leucovorin may delay onset of bone marrow toxicity.
	PLUS			
	Pyrimethamine 75–100 mg po loading dose, then 25–75 mg po qd			
	PLUS			
	Leucovorin calcium (folinic acid) 10–25 mg po qd			
	If sulfa allergy			
	Pyrimethamine 25–100 mg po qd	Same	Same.	Same.
	PLUS			
	Clindamycin (Cleocin™) 600–900 po or IV qid		Nausea, vomiting, diarrhea, abdominal cramps.	

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Table 1. ***Continued.***

System & Organism	Drug Regimen	Duration	Common Adverse Effects	Comments
CENTRAL NERVOUS SYSTEM				
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	6 weeks or total of 1.5–2 g	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.
	OR			
	Amphotericin B with or without 5-flucytosine (as above) followed by fluconazole 400 mg po qd	6–8 weeks total; amphotericin B for first 2–4 weeks or until clinically improved		
	Mild or asymptomatic disease or inability to tolerate amphotericin B			
	Fluconazole *Acute:* 400 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.
	Maintenance: 200 mg po qd	Indefinitely		
	OR			
	Amphotericin 0.5–0.8 mg/kg/d 3–5 times a week	Indefinitely	See above.	
CNS Syphilis	Aqueous crystalline penicillin G 2–4 mIU IV q 4 hr (total 12–24 mIU per day)	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 mIU IM qd	10 days	Same.	
	plus			
	Probenecid 500 mg po qid		Probenecid rash.	

underlying disease. Withdrawal of offending agents is often the only way to make this diagnosis. Because patients use nonprescription (unapproved) and other experimental drugs, a careful drug history is important.

References

A selected bibliography supplements the material in Table 1. Included are additional articles with management and therapeutic implications.[27-32] Further clinical guidance and extensive bibliographies can be found in other articles, texts,[33-35] and computer-based information systems.[36]

References

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