lung disease, a low serum albumin level, the need for mechanical ventilation, and the development of pneumothorax. With advances in supportive critical care, the prognosis for patients with PCP who require intubation and respiratory support has improved and now depends to a large extent on comorbidities and the prognosis of the underlying disease. Since patients typically do not respond to therapy for 4–8 days, supportive care for a minimum of 10 days is a reasonable consideration if such support is compatible with the patient's wishes and the prognosis of comorbidities. Patients whose condition continues to deteriorate after 3 or 4 days or has not improved after 7–10 days should be reevaluated to determine whether other infectious processes are present (either having been missed on initial evaluation or having developed during treatment) or whether noninfectious processes (e.g., congestive heart failure, pulmonary emboli, pulmonary hypertension, drug toxicity, or a neoplastic process) are causing pulmonary dysfunction.

TREATMENT *P. JIROVECII* PNEUMONIA

The treatment of choice for PCP is trimethoprim-sulfamethoxazole (TMP-SMX), given either IV or PO for 14–21 days **(Table 244-1)**. TMP-SMX, which interferes with the organism's folate metabolism, is at least as effective as alternative agents and is better tolerated. However, TMP-SMX can cause leukopenia, hepatitis, rash, and fever as well as anaphylactic and anaphylactoid reactions, and patients with HIV infection have an unusually high incidence of hypersensitivity to TMP-SMX. Monitoring of serum drug levels is useful if renal function or toxicities are issues. Maintenance of a 2-h post-dose sulfamethoxazole level of 100–150 μg/mL has been associated with a successful outcome. Resistance to TMP-SMX cannot be measured by organism growth inhibition in the laboratory because *Pneumocystis* cannot be cultured. However, mutations in the target gene for sulfamethoxazole that confer in vitro sulfa resistance to other organisms have been found in *Pneumocystis*. The clinical relevance of these mutations for the response to therapy is unknown. Sulfadiazine plus pyrimethamine, an oral regimen more often used for treatment of toxoplasmosis, also is highly effective. Dapsone plus pyrimethamine or dapsone plus trimethoprim also can be used.

Intravenous pentamidine or the combination of clindamycin plus primaquine is an option for patients who cannot tolerate TMP-SMX and for patients in whose treatment TMP-SMX appears to be failing. Pentamidine must be given IV over at least 60 min to avoid potentially lethal hypotension. Adverse effects can be severe and irreversible and include renal dysfunction, dysglycemia (life-threatening hypoglycemia that can occur days or weeks after initial infusion and be followed by hyperglycemia), neutropenia, and torsades des pointes. Clindamycin plus primaquine is effective, but primaquine can be given only by the oral route—a disadvantage for patients who cannot ingest or absorb oral drugs.

A major advance in therapy for PCP was the recognition that glucocorticoids could improve survival rates among HIV-infected patients with moderate to severe disease (room air PO_2, <70 mmHg; or alveolar-arterial oxygen gradient, ≥35 mmHg). Glucocorticoids appear to reduce the pulmonary inflammation that occurs after specific therapy is started and organisms begin to die, eliciting inflammation. Therapy with glucocorticoids should be the standard of care for patients with HIV infection and probably is also effective for patients with other immunodeficiencies. This treatment should be started for moderate or severe disease when therapy for PCP is initiated, even if the diagnosis has not yet been confirmed. If HIV-infected or HIV-uninfected patients are receiving high-dose glucocorticoids when they develop PCP, there are theoretical advantages to increasing or decreasing the steroid dose, but there is no convincing evidence on which to base any specific strategy.

No definitive trials have defined the best therapeutic algorithm for patients in whom TMP-SMX treatment for PCP is failing. If no other treatable infectious or noninfectious processes are detected and pulmonary dysfunction appears to be due to PCP alone, many authorities would switch from TMP-SMX to either IV pentamidine or IV clindamycin plus oral primaquine. Some authorities would add the second drug or drug combination to TMP-SMX rather than switching regimens. If patients are not already receiving them, glucocorticoids should be added to the regimen; the dosage and regimen, which are usually chosen empirically, depend on what glucocorticoid regimen (if any) the patient was receiving when PCP therapy was begun.

For patients with HIV infection who present with PCP before the initiation of ART, ART should be started within the first 2 weeks of therapy for PCP in most cases. Immune reconstitution inflammatory syndrome (IRIS) can occur, however, and the decision to initiate ART thus requires considerable expertise in terms of optimal timing relative to PCP recovery as well as in the other factors that are relevant when ART is initiated in any patient.

TABLE 244-1 TREATMENT OF PNEUMOCYSTOSIS (14–21 DAYS)

Drug(s)	Dose, Route	Adverse Effects
First-Choice Agent		
TMP-SMX	TMP (5 mg/kg) plus SMX (25 mg/kg) q6–8h PO or IV (2 double-strength tablets tid or qid)	Fever, rash, cytopenias, hepatitis, hyperkalemia
Alternative Agents		
TMP ***plus*** Dapsone	5 mg/kg q6–8h PO 100 mg qd PO	Hemolysis (G6PD deficiency), methemoglobinemia, rash, fever, gastrointestinal disturbances
Atovaquone	750 mg bid PO	Rash, fever, hepatitis
Clindamycin ***plus*** Primaquine	300–450 mg q6h PO or 600 mg q6–8h IV 15–30 mg qd PO	Hemolysis (G6PD deficiency), methemoglobinemia, neutropenia, rash
Pentamidine	3–4 mg/kg qd IV	Hypotension, azotemia, cardiac arrhythmias (torsades des pointes), pancreatitis, dysglycemias, hypocalcemia, neutropenia, hepatitis
Adjunctive Agent		
Prednisone or methylprednisolone	40 mg bid × 5 d, 40 mg qd × 5 d, 20 mg qd × 11 d; PO or IV	Peptic ulcer disease, hyperglycemia, mood alteration, hypertension

Abbreviations: G6PD, glucose-6-phosphate dehydrogenase; TMP-SMX, trimethoprim-sulfamethoxazole.

PREVENTION

The most effective method for preventing PCP is to eliminate the cause of immunosuppression by withdrawing immunosuppressive therapy or treating the underlying cause, e.g., HIV infection. Patients who are susceptible to PCP benefit from chemoprophylaxis during the period of susceptibility. For patients with HIV infection, CD4+ T cell counts are a reliable marker of susceptibility, and counts below 200 cells/μL are an indication to start prophylaxis **(Table 244-2)**. For patients with HIV infection who are not receiving ART, oral candidiasis or prior PCP also is an indication for chemoprophylaxis, regardless of CD4+ T cell count. For such patients not receiving ART, any prior episode of an AIDS-defining illness or pneumonia should encourage the use of chemoprophylaxis. However, patients who are not adherent to ART are not likely to take PCP chemoprophylaxis.

For patients without HIV infection, there is no laboratory parameter, including the CD4+ T cell count, that predicts susceptibility to PCP with adequate positive and negative accuracy. The period of susceptibility is usually estimated on the basis of experience with the