R.J. is a 34-year-old female with non-Hodgkin’s lymphoma who completed her third course of cyclophosphamide, doxorubicin, vincristine, and prednisone 13 days ago. She presents to the inpatient unit with a fever of 101.4°F, blood pressure of 92/54 mm/Hg, apical pulse of 104 beats per minute, respiratory rate of 24 breaths per minute, and arterial blood oxygen saturation of 96% on room air. Physical examination is within normal limits. No adventitious sounds are noted on chest auscultation; however, she does have a nonproductive cough. In addition to blood and urine cultures, a complete blood count with differential, serum electrolytes, lactate dehydrogenase (LDH), a complete metabolic panel, and a hepatic panel are sent to the laboratory. She is started on ceftriaxone and vancomycin. A portable chest x-ray indicates no abnormalities. Laboratory results include a white blood cell count of 2,400/mm³ with 45% neutrophils and 1% bands, absolute neutrophil count of 1,104/mm³, hemoglobin of 11 g/dl, platelet count of 110,000/mm³, and LDH of 3,245 U/ml. Serum electrolytes, liver enzymes, and urinalysis are within normal limits.

After four days of therapy, R.J. continues to have temperature spikes above 100.5°F. Blood cultures show no growth after 72 hours. Amphotericin B and acyclovir are added to the treatment schedule. A follow-up chest x-ray returns to baseline after two weeks of treatment (see Figure 2).

Pathophysiology

*Pneumocystis carinii* is a fungal infection that is present naturally in the environment (Armstrong & Bernard, 2000; Frame & Wilkin, 2002). Serologic studies indicate that exposure can occur in children as young as two years (Centers for Disease Control and Prevention, 1992; Frame & Wilkin; Kovacs, Gill, Meshnick, & Masur, 2001), and more than 80% of adults have antibodies to *Pneumocystis carinii* pneumonia (PCP). Active cases of PCP may result from reactivation of a latent infection or reinfection with a different strain of the organism. Infection with multiple strains has been noted in 20%–30% of patients with PCP (Agostoni et al., 2000; Beard et al., 2000; Kovacs et al., 2001). The underlying pathophysiology of *P. carinii* also is unknown. The organism possibly attaches to areas on alveolar macrophages, and in binding to type I alveolar epithelial cells, the basement membrane degenerates and normal surfactant function is impaired. An eosinophilic, foamy exudate develops that fills the alveolar space and leads to impaired gas exchange. Although rare, bullous cavities may develop, usually in the lower lung lobe consolidation.

**Key Words:** pneumonia, pneumocystis carinii; HIV; anti-infective agents
apices of the lung. Rupture of these cysts can lead to pneumothorax. Individuals who have had prior PCP or present with profound HIV-related immunodeficiency may exhibit an extrapulmonary disease presentation with or without PCP. Extrapulmonary disease is rare and most likely results from the invasion of pulmonary vessels by P. carinii and hematogenous spread. Organs most frequently involved in extrapulmonary disease are the lymph nodes, spleen, liver, and bone marrow. Cutaneous nodules on the cranium or fluffy, white retinal exudates without associated hemorrhage also may be present (Beard et al., 2000).

Incidence and Risk Factors

P. carinii has been identified as the most common AIDS-defining opportunistic infection in the United States and is a common cause of HIV-associated pneumonia (Murray & Nadel, 2000). Adults and adolescents with HIV and CD4+ T lymphocyte counts less than 200 m/l, children with HIV regardless of their CD4+ T lymphocyte count, and newborns of HIV-infected mothers are at risk for PCP (Armstrong & Bernard, 2000).

Although most of the current literature about PCP is based on patients with HIV because they experience PCP more commonly, the immunosuppressed patient population is another high-risk group. In the non-HIV infected population, patients with cancer and related immunosuppression, severe protein-calorie malnutrition, oral candidiasis, and prolonged systemic corticosteroid therapy are at risk for developing PCP (see Figure 3).

Clinical Presentation

Presenting symptoms are vague and typically include fever, nonproductive cough, and dyspnea on exertion. Dyspnea at rest is an indication of disease progression. Chills, night sweats, purulent sputum, pleuritic chest pain, and diarrhea are uncommon but can occur. HIV-positive patients tend to have a subtle and prolonged clinical presentation and usually seek treatment after three to six weeks of subacute symptomatology. HIV-negative immunosuppressed patients tend to have a more pronounced inflammatory response and present for therapy within a week of symptom development. Unexplained anemia, adenopathy, hepatosplenomegaly, or external auditory canal lesions may be caused by extrapulmonary pneumocystis (Aurora, Milite, & Vander Els, 2000; Frame & Wilkin, 2002; Kovacs et al., 2001; Murray & Nadel, 2000).

Clinical presentation is categorized as “mild” PCP in patients presenting with an alveolar oxygen partial pressure (PaO2) greater than 70 mm Hg and an alveolar-arterial partial pressure of oxygen (PO2) difference of less than 35 mm Hg or “moderate to severe” PCP with a PaO2 less than or equal to 70 mm Hg or alveolar-arterial PO2 difference greater than or equal to 35 mm Hg (Murray & Nadel, 2000). Hypoxemia and hypercapnia because of alveolar hyperventilation are almost always present (Frame & Wilkin, 2002). Pulmonary function testing usually indicates a restrictive defect with decreased lung volumes and increased airflow. A low-diffusing capacity for carbon monoxide (i.e., diffusion lung carbon monoxide level less than or equal to 75% of predictive values) is seen in approximately 90% of patients (Aurora et al., 2000). Desaturation with exercise is strongly predictive of PCP.

Diagnosis

Chest x-ray commonly reveals diffuse, bilateral, symmetrical interstitial or alveolar infiltrates that usually are present in the lower lobes. Rare radiologic findings may include asymmetric or unilateral infiltrates. A normal chest x-ray may be present in 10%–30% of patients with PCP (Armstrong & Bernard, 2000; Frame & Wilkin, 2002). Consolidation, cavitation, and pleural effusions are rare. Occasional intrathoracic adenopathy may be present. Computed tomography (CT) is not indicated routinely but may assist in demonstrating patchy or nodular ground-glass attenuation. Although a gallium scan is a sensitive test that has been used to diagnosis PCP, it may produce nonspecific results.

Hematologic studies are nonspecific. Anemia, neutropenia, thrombocytopenia, and lymphopenia may be present because of HIV infection or immunosuppression following chemotherapy. The presence of leukocytosis may indicate a coexisting bacterial infection. HIV-positive patients present with depressed CD4+ lymphocyte counts. Serum chemistry findings also are nonspecific; however, elevated lactate LDH levels do occur in patients with PCP. Although not specific for PCP, a normal LDH value makes the diagnosis unlikely.

Because of PCP’s vague clinical presentation, differential diagnoses include a variety of conditions such as bacterial infection, drug toxicity, fungal infection, lymphoid interstitial pneumonitis (in children), neoplasms, pulmonary Kaposi’s sarcoma, tuberculosis, and viral infections (e.g., cytomegalovirus) (Armstrong & Bernard, 2000; Dambro, 2001; Frame & Wilkin, 2002; Murray & Nadel, 2000). Although any of the following symptoms may be present in patients with PCP, further workup should be conducted to rule out PCP.
out alternative processes: The presence of purulent sputum, pleuritic chest pain, or severe chills may be indicative of bacterial pneumonia or tuberculosis. Bacterial or fungal pneumonia, tuberculosis, or pulmonary Kaposi’s sarcoma may present with intrathoracic adenopathy or pleural effusion. Transbronchial or lung biopsy is helpful in detecting cytomegalovirus, drug toxicity, lymphocytic interstitial pneumonia, and solid tumors. Additionally, any of these conditions may coexist with PCP. For example, the presence of leukocytosis is unusual and may indicate a coexisting bacterial infection.

Definitive diagnosis of PCP is dependent on demonstrating the presence of P. carinii in pulmonary secretions or lung tissue. Sputum induction, tracheobronchial suction, bronchoalveolar lavage, or lung biopsy may be used to obtain cytologic specimens. Induced sputum usually is nondiagnostic in non-HIV immunosuppressed patients because of a lower organism burden. Biopsy of involved tissue assists in extrapulmonary tissue diagnosis (see Figure 4).

Prophylaxis and Treatment

Prophylactic PCP management is recommended for HIV-positive patients with a CD4+ T lymphocyte count less than 200 m/l or a history of oropharyngeal candidiasis and

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<td>Bronchoscopy with bronchoalveolar lavage with or without biopsy</td>
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**Figure 4. Diagnostic Workup**

• Biopsy may not be possible in patients with cancer with thrombocytopenia or coagulopathy.

**Note:** Based on information from Agostoni et al., 2000; Armstrong & Bernard, 2000; Frame & Wilkin, 2002; Kovacs et al., 2001; Murray & Nadel, 2000.

**When to initiate treatment**

• HIV infection
  - CD4+ T lymphocyte count less than 200 m/l or history of oropharyngeal candidiasis or
  - Non-HIV patients receiving corticosteroids of 20 mg per day or more

**Consider treating**

• CD4+ T lymphocyte percentage less than 14% or history of an AIDS-defining illness but do not otherwise qualify for prophylaxis
• When not possible to monitor counts at least every three months, initiate at CD4+ T lymphocyte more than 200 but less than 250 m/l
• Patients with anticipated prolonged neutropenia

**Primary therapy**

• Trimethoprim-sulfamethoxazole (TMP-SMX), one double-strength dose, orally (PO) every day or TMP-SMX, one single-strength dose, PO every day

**Alternative therapies**

• Dapsone 50 mg PO twice a day or 100 mg PO daily
• Dapsone 50 mg PO daily, pyrimethamine 50 mg PO every week, and leucovorin 25 mg PO every week
• Dapsone 200 mg PO, pyrimethamine 75 mg PO, and leucovorin 25 mg every week
• Aerosolized pentamidine 300 mg every morning via Respigrad II™ Nebulizer (Marquest Medical Products, Inc., Englewood, CO)
• Atovaquone 1,500 mg PO daily
• TMP-SMX, one double-strength dose, PO three times a week

**Figure 5. Primary Prophylaxis of Pneumocystis Carinii Pneumonia**


When treatment is for secondary prophylaxis, treatment should continue because research is inconclusive regarding the withdrawal of therapy (“1999 USPHS/IDSA Guidelines”). For patients receiving corticosteroids, prophylactic therapy should continue for one month after completion (Armstrong & Bernard, 2000; Russian & Levine, 2001).

Treatment of active disease is similar to chemoprophylaxis. The preferred therapy is TMP-SMX administered every eight hours via IV at a dose of TMP 5 mg and SMX 25 mg. Oral regimens consisting of two double-strength tablets every eight hours also may be implemented. Duration of treatment varies. HIV-negative and HIV-positive patients should receive treatment for 14 days and 21 days, respectively (Armstrong & Bernard, 2000; Frame & Wilkin, 2002). Patients who are allergic to TMP-SMX can be treated with IV pentamidine while being desensitized to SMX over three to seven days. Individuals who cannot tolerate TMP-SMX may be treated with several alternative therapies, including pentamidine, trimetrexate plus leucovorin, clindamycin plus primaquine, and atovaquone (Armstrong & Bernard; Frame & Wilkin). However, patients receiving atovaquone have a high frequency of therapeutic failure, possibly because of poor oral absorption (see Figure 6).
Nursing Implications

Patients with HIV, with neutropenia, or who have had prolonged treatment with corticosteroids or prolonged immunosuppression (i.e., following bone marrow transplantation) should be assessed for the development of PCP. Because symptoms are insidious, a prolonged fever that is unresponsive to antibiotics and associated with a nonproductive cough and dyspnea on exertion may indicate infection. In the HIV population, close monitoring of CD4+ lymphocyte counts can alert clinical staff to the need for prophylaxis. In the non-HIV population, prophylaxis should be considered with prolonged neutropenia.

In addition to close patient assessment, nursing staff may be the first to identify and intervene when untoward side effects of prophylaxis and treatment develop. TMP-SMX may lead to the development of neutropenia, a rash, nausea, or hypersensitivity to the sulfonamide component. Patients allergic to the sulfonamide component of TMP-SMX also may lead to the development of neutropenia, rash, nausea, or hypersensitivity to the sulfa component. Patients allergic to the sulfa component of TMP-SMX also may lead to the development of neutropenia. Nursing assessment should include evaluation of respiratory status, presence and productivity of cough, and presence of dyspnea. In addition to physician assessment, nurses should review available pulmonary function and laboratory (i.e., LDH) studies.

Education is an important component in the treatment of patients with PCP. Because treatment is long-term, patients may consider stopping treatment for a variety of reasons. Education should focus on the rationale for the duration of therapy and potential consequences of discontinuing therapy early. Because of the cost of therapy, nurses also may provide information on available financial or pharmaceutical resources.

References


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Conclusion

Untreated PCP typically leads to increasing pulmonary complications and death. Mortality in the HIV population ranges from 15%–20% (Frame & Wilkin, 2002). In addition, non-HIV patients with cancer or patients who use corticosteroids for a prolonged period of time are also at risk for developing PCP. Persistent symptoms in patients at risk for developing PCP should prompt a thorough assessment and workup of the diagnosis.

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Figure 6. Alternative Treatment of Active Disease


