CLINICAL GUIDELINE

# THE PREVENTION AND TREATMENT OF OPPORTUNISTIC INFECTIONS IN HIV-INFECTED ADULTS

**HIV Clinicians Society of Southern Africa**

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A number of lengthy and comprehensive articles and guidelines exist with regard to the treatment and prevention of opportunistic infections, but this guideline is designed to be easy and simple for a practitioner to use. It is presented in a simplified format. The guideline is supported by evidence-based studies and adapted to be appropriate to the local situation. It should be noted that only the drugs that are licensed in South Africa have been recommended and in addition, at all times, the most cost-effective regimen(s) have been endorsed. Alternative regimen(s) have been listed where appropriate, but these are not exhaustive. A practitioner dealing with a more complex problem may find it necessary to consult with a colleague or refer to more comprehensive material.

The best method of preventing opportunistic infections in HIV-infected individuals is to use highly active antiretroviral therapy, which leads to partial immune reconstitution. However, even if antiretroviral therapy is available a substantial proportion of patients will either present with severe immune suppression or remain severely immune-suppressed despite antiretroviral therapy. Many opportunistic infections can be prevented in these patients by using primary prophylaxis (see below) or vaccination (see below). Relapses are common after initial treatment of many opportunistic infections and maintenance therapy (also known as secondary prophylaxis – see Table I) is necessary while patients remain immune-suppressed.

**The following delegates attended the opportunistic infections guideline workshop of the SA HIV Clinicians Society, held in Cape Town on 9 March: Dr Mark Cotton, Professor Gary Maartens, Dr Steve Andrews, Dr Steve Miller, Dr Dave Spencer, Dr Des Martin, Dr Francois Venter, and Pofessor Robin Wood.**

## PRIMARY PROPHYLAXIS

*Tuberculosis preventive therapy was covered in the February 2001 issue of the* SA Journal of HIV Medicine.

### INDICATIONS FOR CO-TRIMOXAZOLE PROPHYLAXIS

- WHO clinical stage 3 or 4
- CD4 count < 200
- Total lymphocyte count < 1.25 x $10^9$/l (should only be used when CD4 count unavailable – may miss 25% of patients CD4 < 200).

### DOSE OF CO-TRIMOXAZOLE PROPHYLAXIS

All the following regimens are equally efficacious against *Pneumocystis carinii* pneumonia (PCP):

- 960 mg daily
- 960 mg three days/week
- 480 mg daily.

All dosages are acceptable, but lower dose regimens are better tolerated. There is scanty evidence for lower dose regimens against toxoplasmosis and strongest evidence for higher-dose regimens.

### CO-TRIMOXAZOLE INTOLERANCE

Co-trimoxazole intolerance is common in late disease and usually presents as a maculopapular rash. Many intolerant patients may continue to receive co-trimoxazole with the addition of an antihistamine unless there are systemic symptoms or mucosal involvement. If co-trimoxazole therapy is discontinued, desensitisation or rechallenge appear to be safe unless there are systemic symptoms or mucosal involvement. Because co-trimoxazole reduces the incidence of many opportunistic infections, rechallenge or desensitisation should be considered. Studies have demonstrated that desensitisation and rechallenge appear safe. Both rechallenge and desensitisation should be done under antihistamine cover starting the day before. Rechallenge should be done with co-trimoxazole 480 mg and the patient observed for several hours. Several desensitisation regimens exist; one of the simplest uses co-

## TABLE I. TREATMENT AND SECONDARY PROPHYLAXIS OF OPPORTUNISTIC INFECTIONS IN ADULTS

Standard adult doses have been given. Every effort has been made to check doses, but readers should check other sources. Usual duration of therapy has been given, but longer courses may be needed in individual cases.

| Infection | Treatment options | Duration | Secondary prophylaxis[1] |
|---|---|---|---|
| Herpes simplex | Valaciclovir 500 mg bid<br>Acyclovir 400 mg tid<br>Famciclovir 125 mg bid | 7 days | Not usually recommended (acyclovir 400 mg bid) |
| Tuberculosis | Standard short-course therapy | 6 months | Not recommended |
| Candida oesophagitis | Fluconazole 100 mg daily<br>Itraconazole 200 mg daily<br>Ketoconazole 400 mg daily | 14 - 28 days | Not recommended |
| *Pneumocystis carinii* pneumonia[2] | Co-trimoxazole[3] 3-4 tabs qid<br>Dapsone 100 mg daily **plus** trimethoprim 300 mg tid<br>Clindamycin 450 mg tid **plus** primaquine 15 mg daily | 14 - 21 days | Co-trimoxazole[3] 2 tabs daily<br>Dapsone 100 mg daily |
| Toxoplasmosis | Co-trimoxazole[3] 4 tabs bid<br>**Then** 2 tabs bid<br>Clindamycin 600 mg qid **plus** pyrimethamine[4] 50 mg daily | 4 weeks<br>12 weeks<br>6 weeks | Cotrimoxazole[3] 2 tabs daily |
| Cytomegalovirus | Ganciclovir 5 mg/kg bid IV **then**<br>Ganciclovir 5 mg/kg/day IV 5 days/week **or**<br>1 g tid PO | 14 days<br>Lifelong[1] | N/A |
| Atypical mycobacteriosis | Clarithromycin 500 mg bid **plus** ethambutol 800 mg daily | Lifelong[1] | N/A |
| Salmonella bacteraemia<br>Isosporiasis | Ciprofloxacin 500 mg bid<br>Co-trimoxazole[3] 4 tablets bid<br>Pyrimethamine[4] 25 mg daily | 6 weeks<br>4 weeks | Not recommended<br>Co-trimoxazole[3] 2 tabs daily<br>Pyrimethamine[4] 75 mg daily |
| Cryptosporidiosis | None available (antimotility drugs) | N/A | N/A |
| Bacterial pneumonia | Cefuroxime 750 mg - 1.5 g tid IV[5]<br>Cefamandole 1 - 2 g qid IV[5]<br>Ceftriaxone 1 - 2 g daily IV[5]<br>Cefotaxime 1 - 2 g bid IV[5]<br>Co-amoxiclav 1.2 g tid IV[5]<br>Moxifloxacin 400 mg daily<br>Gatifloxacin 400 mg daily | 5 - 10 days | Not recommended |
| Cryptococcal meningitis | Amphotericin B 0.7 mg/kg[6] IV daily **then** fluconazole 400 mg daily | 7 - 14 days<br>8 - 10 weeks | Fluconazole 100 - 200 mg daily[4] |
| Herpes zoster (shingles) | Acyclovir 800 mg 5 times/day<br>Valaciclovir 1 g tid<br>Famciclovir 250 mg tid | 7 days | Not recommended |
| Microsporidiosis | Albendazole 400 mg bid[7] | 21 days | Not recommended |

1. Prophylaxis or lifelong therapy can be discontinued if the CD4 count increases to > 200 on antiretroviral therapy.
2. Adjunctive corticosteroids are indicated in hypoxic patients (oral prednisone 40 mg bid followed by taper after 5 - 10 days).
3. Single-strength (480 mg) tablets.
4. Folinic acid (not folic acid) should be used to treat or prevent bone marrow suppression.
5. Therapy should be completed with oral antibiotics (amoxicillin, co-amoxiclav, moxifloxacin or gatifloxacin are recommended). These antibiotics are recommended in the South African Thoracic Society guidelines on community-acquired pneumonia (in press).
6. A test dose of 1 mg should be given over 30 minutes. If this is tolerated then half the daily dose can be infused over 4 hours with the full dose given the next day. Many experts omit the test dose.
7. Only certain species (notably *Encephalitozoon intestinalis*) respond well to albendazole.

trimoxazole syrup (240 mg/5 ml):

| | |
|---|---|
| Day 1 | 1.25 ml daily |
| Day 2 | 1.25 ml bid |
| Day 3 | 1.25 ml tid |
| Day 4 | 2.5 ml bid |
| Day 5 | 2.5 ml tid |
| Day 6 | One tablet (480 mg) daily |

(Leoung GS, Stanford JF, Giordano MF, et al. Trimethoprim-sulfamethoxazole (TMP-SMZ) dose escalation versus direct rechallenge for Pneumocystis carinii pneumonia prophylaxis in human immunodeficiency virus infected patients with previous adverse reaction to TMP-SMZ. J Infect Dis 2001; 184: 992-997).

### THE ALTERNATIVE TO CO-TRIMOXAZOLE

If co-trimoxazole cannot be tolerated, dapsone 100 mg daily should be substituted. Dapsone is as effective as co-trimoxazole for prophylaxis against PCP but does not prevent other opportunistic infections, e.g. toxoplasmosis, isosporiasis and bacterial infections.

## VACCINATION

Aerosolised pentamidine is not cost effective in the local setting.

Live vaccines should generally be avoided in adults. Yellow fever vaccine may be safe if the CD4+ count is > 200. When the CD4+ count is < 200 antigenic responses tend to be poor and short-lived for all types of vaccinations. A transient increase in viral load, experienced following vaccination, can be discounted.

- Influenza vaccination should be administered annually.
- The present 23 polyvalent pneumococcal vaccine should be avoided as there is strong evidence that it is harmful. Further trials on other pneumococcal vaccines are awaited.
- Hepatitis B vaccine should be administered to hepatitis B surface antigen-negative patients.