Current Report—HIV

Recommendations for Treatment of Acute *Pneumocystis carinii* Pneumonia

Ronald H. Goldschmidt, M.D.

Pulmonary disease remains the most common cause of morbidity and mortality in AIDS, but it is also the most treatable complication. *Pneumocystis carinii* pneumonia (PCP), bacterial pneumonias, pulmonary tuberculosis, fungal infections, and other opportunistic infections must be considered in the differential diagnosis and treated promptly.[1] Kaposi's sarcoma and lymphoma, although not readily treated, may also cause pulmonary decompensation.

The focus of attention for pulmonary disease in AIDS is principally on the diagnosis and treatment of *Pneumocystis carinii* pneumonia. *Pneumocystis carinii* is an organism of controversial classification because it has properties characteristic of both a fungus and parasite.[1] *Pneumocystis carinii* is the cause of AIDS pulmonary disease in approximately 85 percent of the patients, either alone or in combination with other processes. *Pneumocystis carinii* pneumonia is usually characterized by fever, shortness of breath, tachypnea, and dry cough. Although the symptoms of acute PCP usually evolve over days to weeks, severe respiratory decompensation can develop within 24 to 48 hours after the onset of symptoms.

The diagnosis of PCP is usually made by examination of specimens obtained at bronchoscopy with bronchoalveolar lavage or biopsy. At medical centers where there has been substantial experience with PCP, sputum induction techniques are highly reliable in establishing the diagnosis of PCP. Purulent sputum makes bronchoscopic examination for PCP technically difficult and diminishes the diagnostic yield of sputum induction. An open lung biopsy is rarely required to make the diagnosis of PCP. Fortunately, the organism can be detected for weeks after the initiation of therapy. Therefore, empiric treatment of acute PCP can be given without diminishing the yield from diagnostic procedures.

Withholding treatment for PCP until a definitive diagnosis can be made is only appropriate when symptoms are mild (such as mild dyspnea or nonproductive cough), when concern about drug toxicity is great, when definitive diagnostic tests can be completed within a day, and when evaluating an abnormal chest radiograph in a patient without significant respiratory signs or symptoms. Otherwise, empiric therapy followed by expeditious diagnostic evaluation is usually advisable.

Indications for immediate empiric treatment for PCP include: substantial shortness of breath, tachypnea, and either marked fever or a toxic appearance in combination with an abnormal chest radiograph. In some patients, the decision to withhold treatment pending diagnostic tests

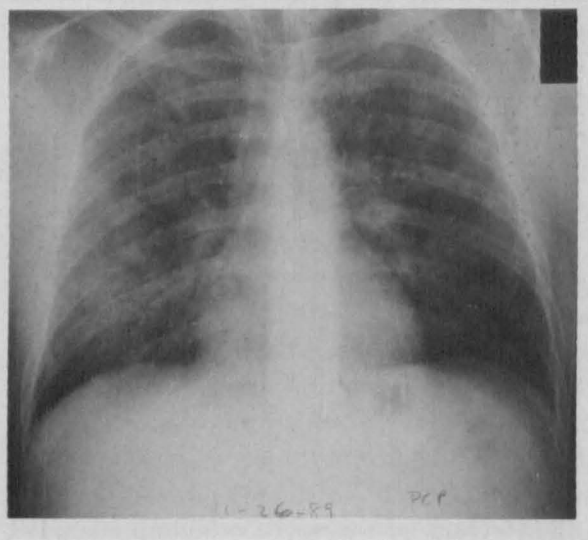

Figure 1. Posteroanterior chest radiograph of a patient with *Pneumocystis carinii* pneumonia showing diffuse bilateral retucular infiltration.

From the Family Practice Residency Program, San Francisco General Hospital. Address reprint requests to Ronald H. Goldschmidt, M.D., Director, Family Practice Inpatient Service, 1001 Potrero Avenue, San Francisco, CA 94110.

Supported in part by Grant No. BRT 000006-03-1, with the Bureau of Health Professions, Health Resources and Services Administration, Department of Health and Human Services.

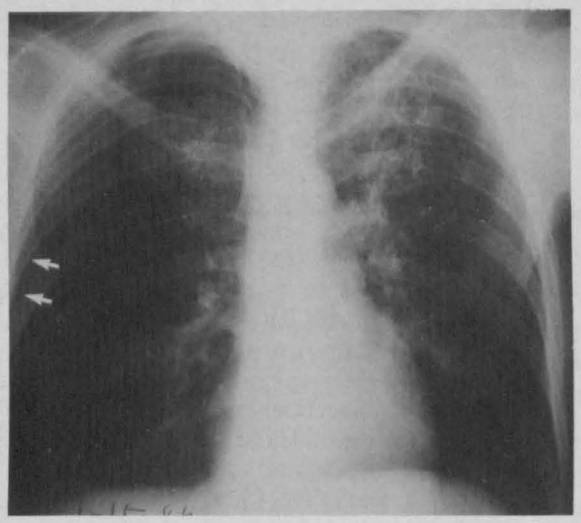

Figure 2. Posteroanterior chest radiograph of a patient with *Pneumocystis carinii* pneumonia showing asymmetric reticular infiltration and a pneumothorax (arrows). Pneumothorax occurs most commonly with *Pneumocystis carinii* pneumonia, especially in patients receiving aerosolized pentamidine prophylaxis.

or to treat empirically is not obvious. Arterial blood gas measurements can provide additional guidance. Significant hypoxemia, with a PaO_2 less than 80 mmHg on room air, is a reasonable threshold to justify immediate therapy. Chest radiographs in patients with PCP are usually abnormal (Figures 1,2), but normal findings are present in 5–10 percent of patients.

Treatment of acute PCP is with trimethoprim-sulfamethoxazole or with pentamidine (Table 1). Trimethoprim-sulfamethoxazole is usually the drug of first choice because it is also effective against most pulmonary bacterial pathogens, whereas pentamidine is not. Both drugs appear equally effective and equally toxic. Although toxicities from either drug may occur in as many as 50 percent of patients, most cases require careful monitoring and dosage adjustment rather than discontinuation of the drug. Modest degrees of hepatotoxicity and nephrotoxicity can usually be corrected by decreasing the dosage or temporarily discontinuing the drug.[2] Severe allergic reactions (such as the Stevens-Johnson syndrome) and drug fevers (which may be difficult to diagnosis in the face of active acute pulmonary disease) necessitate changing to the alternative drug. Dapsone plus trimethoprim can be used to treat acute PCP, but most successful use of this drug combination has been reported for mild PCP.[3]

Table 1. Treatment of Acute *Pneumocystis carinii* Pneumonia.

Drug	Dosage
Trimethoprim-sulfamethoxazole (Septra™, Bactrim™)	15 mg TMP/75 mg SMX per kg daily given in 3–4 doses po or as 1–2 hour IV infusion
or	
Pentamidine isethionate (Pentam™)	4 mg per kg daily as 1–2 hour IV infusion once daily
For patients with $PaO_2 \leq 70$ mmHg add	
Methylprednisolone (IV) or Prednisone (po)	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)

Treatment should be continued for 3 weeks. Although a 3-week course of antibiotics is generally recommended, some authorities believe that 2 weeks of therapy is adequate in some cases because chronic suppressive therapy after acute PCP (secondary prophylaxis) is now standard.[1] Prophylaxis against PCP[4,5] can be with aerosolized pentamidine, oral trimethoprim-sulfamethoxazole, or dapsone. There are no studies comparing these prophylactic regimens. Aerosolized pentamidine is most commonly used in the United States.

Recently, there has been an important change in recommendations for treatment of acute *Pneumocystis carinii* pneumonia. Based on published[6-8] and unpublished studies, it is recommended that when significant hypoxemia is present, corticosteroids be used concurrently with antimicrobial drugs in the treatment of acute *Pneumocystis carinii* pneumonia (Table 1).[9,10] A trend toward faster resolution of PCP, reduced need for mechancially assisted ventilation, fewer deaths, and better long-term outcomes was noted for selected patients treated with corticosteroids. Patients with a PaO_2 less than or equal to 70 mmHg on room air appeared to benefit most. Withholding corticosteroids until late in the course of severe PCP when PaO_2 values are less than 50 mmHg (salvage therapy) was not shown to be effective.

Indications for hospitalization include respiratory distress, severe hypoxemia, and high fevers. In addition, when the diagnosis of acute

pulmonary disease is the initial (index) AIDS-defining diagnosis, admission to the hospital for medical monitoring and psychological support is appropriate.

I wish to acknowledge Mary A. Hanville for her thoughtful comments and Philip C. Goodman, M.D., for the chest radiographs.

References

1. Murray JF, Mills J. Pulmonary infectious complications of human immunodeficiency virus infection. Am Rev Respir Dis 1990; 141:1356-72, 1582-98.
2. Sattler FR, Cowan R, Nielsen DM, Ruskin J. Trimethoprim-sulfamethoxazole compared with pentamidine for treatment of *Pneumocystis carinii* pneumonia in the acquired immunodeficiency syndrome: a prospective, noncrossover study. Ann Intern Med 1988; 109:280-7.
3. Medina I, Mills J, Leoung G, et al. Oral therapy for *Pneumocystis carinii* pneumonia in the acquired immunodeficiency syndrome: a controlled trial of trimethoprim-sulfamethoxazole versus trimethoprim-dapsone. N Engl J Med 1990; 323:776-82.
4. Goldschmidt RH. Prophylaxis against *Pneumocystis carinii* pneumonia. J Am Board Fam Pract 1989; 2:153-4.
5. Guidelines for prophylaxis against *Pneumocystis carinii* pneumonia for persons with human immunodeficiency virus infection. MMWR 1989; 38(Suppl S-5): 1-9.
6. Montaner SG, Lawson LM, Levitt N, et al. Corticosteroids prevent early deterioration in patients with moderately severe *Pneumocystis carinii* pneumonia and the acquired immunodeficiency syndrome (AIDS). Ann Intern Med 1990; 113: 14-20.
7. Gagnon S, Boota AM, Fischl MA, Baier H, Kirksey OW, La Voie L. Corticosteroids as adjunctive therapy for severe *Pneumocystis carinii* pneumonia in the acquired immunodeficiency syndrome: a double-blind, placebo-controlled trial. N Engl J Med 1990; 323:1444-50.
8. Bozzette SA, Sattler FR, Chiu J, et al. A controlled trial of early adjunctive treatment with corticosteroids for *Pneumocystis carinii* pneumonia in the acquired immunodeficiency syndrome. N Engl J Med 1990; 323:1451-7.
9. Kovacs JA, Masur H. Are corticosteroids beneficial as adjunctive therapy for *Pneumocystis carinii* pneumonia in AIDS? Ann Intern Med 1990; 113:1-3.
10. The National Institutes of Health—University of California Expert Panel for Corticosteroids as Adjunctive Therapy for *Pneumocystis carinii* Pneumonia. Consensus statement on the use of corticosteroids as adjunctive therapy for *Pneumocystis carinii* pneumonia in the acquired immunodeficiency syndrome. N Engl J Med 1990; 323:1500-4.