Pneumocystis jiroveci (formerly Pneumocystis carinii)

Introduction

Pneumocystis jiroveci remains an important pathogen in immunocompromised individuals despite a variety of effective antimicrobial strategies. In most solid organ transplant recipients with standard immune suppression the risk of Pneumocystis jiroveci pneumonia is of the order of 5–15% (1–4) (See Table 1). The risk of Pneumocystis jiroveci pneumonia increases with the intensity of immune suppression. With increased success of transplantation due to enhanced immune suppression, and improved diagnostic capabilities, in the absence of prophylaxis the incidence of infection has increased from 0.6 to 1.1% prior to 1990 to 9–11.5% in more recent transplant recipients (5–7).

Clinical manifestations of Pneumocystis infection

Pneumocystis pneumonia is usually subacute to acute in onset, developing over a few days to weeks. The patient develops progressive dyspnea, tachypnea, cyanosis, and a nonproductive cough. Patients may report low-grade fevers, sweats, or systemic flu-like symptoms. Auscultatory findings at the onset are minimal, generally no more than scattered rales and somewhat diminished breath sounds. Dyspnea and arterial hypoxemia often occur in the face of a normal chest radiograph. Pleurisy and pneumothorax may occur acutely. Relapsed infection may evolve more rapidly, especially in the setting of other infections (e.g. CMV) or fibrosis or emphysematous changes from previous infections. Arterial hypoxemia is generally moderate to severe, and may be out of proportion to physical and radiologic findings. The use of corticosteroids, cyclosporine, or tacrolimus therapy may mask the signs and symptoms of Pneumocystis pneumonia until late in the course of disease. Extrapulmonary disease due to P. jiroveci is rare in organ transplantation.

In children, early signs of pneumocystosis include diarrhea, poor feeding, and coryza. The respiratory manifestations progress to nasal flaring, intercostal retraction, and cyanosis. Fever may be absent. As in the adult, arterial hypoxemia is generally present along with respiratory alkalosis.

In the organ transplant recipient, the incidence of Pneumocystis pneumonia depends on the center where transplantation is performed and the immunosuppressive and prophylactic regimens employed. P. jiroveci pneumonia will generally occur approximately 6–8 weeks after the initiation of immunosuppressive therapy, with cytomegalovirus infection, or during periods of increased immunosuppression for treatment of episodes of graft rejection. Unprophylaxed liver transplant recipients treated with corticosteroids for autoimmune hepatitis prior to surgery, may develop Pneumocystis infection within days of transplantation. Patients receiving heart-lung and single-lung transplants have an incidence of asymptomatic Pneumocystis isolation approaching two thirds of the total number of patients (8). Of these, up to half will develop symptomatic disease in the absence of treatment or prophylaxis. During infection, lung transplant recipients develop a neutrophil and lymphocyte-predominant response, with the recruitment of macrophages during and after therapy. Despite calcineurin inhibitors, T lymphocytes are found in large numbers. Over half of this group of patients with Pneumocystis pneumonia will also have a secondary bacterial or viral infection. By contrast, among all other organ transplant recipients, only 5–15% will be expected to carry or develop Pneumocystis infections.

Heart and heart-lung transplant recipients are particularly susceptible to coinfection with CMV. The cytotoxic T-lymphocyte-mediated response to pulmonary CMV may be difficult to separate from graft rejection. A number of centers have noted that patients with Pneumocystis pneumonia while on cyclosporine have an increased mortality over other immunocompromised patients with Pneumocystis.

Diagnosis

A definitive diagnosis of PCP is made by demonstration of organisms in lung tissue or respiratory tract secretions. The use of imaging tests may identify the presence of a pneumonic process, but none of these offers diagnostic specificity. No specific diagnostic pattern exists for Pneumocystis pneumonia on routine chest radiograph. The chest radiograph may be entirely normal despite significant hypoxemia and diffuse parenchymal involvement. Diffuse, fine, ‘ground-glass’ interstitial infiltrates with a perihilar predominance are common and may progress to involve the entire lung with progressive consolidation. Atypical features are often seen. The use of aerosolized pentamidine for prophylaxis against P. jiroveci in AIDS non-AIDS patients has resulted in a series of otherwise unusual...
**Pneumocystis jiroveci**

Table 1: *Pneumocystis jiroveci* pneumonia in transplantation

<table>
<thead>
<tr>
<th>Incidence</th>
<th>5–14% without prophylaxis – varies by center (A)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sequelae</td>
<td>Significant morbidity and mortality</td>
</tr>
<tr>
<td>Rationale</td>
<td>Prophylaxis is well-tolerated and effective</td>
</tr>
<tr>
<td>Recommendations</td>
<td>Trimethoprim-sulfamethoxazole is first choice agent; other agents are less effective (A1)</td>
</tr>
<tr>
<td></td>
<td>Prophylaxis for first 6 months after any solid organ transplant is safe and effective (A1)</td>
</tr>
<tr>
<td></td>
<td>Insufficient data to determine optimal duration and dose for each organ (B)</td>
</tr>
<tr>
<td></td>
<td>May choose to prolong prophylaxis for liver and lung transplant recipients (B)</td>
</tr>
<tr>
<td></td>
<td>Prophylaxis during periods of intensified immune suppression (A)</td>
</tr>
</tbody>
</table>

Table 2: Treatment of infection due to *Pneumocystis jiroveci*

<table>
<thead>
<tr>
<th>Agent (route)*</th>
<th>Dose*</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug of choice</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trimethoprim-sulfamethoxazole (TMP-SMX) (IV/PO)</td>
<td>15–20 mg/kg/d TMP / 75–100 mkg/d (divided 3–4 doses)</td>
<td>May treat through mild rash (common); desensitization often not useful in transplants; rise in serum creatinine with TMP</td>
</tr>
<tr>
<td>For acute illness (pAO2 &lt; 70 mmHg) or prednisolone</td>
<td>Add prednisone (40–80 mg BID)</td>
<td>Must taper steroids if used; may activate herpes simplex</td>
</tr>
<tr>
<td>Alternatives (or for less seriously ill)</td>
<td>Pentamidine isethionate (IV) 4 mg/kg/d</td>
<td>300 mg/d maximum; lower dose (2–3 mg/kg) common; IM not advised; occasional pancreatitis, hypoglycemia</td>
</tr>
<tr>
<td>Atovaquone liquid (PO)</td>
<td>750 mg bid (–QID)</td>
<td>Best with meals; absorption variable; stains clothes</td>
</tr>
<tr>
<td>Dapson (PO) &amp; TMP (PO)</td>
<td>100 mg/d (TMP 5 mg/kg TID)</td>
<td>May be tolerated with allergy to SMX; long half-life; check G6PD; methemoglobinemia</td>
</tr>
<tr>
<td>Primaquine (PO) and clindamycin (IV/PO)</td>
<td>30 mg base QD</td>
<td>Diarrhea (<em>C. difficile</em>); may use primaquine instead of pyrimethamine; check G6PD for primaquine; methemoglobinemia</td>
</tr>
<tr>
<td>Pyrimethamine (PO) &amp; sulfa diazine (PO)</td>
<td>600 mg IV q8 h or 300–450 mg PO QID</td>
<td>TMP-SMX better; few data</td>
</tr>
<tr>
<td>then 75 mg/kg</td>
<td>load 50 mg BID x 2 d then 25–50 mg/d</td>
<td>Maximum 4 g in 2 doses</td>
</tr>
<tr>
<td>then 100 mg/kg/d</td>
<td>Maximum 8 g</td>
<td></td>
</tr>
<tr>
<td>Trimetrexate (IV) &amp; folinic acid (PO/IV)</td>
<td>45 mg/d</td>
<td>marrow suppression; anemia; early relapse</td>
</tr>
<tr>
<td>Pirithrexim and folic acid</td>
<td>20 mg/m² q6 h</td>
<td>under study</td>
</tr>
<tr>
<td>Macrolide and sulfonamide</td>
<td></td>
<td>possible synergy; limited data</td>
</tr>
</tbody>
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*All doses may need adjustment for renal or hepatic dysfunction. Avoid agents with history of prior allergy including hives, severe rash, renal or hepatic toxicity, respiratory distress. Reduce immune suppression other than steroids if possible. Usual course 21 days of therapy based on clinical response, followed by life-long prophylaxis. Check for G6PD deficiency prior to use of dapson or primaquine.

Radiologic presentations of *Pneumocystis* pneumonia, often involving the upper lobes. Alternatives to plain radiographic imaging include the computerized tomography (CT) and nuclear magnetic resonance imaging (MRI) scans, ultrasound, and nuclear medicine imaging including gallium, radiolabeled immunoglobulin, and white blood cell scans. While these studies may identify the presence of a pulmonary process consistent with PCP, they can be not specific for this disease.

Direct demonstration of *P. jiroveci* is the diagnostic method of choice and can be accomplished through either noninvasive or invasive methods. In general, noninvasive testing may be attempted to make the initial diagnosis, but invasive techniques should be used when clinically feasible. The choice of invasive procedure depends on the patient and the institution. The yield of diagnostically useful material is generally greater from tissue biopsies than from induced sputa or bronchoalveolar lavage specimens.

The diagnosis of *P. jiroveci* infection has been improved by the use of induced sputum samples and of immunofluorescent monoclonal antibodies to detect the organism in clinical specimens. Direct immunofluorescent staining of organisms using monoclonal antibodies is useful for screening induced sputum specimens. These antibodies bind both cysts and trophozoites. The cyst wall can be displayed by a variety of staining techniques; of these, the Gomori methenamine-silver nitrate method (which stains organisms brown or black) is most reliable, even though it is susceptible to artifacts and stains only the cyst forms of the organism which represent only 5–10% of the total infectious burden of *Pneumocystis* in the lungs. Sporozoites and trophozoites are stained by polychrome
stains, particularly the Giemsa stain. The Giemsa, Wright’s, toluidine blue O, or Grocott’s rapid silver stain technique is most useful in dealing with the lung imprints, bronchial lavage fluid, or pulmonary aspirates. Rapid polychrome staining (Diff-Quick, American Scientific Products, Inc.) and a rapid silver staining technique are useful in screening smears.

On histopathology, *P. jiroveci* produces a characteristic interstitial and alveolar infiltrate. In the adult, the alveolar space is filled with a frothy eosinophilic material that contains organisms and debris of macrophages and alveolar epithelial cells as well as edema fluid and protein. The distribution of disease is often patchy.

**Therapy**

The recommended treatment for *P. jiroveci* infections are shown in Table 2.

1. The most effective systemic therapy for the treatment of *P. jiroveci* pneumonia in all patients remains trimethoprim-sulfamethoxazole (cotrimoxazole, TMP-SMZ) (AII). This consideration includes such factors as the rapidity of clinical response and the ease of administration (oral bioavailability).

2. The transplant patient with significant hypoxemia may benefit from high dose corticosteroids (AII). The use of other adjunctive therapies (colony-stimulating factors, immune modulators, aerosolized pentamidine, antibodies) must be tailored to the individual patient.

3. *Pneumocystis jiroveci* that is resistant to antimicrobial agents has been described in vitro by a number of authors but, has not been demonstrated as a cause of clinical therapeutic failure. While there are patients who appear to ‘do better’ on one agent instead of another, it is much more common to recognize a second process (infection, tumor, allergy, ARDS) complicating *Pneumocystis* pneumonia than ‘resistant’ infection.

4. Coinfection with pathogens in addition to *P. jiroveci* is common.

5. The duration of therapy in the immunocompromised patient with *Pneumocystis* has not been well studied. The use of 14 days of therapy in non-AIDS patients is arbitrary.

6. Residual organisms present in bronchoalveolar lavage specimens at the completion of therapy are of uncertain importance, but are largely nonviable.

Trimethoprim-sulfamethoxazole is the drug of first choice for the treatment of *P. jiroveci* pneumonia in patients who tolerate this agent (AII). This preference is based on (1) the availability of both intravenous and oral formulations of the drug and (2) on the efficacy of this drug for both therapy and prophylaxis. Further, TMP-SMZ may prevent infection due to a broad spectrum of organisms, including *Listeria*, most *Nocardia*, and many of the common bacterial pathogens including both encapsulated and unencapsulated Gram-negative and Gram-positive organisms. The onset of action for cotrimoxazole is rapid; clinical responses are seen as early as 3–4 days into therapy. Serum levels with orally administered drug are equivalent to intravenous levels with normal GI function. Therapy is generally initiated with a total dose of 20 mg/kg per day of TMP coupled with 100 mg/kg per day of SMZ divided into 4 daily doses. A course of 14 days of therapy is adequate (followed by secondary prophylaxis) only if immune suppression can be reduced. Solid organ transplant recipients, particularly with renal and hepatic transplants, frequently suffer nephrotoxicity with intravenous TMP-SMX treatment. Both components in the combination can produce bone marrow suppression, including thrombocytopenia and neutropenia; these side-effects are frequently reversible by reducing the total dose of the drug. Drug-related toxicities are relatively common in transplant recipients and may necessitate the switching of antimicrobial agents.

Pentamidine isethionate is given intravenously by infusion over 1–2 h in a 5% glucose solution at a dose between 2 and 4 mg/kg per day. Because of the prolonged half-life of this drug and the high levels of tissue binding, it may be advantageous to begin therapy at the 4 mg/kg per day level and to use lower doses subsequently. Therapeutic efficacy is achieved more slowly than with other agents, often requiring 5–7 days before clinical improvement is observed. Therapeutic levels persist in the lungs long after treatment is completed. The incidence of side-effects with intravenous pentamidine is roughly equivalent to that seen with cotrimoxazole in AIDS patients. Adverse reactions are both idiosyncratic and dose-related. Administration of pentamidine in the presence of renal dysfunction is associated with an increased incidence of most of the side-effects of pentamidine therapy. These adverse reactions include hypoglycemia, hyperglycemia, neutropenia, thrombocytopenia, azotemia, pancreatitis, nausea, and altered taste sensation. Pancreatic dysfunction is more common after a total dose exceeding 3 g pentamidine. This injury may present after the cessation of therapy because of the prolonged half-life of the drug, which is frequently over 2 months. Hypoglycemia or hyperglycemia may precede permanent insulin dependence. Pentamidine should be avoided in pancreas transplant recipients due to the potential for islet cell necrosis.

Alternative drug combinations are available for the treatment of *Pneumocystis*. Dapsone (100 mg d PO) has been used in combination therapy with trimethoprim (15 mg/kg/d PO divided into three doses) as an effective alternative oral therapy. The long half-life and side-effect profile (neutropenia in 19%, anemia, fever, hemolysis in G6PD-deficiency, rash, hepatitis) is a concern in patients allergic to TMP-SMZ.

Atovaquone (750 mg suspension PO TID-QID) is useful in the treatment of mild to moderately severe
**Pneumocystis jiroveci**

*Pneumocystis* pneumonia. Side-effects of atovaquone are relatively uncommon and are generally mild. The incidence of rash, the most common side-effect of atovaquone, correlates with increasing serum drug levels. Other toxicities include diarrhea, nausea, vomiting, fever, and increased liver function tests. There does not appear to be any interaction between atovaquone and cyclosporine or tacrolimus (BII).

Trimetrexate (45 mg/m²/day) with folinic acid (80 mg/m²/day) has been approved for use in moderately severe pneumonia, but has not been studied in transplantation. Trimetrexate is a dihydrofolate reductase inhibitor and is lipid soluble with a serum half-life up to 34 h. It will produce severe neutropenia in the absence of folinic acid supplementation (which should be continued for 3–5 days after cessation of trimetrexate). Side-effects include fever, rash, leukopenia, and transaminase elevation. Relapses may be more common with this agent.

The combination of clindamycin (600–900 mg IV or PO Q6–8 h) and primaquine (15–30 mg of base/day PO) is effective in mild to moderate infection (in AIDS). The main toxicities of clindamycin include rash (16% (48)) methemoglobinemia, anemia, neutropenia and the development of *Clostridium difficile* colitis. Primaquine should not be used in G6PD deficiency. Pyrimethamine (60–100 mg/day PO after 100–200 mg load) with sulfadiazine or tri sulfapyrimidines (4–8 g/d) are also effective, but require folinic acid (10 mg/d) supplementation. Pyrimethamine will decrease the renal clearance of creatinine without altering the glomerular filtration rate.

**Use of corticosteroids in treatment**

Many patients with *P. jiroveci* pneumonia will suffer disease progression despite appropriate antimicrobial therapy. Clinical trials have demonstrated that corticosteroids administered in the first 72 h of therapy for *Pneumocystis* pneumonia are of significant benefit in AIDS patients in terms of morbidity, mortality, and the avoidance of intubation in patients with an arterial PO₂ on room air between 35 and 72 mmHg or with a hypoxemia ratio (Pa₂/ FiO₂) between 75 and 350. Experience with both neutropenic and organ transplant patients with *Pneumocystis* pneumonia has been equally gratifying. Patients in whom steroid therapy is not tapered are prone to recrudescence of hypoxemia and of acute pulmonary symptoms. The optimal dose of steroids has not been established. One useful regimen is a dose of 40–60 mg prednisone or prednisolone given orally or intravenously twice a day. After 5–7 days, the steroids are tapered over a period of 7 days to 2 weeks. There may be an increased incidence of oral herpes simplex with oral thrush, both of which are improved with careful attention to oral care.

**Prophylaxis**

Routine anti-*Pneumocystis* prophylaxis has been reserved, in general, for centers or patient groups that are known to have a fixed high incidence of disease (i.e. on the order of 3–5% of susceptible hosts), for individuals with a history of documented *Pneumocystis* disease, for patients requiring more intensive immune suppression on an acute or chronic basis, and/or for those with chronic viral infection (e.g. cytomegalovirus) (4,9,10). The relative risk of infection with *Pneumocystis* is greatest in: the first six months after solid organ transplantation; in lung transplant recipients; in patients receiving prolonged courses of corticosteroid therapy (e.g. >20 mg/d of prednisone for a period of over 2–3 weeks); with prolonged neutropenia; and with acutely increased immune suppression for graft rejection, graft-vs.-host disease, or flares of autoimmune diseases (11).

In solid organ transplant recipients, antilymphocyte antibodies, bolus corticosteroids and the calcineurin inhibitors also contribute to the risk of *Pneumocystis* pneumonia (12–14). While mycophenolate mofetil may have some intrinsic anti-*Pneumocystis* activity (15) we have observed multiple patients with *Pneumocystis* pneumonia while on full-dose mycophenolate and either this agent is not protective in vivo or the immunosuppressive effect outweighs the degree of protection. Patients who have undergone transplantation during or shortly after a course of corticosteroids (e.g. for COPD or autoimmune hepatitis) are at increased risk of *P. jiroveci* pneumonia in the first weeks after transplantation rather than 1–6 months after surgery.

In general, anti-*Pneumocystis* prophylaxis is used for all solid organ transplant recipients for 6 months to a year post-transplant for kidney recipients and up to life-long for heart, liver, intestine and lung recipients. These recommendations are based on the periods of greatest risk due to intensity of immune suppression and the incidence of infection observed in each group. If immune suppression cannot be reduced after a course of treatment for *Pneumocystis* pneumonia, prophylaxis should be maintained indefinitely.

Prophylaxis for *Pneumocystis* pneumonia is highly effective. In one prospective series, the incidence of *Pneumocystis* pneumonia in patients receiving prophylaxis with ciprofloxacin was 14% while no infection was observed in those receiving trimethoprim-sulfamethoxazole therapy (16). Retrospective series confirm the efficacy of prophylaxis (2,5,7,17–20). Breakthrough *Pneumocystis* infections in patients on non-TMP-SMX regimens are often atypical in appearance. In these patients, bronchoalveolar lavage samples are often negative for *P. jiroveci*, and lung biopsy is often required for diagnosis.

**Specific agents**

Trimethoprim-sulfamethoxazole (TMP-SMX, cotrimoxazole) is the agent of choice for the prevention of *Pneumocystis* infection in patients who tolerate this agent (21–27). At a dose of one single strength tablet per day (80 mg TMP/160 mg SMZ) or one double strength tablet per day,
a wide variety of opportunistic infections are generally prevented including *P. jiroveci*, most *T. gondii*, and many community acquired respiratory, gastrointestinal, and urinary tract pathogens. In addition, TMP-SMX will suppress *Isospora belli* (based on experience in AIDS), and most *Nocardia asteroides* (based on susceptibility data) (28–31). However, infections due to *Nocardia* species have been observed in both bone marrow and solid organ transplant recipients receiving TMP-SMX. Protection against *T. gondii* is incomplete in seronegative cardiac transplant recipients. Studies of low and high dose regimens (single or double strength TMP-SMX) for prophylaxis in AIDS suggest no mortality advantage to the higher dose (12% incidence vs. 15% in the lower dose group) and earlier occurrence of toxicity in the high dose group (23, 32). For *Pneumocystis* prevention, it is equally effective to administer TMP-SMX (single or double strength) three days per week (23,33–35). Other agents have not been studied in this regard.

Drug toxicity is common with any regimen, especially as mild hematopoietic suppression and reversible decrease in renal tubular secretion of creatinine (36). Hematopoietic toxicity is notable in combination with other marrow-suppressive agents (e.g. azathioprine, ganciclovir, cytoxan, allopurinol), malnutrition, or infection (CMV, hepatitis C virus). Anemia, neutropenia, and azotemia have been related to trimethoprim levels in AIDS (37) while rash and hepatotoxicity have been related to serum sulfa levels. Some patients will not tolerate any dose of sulfa drugs due to significant rash, Stevens–Johnson syndrome, hepatitis (particularly in liver allograft patients), eosinophilic nephritis, or neutropenia. Interstitial nephritis, hepatitis, and severe skin reactions are contraindications to the use of this agent in solid organ transplant recipients. Toxicity to transplanted organs may occur at any level of drug and, once established, rarely resolves without complete discontinuation of the agent. Hyperkalemia may result from interference by trimethoprim with the secretion of potassium at the renal distal tubule.

Alternative prophylactic regimens are available for the patient intolerant of TMP-SMX (4). All other prophylactic agents should be considered “second line”, in part because of diminished activities of most alternative regimens against pathogens other than *P. jiroveci*.

*Pentamidine*. Aerosolized pentamidine (AP) isethionate (300 mg q 3–4 weeks) is well tolerated in small series of solid organ and hematopoietic transplant recipients (20,38–40). Pentamidine aerosol prophylaxis is most effective when administered by experienced personnel with a nebulizer producing droplets in the 1–3 micron range. Up to 600 mg per month, accumulation of pentamidine in plasma does not occur. Breakthrough infection exceeds 10% with pentamidine (IV or aerosol) in solid organ recipients, making this a less than optimal agent. Breakthroughs are generally in patients who have not yet received two or more doses of pentamidine (i.e. in the first 8 weeks of prophylaxis), and in individuals with more intense immune suppression or coinfection with CMV. Cough and bronchospasm are the common side-effects of aerosolized pentamidine therapy, and are generally reversible with bronchodilator therapy. Hypoglycemia or hyperglycemia have been observed, and may be a concern in pancreas transplant recipients.

*Dapsone* (diaminodiphenylsulfone) with or without trimethoprim or pyrimethamine is widely used for prophylaxis in a variety of combinations. Because of a long serum half-life, dapsone is generally administered in doses of 50–100 mg/d. Breakthrough infection has been observed in transplant patients at doses up to 50 mg/d; toxicity may be limiting at 100 mg/d. Pyrimethamine may be administered weekly (25 or 50 mg) to supplement dapsone (50–100 mg/d). TMP-SMX and dapsone have equal anti-*Toxoplasma* efficacy (23). The transplant recipient who is intolerant of TMP-SMX may tolerate dapsone (41). Switching from TMP-SMX to dapsone cannot be recommended for individuals with severe side-effects from either agent including desquamation, neutropenia, severe nephritis or hepatitis, or in documented G6PD deficiency. Toxicities observed with dapsone are long lived and may limit utility, especially in liver transplantation recipients (42–44). Dapsone is metabolized via the hepatic P450 system (CYP3A).

Atovaquone has been studied in small prospective trials of in transplant recipients intolerant of TMP-SMX (4). Atovaquone (1500 MG PO QD) with daily fluoroquinolone for urinary prophylaxis was effective in 39/44 renal, hepatic, and cardiac transplant recipients intolerant of TMP-SMX (4).

Atovaquone is a hydroxynaphthoquinone and inhibitor of mitochondrial electron transport. Rash, nausea, and elevated liver transaminases are occasionally documented. The incidence of rash correlates with the serum concentration. No interactions of atovaquone with cyclosporine have been documented. Some patients complain about the flavor and color of atovaquone liquid (which stains clothes).

Clindamycin and pyrimethamine. Prophylaxis with the combination of clindamycin and pyrimethamine are effective as alternatives to TMP-SMX (45). However, while small, prospective trials have indicated some efficacy for prophylaxis, clinical trials of the combination of clindamycin and primaquine for the prevention of pneumocystosis have been complicated by a high incidence of *C. difficile* colitis, and of anemia (especially in G6PD-deficient hosts).

Patients receiving prophylaxis for toxoplasmosis (sulfadiazine, triple sulfa, atovaquone, clindamycin with pyrimethamine or primaquine) have also been protected against *P. jiroveci*. Patients receiving quinolone...
antimicrobial agents (e.g. for urinary prophylaxis following renal transplantation) will be at the same risk for Pneumocystis pneumonia as if they were unprophylaxed.

References


