

HATiP

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HIV and TB in Practice for nurses: cotrimoxazole prophylaxis

By Keith Alcorn

This edition of HATIP targeted to nurses and other health care workers involved in task shifting in sub-Saharan Africa is kindly supported by the Stop TB Department of the World Health Organization.

These special editions of HATIP are intended to support the capacity development of nurses and other health care staff as they take on new roles and tasks in the scale-up of HIV counselling and testing, antiretroviral treatment, HIV/TB activities, TB case finding, diagnosis, treatment and cure.

One of our goals with these editions is to draw out key messages and issues within the last several months addressed in HATIP, the HATIP Blog, and www.aidsmap.com news coverage relevant to nurses, and others providing counselling, medical care and support services; and then to link these to related job aids, training materials, posters and training manuals that may be useful.

This edition looks at the importance of cotrimoxazole prophylaxis, which sometimes gets overlooked when talking about antiretroviral therapy and TB treatment in people living with HIV.

What is cotrimoxazole?

Cotrimoxazole is an antibiotic that is widely available in low and middle-income countries. It forms an essential part of the formulary in most health facilities. It is an Essential Medicine in most countries – this means that it plays an important role in the treatment of widespread diseases, so stocks of this drug need to be maintained at high enough levels to meet the needs of all people who might benefit from it.

Cotrimoxazole is a broad-spectrum antibiotic. This means it treats a wide range of bacterial infections. It is also effective against the malaria parasite, and against some other diseases too.

Cotrimoxazole is an important medicine in the treatment and prevention of infections in people living with HIV. It is especially important as a preventive medicine, or prophylaxis. For this reason the national guidelines of most countries recommend that all people living with HIV who have HIV-related symptoms including TB – and those without symptoms who have CD4 cell counts below 350 – should receive cotrimoxazole to prevent infections, even if they are not eligible to start antiretroviral therapy. Some countries have chosen to provide cotrimoxazole prophylaxis for everyone living with HIV regardless of CD4 count.

The benefits of cotrimoxazole prophylaxis in adults and adolescents

There is now a lot of compelling evidence that cotrimoxazole benefits people with HIV – but also evidence that many people living with HIV are not getting this medicine.

Cotrimoxazole's impact on survival, serious illness and hospitalisation in people with HIV is largely due to its anti-bacterial and anti-protozoal properties. It protects against severe bacterial

infections and malaria, and against toxoplasmosis and pneumocystis carinii pneumonia, serious opportunistic infections.

[Cotrimoxazole improves survival](#) in TB patients with HIV even if they are already receiving treatment for TB; this has been demonstrated in two studies, [most recently in 2008](#). This effect was stronger after people had completed a course of TB treatment, but began to dwindle after 18 months, probably because people in the study began to take cotrimoxazole less regularly, or stopped taking it altogether. WHO recommends that all people with HIV who are diagnosed with TB should receive cotrimoxazole prophylaxis regardless of CD4 count.

[Free cotrimoxazole improves retention in care](#) for adults not yet eligible for ART. Giving a person medication which helps to keep them healthy is a good way of ensuring that they will remain in touch with their health care provider. It is also a good opportunity for beginning the process of educating patients about HIV and antiretroviral treatment, so that when they need to start antiretroviral therapy they know what to expect.

Cotrimoxazole prophylaxis even [appears to provide benefit to HIV-negative members of the household](#) when an HIV-positive member takes it. By preventing adult deaths, it also protected children under the age of 10 years, who are likely to be vulnerable if a parent dies, in a study in Uganda which looked at the effect on the household of providing cotrimoxazole to a family member with HIV. It also reduced other illnesses, such as diarrhoea, among all household members, and there were fewer cases of malaria throughout the household.

Cotrimoxazole for people taking ART

Cotrimoxazole prophylaxis also reduces the death rate in people taking antiretroviral therapy by around 60%. ([Read our report here.](#)) People starting antiretroviral treatment with low CD4 counts (especially below 100) may still be vulnerable to bacterial infections and other conditions until their CD4 cell counts rise substantially after starting antiretroviral therapy. Cotrimoxazole prevents these infections during the period that the immune system is regaining its strength.

It is still not clear how long cotrimoxazole prophylaxis should continue after starting antiretroviral therapy in settings where there are high background rates of bacterial infections or malaria. The World Health Organization recommends that if CD4 testing is not available, cotrimoxazole prophylaxis should not be stopped in settings where bacterial infections and malaria are common.

Where CD4 counts are available, cotrimoxazole prophylaxis may be discontinued in settings where bacterial infections and malaria are common only after the CD4 cell count has risen above 350, after at least six months of antiretroviral therapy. In settings where these infections are not common, and where the primary purpose of cotrimoxazole prophylaxis is to protect against pneumocystis carinii pneumonia and toxoplasmosis, it may be discontinued after the CD4 cell count has risen above 200 after at least six months of antiretroviral therapy.

Malaria prevention

[Cotrimoxazole reduces the risk of developing malaria](#) in adults taking ART, and is [a better form of prophylaxis](#) than standard malaria preventive treatment in pregnant women with HIV. A study in Uganda which looked at how well cotrimoxazole protected against malaria found that new cases shot up within a month of stopping cotrimoxazole in people who were taking antiretroviral therapy. This underlines the importance of maintaining a regular supply of the

drug and making sure that patients return regularly to the clinic, even when they are taking ART.

Cotrimoxazole dosing and side-effects

The adult dose is one 960mg or two 480mg tablets once daily.

The most frequent side-effects are headache, nausea and diarrhoea. These affect fewer than one in ten patients. Nausea may be reduced if the drug is taken with food. It should be taken with plenty of water.

Some people are allergic to cotrimoxazole and develop reactions such as a red rash, sometimes with fever or skin peeling and blistering. In affected people, this usually occurs during the second week of taking the drug.

In rare cases these reactions are extremely serious, so patients should be educated to report these side-effects if they worsen.

Health care workers should monitor for side-effects every three months in all patients taking cotrimoxazole, but side-effects of rash and fever are most likely to occur in the first two to four weeks of treatment, so it is especially important to warn patients to report skin reactions and fever that appear soon after starting this medication.

Although this side-effect is rare it is important to be aware of the different grades of rash that may appear and the recommendations for managing rash.

Management of adverse events		
Toxicity	Clinical description	Recommendations
Grade 1	Erythema (reddening of the skin)	Continue cotrimoxazole prophylaxis with careful and repeated observation and follow-up. Provide symptomatic treatment, such as antihistamines, if available.
Grade 2	Diffuse maculopapular rash (skin rash of small bumps), dry desquamation (skin peeling)	Continue cotrimoxazole prophylaxis with careful and repeated observation and follow-up. Provide symptomatic treatment, such as antihistamines, if available.
Grade 3	Vesiculation (blisters), mucosal ulceration	Cotrimoxazole should be discontinued until the adverse effect has completely resolved (usually two weeks) and then reintroduction or desensitisation can be considered.
Grade 4	Exfoliative dermatitis (skin loss), Stevens-Johnson syndrome or erythema multiforme, moist desquamation (severe rash, potentially life-threatening).	Cotrimoxazole should be permanently discontinued.
Source: WHO Guidelines on Cotrimoxazole Prophylaxis for HIV-related infections among children, adolescents and adults, 2006.		

Desensitisation means using small doses, followed by ascending doses, in order to get the body accustomed to the presence of the drug. After a week the patient is taking the full dose. Nurses should

follow a local protocol for doing this, because it depends on the availability of liquid formulation and lower-dose tablets.

Bone marrow suppression is a rare side-effect of cotrimoxazole and may lead to neutropenia and anaemia, so caution is needed when using cotrimoxazole with other drugs known to cause these toxicities.

Another rare side-effect is hepatitis, or asymptomatic increase in liver enzymes (transaminitis).

Contraindications to cotrimoxazole include:

- Sulfa drug allergy
- Severe renal insufficiency (creatinine > 3 times normal)
- Severe hepatic insufficiency (LFTs > 5 times normal)

Dapsone may be used in place of cotrimoxazole when necessary.

When a patient is eligible to start ART and cotrimoxazole prophylaxis, start cotrimoxazole two to four weeks before ART due to the risk of rash, which is a common side-effect of efavirenz and nevirapine and some other antiretroviral drugs, unless ART is needed urgently (for example in persons with TB and a CD4 cell count below 50). This interval will allow nursing staff to assess patient readiness for ART and to prepare the patient for ART, and will also allow the patient to become used to taking medication.

Cotrimoxazole and isoniazid may be safely co-administered.

Cotrimoxazole can be safely initiated during pregnancy or breastfeeding.

Cotrimoxazole prophylaxis in infants and children

Cotrimoxazole reduces the risk of death in children with symptomatic HIV disease and it is highly cost-effective. It is also recommended for HIV-exposed infants from 4-6 weeks of age until HIV infection is excluded, and for any child with HIV below the age of one year, and for children above this age with any symptoms of HIV disease or a CD4 cell percentage below 25. In settings with a high burden of infectious diseases, national guidelines may recommend cotrimoxazole prophylaxis for all children.

Indeed in 2006 WHO recommended that cotrimoxazole prophylaxis for children should be [part of any national AIDS programme](#)

WHO 2006 recommendations on cotrimoxazole prophylaxis for infants and children			
HIV-exposed infants and children	Infants and children confirmed to be living with HIV		
	< 1 year	1 – 4 years	5 years and over
Universally indicated from 4-6 weeks of age until cessation of risk of HIV transmission and exclusion of HIV infection	Cotrimoxazole indicated regardless of CD4 percentage or clinical status	WHO clinical stages 2,3 and 4 regardless of percentage OR Any WHO stage and CD4% <25%	Follow adult recommendation

- Cotrimoxazole prophylaxis should start after ART where ART is urgently indicated, for example in infants under one year of age, who are at particularly high risk of disease progression.
- Cotrimoxazole must be continued, unless the child is proven to be HIV negative.
- Cotrimoxazole may be stopped in children on ART who are over one year of age and where there is evidence that the immune system is functioning well.

- In order to stop cotrimoxazole, the child must have two CD4 counts greater than 15% or 500 cells, taken at least three months apart.

Improving cotrimoxazole coverage in children: the role of nurses

Research shows that by 2008 Swaziland, Botswana and Rwanda had achieved relatively high levels of infant coverage, although other countries such as Nigeria, Lesotho and Kenya were providing cotrimoxazole to very few infants of HIV-positive mothers.

High levels of infant coverage in Botswana, Rwanda and Swaziland appear to be linked with national-level efforts to improve the follow-up and care of mothers with HIV and their infants through:

- Specialised training for all health care workers in maternal and newborn health in how to screen for and recognise infants with HIV
- Greater linkage of **all** programmes diagnosing mothers with HIV to promote follow-up and testing of children
- Use of community-based organisations to follow up mothers in the community to ensure continued engagement with newborn services
- Integration of paediatric HIV activities into district and regional health plans.

In Swaziland, [operations research carried out by the Ministry of Health, Population Council, USAID and the Elizabeth Glaser Pediatric AIDS Fund](#) observed a 24% increase in paediatric cotrimoxazole uptake after the implementation of a project to improve access to quality postnatal care for all women. This project involved a training programme for all health care workers in the full spectrum of high quality post-natal care, of which the offer of cotrimoxazole prophylaxis was one element. The pilot project also looked at ways of reducing waiting times and improving the experience of mothers during their visit to the facility. Confidentiality and privacy were promoted, and there was an ongoing mentoring programme to support facilities in making changes and to identify continuing gaps in knowledge.

A review [conducted by AIDSTAR-One for USAID in 2010](#), which reviewed cotrimoxazole management and availability in 15 countries found that where national programmes and non-governmental organisations had worked together to assess demand, plan procurement to meet the anticipated need and manage the supply chain, cotrimoxazole was widely and consistently available. But, in countries where partners were not well co-ordinated, availability was less reliable.

Cotrimoxazole dosing for infants and children

Dosing of cotrimoxazole in infants and children varies by age and weight. Cotrimoxazole is a combination of two compounds, sulphamethoxazole (SMX) and trimethoprim (TMP), so dosing must ensure that the correct doses of both compounds are contained in liquids or split tablets. WHO has produced this useful guide to the different doses by age, weight and formulation.

Age or weight of child	Dose (SMX / TMP)	Suspension (5ml = 200mg SMX + 40mg TMP)	Single strength tablet (400mg SMX + 80mg TMP)	Double strength tablet (800mg SMX + 160mg TMP)
< 6 months or <5kg	100mg / 20mg	2.5ml	One-quarter tablet	
6 months – 5 years or 5 – 15kg	200mg / 40mg	5ml	One-half tablet	
6 – 14 years or 15 – 30kg	400mg / 80mg	10ml	One tablet	One-half tablet
>14 years or > 30kg	800mg / 160mg		Two tablets	One tablet

Side-effects and contraindications are the same in infants and children as in adults.

Resources for health care workers

Research for the Interagency Task Team for Prevention of HIV Infection in Pregnant Women, Mothers and Children has also shown that access to cotrimoxazole has been impeded by:

- Lack of national policy support for cotrimoxazole to be prescribed or dispensed by lower-level health care workers.
- Insufficient training on the importance of cotrimoxazole prophylaxis.

AIDSTAR has produced [a number of tools and job aids](#) for health care workers to support making cotrimoxazole available, increasing community awareness and demand.

WHO & UNICEF [published practical guidance on implementation and scale-up](#) of cotrimoxazole prophylaxis for infants and children in 2009.

WHO published [Guidelines on cotrimoxazole prophylaxis for HIV-related infections among children, adolescents and adults](#) in 2006.

I-TECH [Clinical Mentoring Toolkit](#): Cotrimoxazole prophylaxis case study ([Download Word document](#)).