Chapter 4. Pneumocystis Pneumonia Prophylaxis

Background

Despite advances in the management of HIV disease, *Pneumocystis jiroveci* (previously known as *carinii*) pneumonia (PCP) remains an important complication and cause of morbidity. PCP antimicrobial prophylaxis is very effective and has been demonstrated to prolong life. The risk of developing PCP becomes significant when the patient's CD4 cell count falls to about 200/mm^3 and increases progressively as it further declines.

PCP presents subacutely with fever, malaise, dyspnea on exertion, and a nonproductive cough. Physical examination may be normal or show scattered rales on auscultation of the lungs. The chest x-ray typically reveals diffuse interstitial infiltrates but may be normal in early infection. Oximetry often shows decreased oxygen saturation following exertion. Diagnosis is generally made by induced sputum with identification of the organism on direct fluorescent antibody test; bronchoscopy with lavage may be necessary in a minority of cases. Treatment of PCP consists of trimethoprim-sulfamethoxazole (TMP-SMX) or an alternative drug for three weeks. Adjuctive corticosteroid therapy is used in patients with significant respiratory dysfunction.

Guidelines

An algorithmic approach to PCP prophylaxis is presented in Figure 4-1. Effective agents for PCP prevention include TMP-SMX, dapsone, aerosol pentamidine (AP), and atovaquone (Table 4-1).

- All HIV-infected patients whose CD4 cell count is less than 200/mm^3 or CD4 percentage is less than 14, who have thrush, or who have a history of PCP and have not been immune reconstituted on antiretroviral therapy (see below) should receive prophylaxis.

- Primary prophylaxis can be safely discontinued in patients whose CD4 cell count rises above 200/mm^3 for 3 months on combination antiretroviral therapy. Secondary prophylaxis (maintenance therapy) in patients with a history of PCP can also be stopped in this context.

- TMP-SMX is the drug of choice for PCP prophylaxis. The recommended dose is one double-strength (DS) or single-strength (SS) tablet per day. It can also be given as one DS three times per week.

- TMP-SMX is preferred to dapsone because of increased efficacy and protection against conventional bacterial infections. It is preferred to AP because of increased efficacy, lower cost, protection against toxoplasmosis and conventional bacterial infections, and lower risk of extrapulmonary pneumocystosis. It is preferred to atovaquone because of much lower cost.

- Twenty-five to 50% of patients with HIV infection develop toxicity to TMP-SMX. The most common side effects include fever, rash, and leukopenia. Strategies for managing mild reactions include discontinuation of the drug and resuming it at same or lower dose or use of a desensitization protocol (gradually increasing doses administered over several days). Many patients can be treated through mild drug reactions using acetaminophen and/or antihistamine for symptom management.

- Dapsone 100 mg po qd is recommended as the alternative agent in patients who cannot tolerate TMP-SMX. Side effects include fever, rash, and hemolytic anemia. G6PD qualitative assay should be performed before starting dapsone therapy; the drug is contraindicated in patients with G6PD deficiency. For dapsone to be effective as toxoplasmosis prophylaxis, which is indicated in context of CD4 cell count < 100/mm^3 and positive IgG serology, it should be given as 50 mg po qd in conjunction with pyrimethamine 50 mg po weekly. Folinic acid is advised to prevent bone marrow suppression from pyrimethamine.

- For patients who cannot tolerate dapsone, AP or atovaquone is recommended.

- AP 300 mg per month is given by Respirgard II jet nebulizer using 6 ml sterile water delivered at 6 L/min from a 50-psi compressed air source until the reservoir is dry, usually over 45 minutes. Active tuberculosis (TB) should be ruled out with PPD, chest x-ray, and other studies if necessary before initiating AP. Appropriate measures should be in place to prevent TB transmission in persons receiving AP. These include use of individual rooms or booths with negative pressure ventilation, air exhaust to the outside, scheduling to permit air exchange prior to use by another patient, use of particulate respirators by workers administering the drug, and restriction of patients from returning to waiting areas until their coughing subsides.

- Atovaquone is dosed as 1500 mg of suspension po qd with food. Side effects include gastrointestinal intolerance, rash, headache, and fever.

Table 4-1. Comparison of PCP Prophylaxis Regimens

Issue	TMP-SMX	Dapsone	AP	Atovaquone
Efficacy	High	Moderate	Moderate	Moderate
Toxicity	Moderate	Low-Moderate	Low	Low
Cost	Low	Low	High	High
Toxoplasmosis Protection	Yes	Yes *	No	Probably
Bacterial Infection protection	Yes	?	No	No
Risk of Extrapulmonary Pneumocystosis	No	No	Yes	No

* In conjunction with weekly pyrimethamine

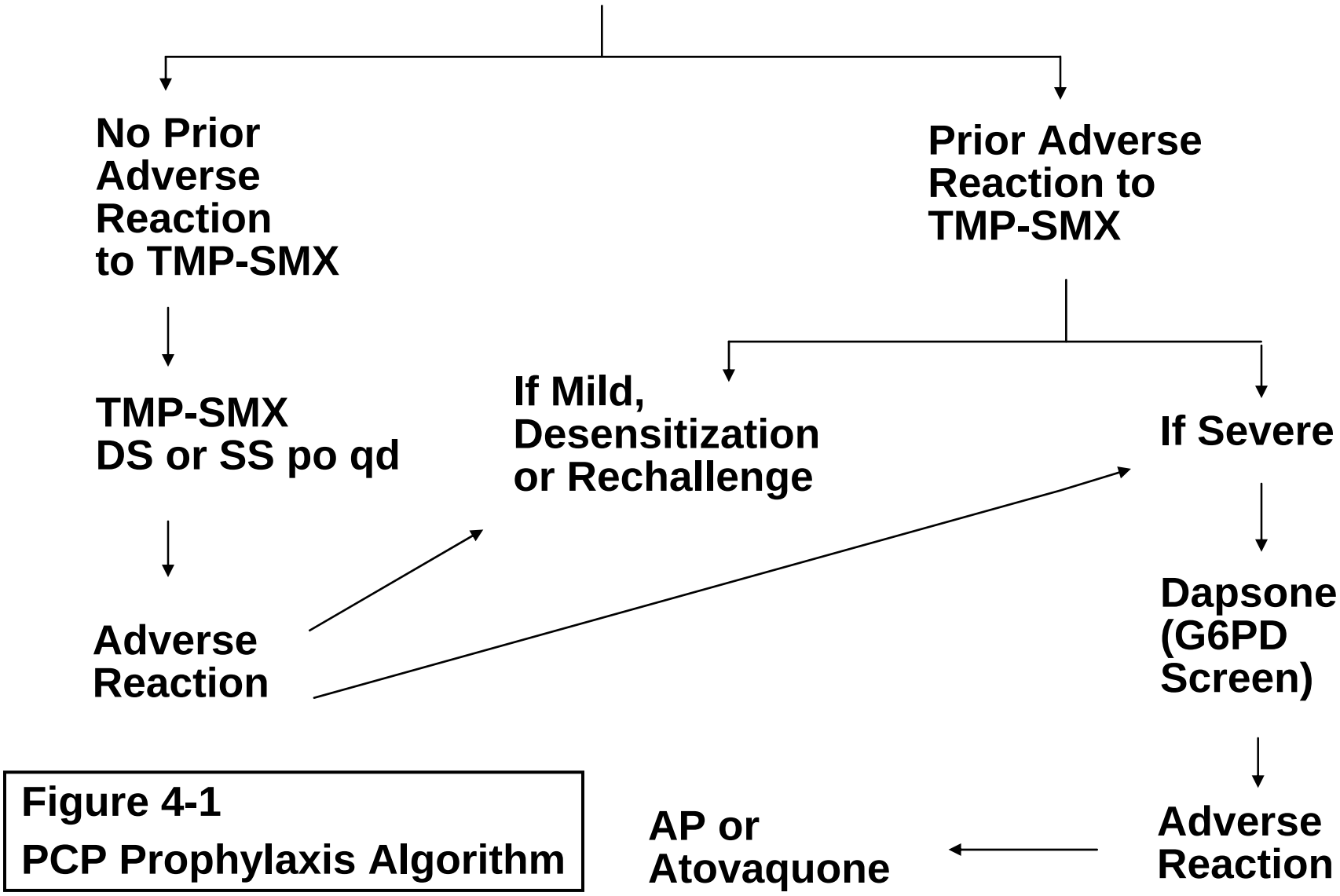

Figure 4-1
PCP Prophylaxis Algorithm