Pneumocystis Pneumonia (PCP) Treatment

Pneumocystis pneumonia (PCP) is a fungal pneumonia that occurs in immunocompromised individuals. It may be fatal without prompt therapy. While historically associated with poorly-controlled HIV, PCP is now more commonly seen at the MUHC with other forms of immunodeficiency.

Clinically, individuals with PCP often present with **hypoxemia** (either at rest or with exertion) **and dry-cough**. Fever may occur, but purulent sputum is rare (look for other causes of pneumonia).
Consultation with **Infectious Diseases and Respirology is encouraged** for clinical concerns of PCP.

Risk factors for PCP
Low CD4 lymphocyte counts <200 cells/mm^3 (200 × 10^6 cells/L) for any reason (eg: HIV)
Exposure to medication (antineoplastic therapy, anti-inflammatory, or immunosuppressive treatment) associated with T-cell dysfunction
Use of therapeutic doses of ≥0.3 mg/kg prednisone equivalent for ≥2 weeks in the past 60 days
Solid organ transplant recipient
Glioblastoma multiforme receiving steroids, radiotherapy and temozolamide

Diagnostic considerations:

- Chest x-ray poorly predicts the diagnosis of PCP with increased interstitial markings most commonly seen; a CT Thorax is recommended when clinical suspicion is high.
- On CT Thorax the most helpful findings are ground glass opacities (seen in 95%), increased interstitial markings (seen in 47%), the absence of a pleural effusion (seen in 25%), and the absence of nodules (seen in 25%).
- Induced sputum or bronchoscopy/BAL for PCP staining (cytology) and PCR.
    - PCR: cannot discriminate between colonization and infection, so **should not be requested if low pre-test probability of PJP and likely alternate diagnosis** (eg: COVID-19, CAP…).
        - Specific forms must be completed for sample to be sent for PCR.
        - Nasopharynx samples should not be used outside of a research protocol.
    - Transbronchial biopsy is seldom required if PCR can be performed and should be reserved for cases where alternative diagnoses requiring biopsy need to be excluded.
- Serum 1,3 beta-D-glucan (BDG) is helpful in HIV with good operating characteristics. Unfortunately, outside of HIV, the diagnosis cannot be excluded above a 20% pre-test probability and positive predictive value is low. BDG= cell wall component of most fungi, including *Pneumocystis*. Elevated levels of BDG may indicate PCP, but low or negative results do not rule out PCP.
- LDH is neither sensitive nor specific at any cut-off for the diagnosis of PCP

PHARMACOLOGICAL THERAPY

Preferred regimen **MILD disease** O_2 sat > 92% on room air **SEVERE Disease** O_2 sat<92% on RA, or PaO_2 <70 mmHg, or alveolar-arterial (A-a) oxygen gradient ≥35 mmHg,	**TMP-SMX**[1] 15 mg/kg (of the TMP component) PO or IV total daily divided q8h [once clinical improvement after 5 days, may decrease to 10mg/kg daily divided q8h to avoid nephrotoxicity] **TMP-SMX**[1] 15 mg/kg (of the TMP component) PO or IV daily divided q8h *AND* **Prednisone**[2] 40 mg po BID x 5d, then 40 mg po die x 5d then 20 mg po die x 11 d (or equivalent dose of methylprednisone, if unable to take PO).	Total duration of treatment: 14-21 days based on clinical response and use of secondary prevention
Alternative regimens **If significant nephrotoxicity or severe sulfa allergy**[3] For patients with mild sulfa allergies, consider desensitization or the use of DAPSONE with TMP Need to exclude G6PD deficiency if using PRIMAQUINE or DAPSONE. .	Severe disease: **Clindamycin**[4]: 900 mg IV q8h AND **Primaquine**[5]: 30 mg (base) po die AND **Prednisone** 40 mg po BID x 5d, then 40 mg po die x 5d then 20 mg po die x 11d (or equivalent dose of methylprednisone, if unable to take PO). ***OR (if G6PD-deficient)*** **Pentamidine** 4mg/kg per day IV AND **Prednisone** 40 mg po BID x 5d, then 40 mg po die x 5d then 20 mg po die x 11d (or equivalent dose of methylprednisone, if unable to take PO). Mild disease: **Dapsone**[5]: 100mg po DIE AND **Trimethoprim**: 5mg/kg PO q8h OR **Atovaquone** suspension 750 mg orally BID (must be taken with food)* *In randomized trials ATOVAQUONE was associated with higher rates of clinical failure and mortality than TMP-SMX and should be reserved for select cases	Secondary prevention with TMP-SMX should be considered for most patients Antiretroviral therapy should be started approximately day 10-14 in patients with AIDS

[1] TMP-SMX: IV preferred in patients with significant hypoxemia; Adjust dose for renal dysfunction. Consult pharmacy for TMP-SMX dosing in obesity (use adjusted body weight and add 8mg/kg/day).
[2] Adjunctive glucocorticoids may be beneficial, extrapolated from HIV patients with PCP.
[3] Rash (rarely SJS/TEN), fever, neutropenia, transaminase elevations.
[4] Clindamycin may cause *Clostridioides difficile* colitis, abdominal pain.
[5] Primaquine, Dapsone: measure G6PD prior to administration. May cause methemoglobinemia, hemolytic anemia, leukopenia, neutropenia, rash.

REFERENCES

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Drafted by C. Boodman (ID); Reviewed by M. Semret (ID), D. Vinh (ID), M. Cheng (ID), F. Bourdeau (pharmacy). Approved by ASP committee on May 19, 2021; approved by P&T committee on June 23, 2021