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ONE MINUTE CONSULT
BRIEF ANSWERS TO SPECIFIC CLINICAL QUESTIONS

Q: When should I give corticosteroids to my patient with *Pneumocystis* pneumonia?

A: Nonpregnant adult patients with human immunodeficiency virus (HIV) and *Pneumocystis jirovecii* (formerly *carinii*) pneumonia (PJP) with hypoxemia should receive early adjunctive corticosteroids, along with anti-*Pneumocystis* therapy. Hypoxemia is defined as oxygen saturation less than 92% on room air, partial pressure of arterial oxygen (PaO_2) less than 70 mm Hg, or an alveolar-arterial oxygen (A-a O_2) gradient of 35 mm Hg or greater. Select patients without HIV infection who have hypoxemia may benefit from early adjunctive corticosteroids, but there is no clear evidence that they should be used routinely.

WHEN SHOULD YOU SUSPECT PJP?

PJP is a fungal infection that most commonly affects immunocompromised persons, such as those with HIV infection, those taking long-term corticosteroids or other immunosuppressive medications, and transplant recipients.[1] PJP should be considered in any immunocompromised patient who presents with fever and dyspnea, with or without nonproductive cough.[2] This is especially important in patients with defects in cell-mediated immunity. Almost all patients with PJP will have hypoxemia at rest or with exertion.

Typical radiographic findings include bilateral, diffuse, perihilar interstitial infiltrates with ground-glass opacities.[3] Diagnosis is typically made by identification of the organism on polymerase chain reaction testing or direct fluorescence antibody staining of a respiratory specimen from a sputum sample, bronchoalveolar lavage fluid, or endotracheal aspirate. If respiratory samples cannot be obtained, significantly elevated serum 1,3-beta-D-glucan—a cell wall component of many fungi, including *Pneumocystis*—and elevated serum lactate dehydrogenase levels can also support a PJP diagnosis in the appropriate clinical and radiographic context.

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SEVERITY OF DISEASE

PJP severity can be classified as mild, moderate, or severe as follows:

- Mild: A-a O_2 gradient of less than 35 mm Hg, PaO_2 greater than or equal to 70 mm Hg, or both
- Moderate: A-a O_2 gradient of 35 mm Hg or greater but less than 45 mm Hg, PaO_2 greater than or equal to 60 but less than 70 mm Hg, or both
- Severe: A-a O_2 gradient greater than or equal to 45 mm Hg, PaO_2 less than 60 mm Hg, or both.[4]

Additional signs pointing to severe disease include fatigue with impending respiratory failure or intubation. Some trials defined disease severity by the hypoxemia ratio, ie, PaO_2 divided by the fraction of inspired oxygen, with mild disease defined as a ratio greater than 350, moderate disease as greater than 250 but less than or equal to 350, and severe disease as less than or equal to 250 but greater than 75.[5]

TREATMENT

The mainstay of treatment of PJP for patients with and without HIV infection is antimicrobial therapy with trimethoprim-sulfamethoxazole (TMP-SMX).[6,7] Dosing of TMP-SMX is typically 15 to 20 mg/kg daily divided into 3 or 4 doses, with oral and intravenous formulations having equal bioavailability.[8] Although TMP-SMX is strongly preferred as first-line PJP treatment, its side

TABLE 1
Recommendations for adjunctive corticosteroids in patients with *Pneumocystis* pneumonia

Patient population	Recommendation
HIV-positive **WITH** baseline hypoxemia	**Strong** recommendation that adjunctive corticosteroids improve outcomes with *Pneumocystis jirovecii* pneumonia treatment
HIV-positive **WITHOUT** baseline hypoxemia	Steroids should be **considered** if respiratory status worsens after *Pneumocystis jirovecii* pneumonia treatment is started
HIV-negative **WITH** hypoxemia or respiratory failure	Steroids should be **considered**—evidence is unclear
HIV-negative **WITH** mild to moderate respiratory disease	Steroids **should not** be given routinely and may result in worse outcomes

HIV = human immunodeficiency virus

Based on information in references 5–13.

effects can include myelosuppression, hyperkalemia, and acute kidney injury. In the case of intolerance, alternatives include dapsone-trimethoprim or clindamycin-primaquine in patients with mild to moderate disease, or clindamycin-primaquine or intravenous pentamidine for patients with moderate to severe disease.[8] The recommended duration of treatment is 21 days, regardless of regimen.[8]

WHAT IS THE EVIDENCE FOR CORTICOSTEROIDS?

Multiple studies suggest that patients with HIV infection and PJP who are hypoxemic should be treated with glucocorticoids. In this clinical scenario, the use of adjunctive corticosteroids in patients with HIV can decrease mortality and respiratory failure associated with PJP, specifically in patients with substantial hypoxemia (moderate or severe disease) at the time of presentation.[5,9–11] Current guidelines suggest that steroids should be initiated within 72 hours of starting anti-*Pneumocystis* therapy in patients with PJP and resting room air oxygen saturation less than 92%, PaO_2 less than 70 mm Hg on room air, or A-a O_2 gradient greater than 35 mm Hg.[8,12] Many clinicians also advocate for giving corticosteroids to patients whose respiratory symptoms worsen after starting anti-*Pneumocystis* therapy. No studies have determined the optimal corticosteroid regimen, but clinicians often administer a 21-day course, starting with prednisone 40 mg twice daily (or equivalent) for 5 days, followed by 40 mg once daily for 5 days, and then 20 mg once daily for 11 days.

There is limited evidence, however, on the role of adjunctive corticosteroids for PJP treatment in patients without HIV. Society guidelines also do not address this topic. A meta-analysis from 2020 found a probable decrease in mortality in patients negative for HIV who had PJP with hypoxemia (PaO_2 < 70 mm Hg) and were treated with adjunctive corticosteroids compared with those not given steroids (odds ratio [OR] 0.69, 95% confidence interval [CI] 0.47–1.01, P = .05).[13] Mortality was significantly lower in patients without HIV who had respiratory failure (PaO_2 < 60 mm Hg) and were treated with adjunctive corticosteroids vs those not given steroids (OR 0.63, 95% CI 0.41–0.95, P = .03). However, the meta-analysis also found increased mortality in a mixed population of HIV-negative patients with PJP treated with adjunctive corticosteroids (OR 1.37, 95% CI 1.07–1.75, P = .01), leading to the conclusion that corticosteroids should be considered for patients without HIV who have hypoxemia or respiratory failure, but not added to PJP treatment for other patients without HIV.[13]

Another retrospective cohort study evaluated PJP treatment in 323 adults without HIV, 80% of whom received adjunctive corticosteroids within the first 48 hours of antimicrobial treatment or PJP diagnosis.[14] After adjusting for baseline hypoxemia severity, the authors found that early corticosteroid administration was associated with less improvement in the Sequential Organ Failure Assessment score at day 5 compared with no steroids (P = .001), indicating a possible negative effect of steroid administration on organ recovery. Adjunctive corticosteroid administration also was not associated with changes in mortality, length of stay, intensive care unit admission, or need for mechanical ventilation,[14] leading to the conclusion that adding corticosteroids to anti-*Pneumocystis* therapy did not benefit patients without HIV.

THE BOTTOM LINE

The data are clear and compelling regarding the use of adjunctive corticosteroids in patients with PJP who are positive for HIV and are hypoxemic on presentation. Based on the currently available evidence, these patients should be started on adjunctive corticosteroids within 72 hours of initiating antimicrobial therapy. Adjunctive corticosteroids should also be considered for HIV-positive patients with PJP who are not hypoxemic at baseline but develop worsening respiratory status after starting anti-*Pneumocystis* therapy.

The data regarding adjunctive corticosteroid therapy for patients with PJP who don't have HIV infection are less robust. There may be a mortality benefit in some HIV-negative patients with PJP who are hypoxemic and have severe respiratory disease, but worse outcomes have been reported in patients without HIV who have mild to moderate disease and are treated with steroids. Corticosteroids should not be routinely used for adjunctive treatment of PJP in patients without HIV. **Table 1** summarizes these recommendations.[5-13]

DISCLOSURES

The authors report no relevant financial relationships which, in the context of their contributions, could be perceived as a potential conflict of interest.

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