Prophylaxis for Pneumocystis Pneumonia (PCP) in non-HIV infected patients

Pneumocystis pneumonia (PCP) is a potentially life-threatening opportunistic infection that occurs in immunocompromised individuals and is caused by Pneumocystis Jiroveci (formerly known as Pneumocystis carinii), a ubiquitous organism that is classified as a fungus, but also shares biologic characteristics with protozoa. P. Jiroveci was first recognized as a pathogen in severely malnourished and premature infants developing an epidemic form of interstitial plasma cell pneumonitis in Central and Eastern European countries during the Second World War. PCP is the most common opportunistic infection in HIV-infected patients and very often the AIDS-defining illness. Apart from seropositive individuals, patients receiving chronic immunosuppressive medication or those who have an altered immune system are considered to be at high risk for PCP. In the absence of appropriate antibiotic therapy, the mortality rate from PCP in non-HIV-infected patients is 90 to 100 percent. PCP rarely occurs in patients without apparent immunodeficiency.

Patients who are not infected with HIV but are receiving immunosuppressive medications or who have an underlying acquired or inherited immunodeficiency should receive prophylaxis against pneumocystis pneumonia, as it appears to dramatically lower the risk of disease in susceptible populations. There are no published guidelines for PCP prophylaxis among patients with rheumatologic diseases receiving immunosuppressive drugs, but some suggest PCP prophylaxis when they are receiving high-dose immunosuppressive therapy. The most significant risk factors for PCP in patients without HIV infection are glucocorticoid use and defects in cell-mediated immunity.

PCP usually develops within one month of glucocorticoids administration, with a median dose of prednisone 30 mg/day, but some patients develop PCP with as little dose as 16 mg/day. The median duration of glucocorticoid therapy before the development of PCP in a series of 116 patients in Mayo Clinic was 12 weeks, but 25 percent of patients had been receiving glucocorticoids for ≤8 weeks.

Risk factors warranting prophylaxis for PCP are listed below:

1. Glucocorticoid dose equivalent to ≥20 mg of prednisone daily for one month or longer plus another cause of immunocompromise.
2. Combination of immunosuppressive drugs, such as TNF-α inhibitors plus high dose glucocorticoids or other immunosuppression.
3. Treatment of polymyositis/dermatomyositis with interstitial pulmonary fibrosis with glucocorticoids.

4. Certain primary immunodeficiencies (severe combined immunodeficiency, idiopathic CD4 T-lymphocytopenia, hyper-IgM syndrome).

5. Patients with rheumatologic diseases, receiving ≥20 mg of prednisone daily for one month or longer in combination with a second immunosuppressive drug.

6. Patients with granulomatosis with polyangiitis [Wegener’s] receiving methotrexate in combination with high doses of glucocorticoids.


8. Allogeneic or autologous hematopoietic stem cell transplantation.

9. Solid organ transplantation and antirejection medications.

10. Treatment with a purine analog (fludarabine, another T-cell depleting agent).

11. Severe malnutrition (especially protein malnutrition).

**Trimethoprim-sulfamethoxazole (TMP-SMX)** is the first-line agent used for PCP prophylaxis due to its high efficacy. It can be administered as one double-strength tablet daily or three times a week or as one single-strength tablet daily. In patients who cannot tolerate the use of TMP-SMX there must be an attempt of desensitization. If the patient cannot tolerate TMP-SMX, alternatively can be administered atovaquone, dapsone with or without pyrimethamine, pentamidine, clindamycin plus primaquine or sulfadoxine plus pyrimethamine (table 1).

Prophylaxis can often be discontinued after the risk factors for the disease, such as significant dose systemic corticosteroid or other immune suppressant agents are no longer present. However, it should be kept in mind that the immunosuppressed state can persist for months after discontinuation of some cytotoxic agents, such as cyclophosphamide.

Caution is needed regarding PCP prophylaxis in patients with **systemic lupus erythematosus** (SLE), since there are data suggesting that sulfonamide-containing antibiotics, including TMP-SMX, can cause exacerbations of SLE, particularly in patients with adverse reactions to these agents. Atovaquone is suggested as an alternative agent.

**REFERENCES**


17. Suryaprasad A, Stone JH. When is it safe to stop Pneumocystis

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**TABLE 1.** Regimens for PCP prophylaxis

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Adverse reactions</th>
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<tbody>
<tr>
<td><strong>TMP-SMX</strong></td>
<td>1 double strength tbl daily</td>
<td>Fever, rash, neutropenia, elevation of transaminases</td>
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<tr>
<td></td>
<td>or 1 double strength tbl three times a week</td>
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<tr>
<td></td>
<td>or 1 single strength tbl daily</td>
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</tr>
<tr>
<td>Sir Atovaquone</td>
<td>1500 mg once daily</td>
<td>Rash gastrointestinal, upset</td>
</tr>
<tr>
<td>Dapsone</td>
<td>50 mg twice daily</td>
<td>Fever, rash, hemolytic anemia, methemoglobinemia</td>
</tr>
<tr>
<td></td>
<td>or 100 mg daily</td>
<td></td>
</tr>
<tr>
<td>Aerolized pentamidine</td>
<td>300 mg monthly</td>
<td>Cough, wheezing</td>
</tr>
<tr>
<td>Intravenous pentamidine</td>
<td>4 mg/kg monthly</td>
<td>Nephrotoxicity, hypercalcemia, hypoglycemia, hypotension, pancreatitis, elevation of transaminases</td>
</tr>
<tr>
<td>Clindamycin/ primaquine</td>
<td>600 mg 3-4 times a day/15-30 mg PO</td>
<td>Rash, diarrhea, fever, abdominal pain, hemolytic anemia</td>
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