

# HATiP

HIV & AIDS Treatment in Practice

Issue 194 | 08 June 2012



## In this issue:

### **HIV and TB in Practice for nurses: ART and TB prevention; by Theo Smart *page 2***

- Latent TB and active TB
- Risks for TB in people living with HIV
- Preventing HIV-related TB
- Further resources

# HIV and TB in Practice for nurses: ART and TB prevention

By Theo Smart

This is the fifth edition of HATiP targeted to nurses and other health care workers involved in task shifting in sub-Saharan Africa, 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](http://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.

If you have validated materials targeting nurses and others involved in task shifting that you would like to share, or are a nurse or health care provider and want to see particular issues addressed, or would like to share your personal experience in task shifting, please contact us at [info@nam.org.uk](mailto:info@nam.org.uk). We would particularly like to thank Dr Varanna Dogan, Programme Advisor in the TB/HIV Technical Team at Wits Reproductive Health and HIV Institute, for contributing materials to support this edition, and to the Institute for allowing us to make these materials available for download to HATiP readers (see *Further resources* section of this edition).

This fifth issue is about how people living with HIV have a much greater risk of active TB— and how ART can reduce, but not entirely wipe out the threat of TB. We also look at isoniazid preventive therapy in relation to ART. [HATiP 183](#) covered the same topic in a more technical way (and the references for most of the points below can be found there unless otherwise noted).

## Did you know?

**Did you know that the risk of TB in people living with HIV is much higher than in HIV-negative people:**

- **At any CD4 cell count**
- **Even just after becoming HIV-infected, and**
- **Even after going on ART**

## Latent TB and active TB

It is estimated that about a third of the people on the planet have been exposed to mycobacterium tuberculosis (M.TB — the small bacteria that causes TB) and have developed a latent infection. That means the infection is still there in the lungs, but it lies inactive, walled off by cells from the immune system within nodules called granulomas.

That is how the TB infection will remain in most people with latent TB. But in one person out of ten, the dormant M.TB will wake

up or 'reactivate' to become active TB —usually pulmonary TB (TB in the lungs). In about half of the cases, this happens within one or two years of becoming infected with TB. The rest may only develop active disease years later, often when they have other illnesses or as a result of the declining health that comes with old age.

TB has been around as long as recorded history (there is an interesting illustrated timeline, 'A Brief History of TB', on page 4 and 5 of the [September 2011 issue of the Treatment Action Campaign's magazine, Equal treatment](#)), but we still don't fully understand everything there is to know about the disease.

For example, although we know how TB is spread and contracted (in crowded conditions, with poor ventilation and repeated exposure), it is still a bit of a mystery why some people exposed to TB in the household get infected and others with similar exposure do not.

Nevertheless we do know that by the time they reach adulthood, most South Africans living in townships and informal settlements have latent TB infections — in fact, WHO estimates that 88% of those between the ages of 30 and 39 harbour latent TB infections.

How many will progress to full-blown active TB? At least 10%, and probably more in regions like southern Africa where a number of factors known to increase the risk of developing TB are very common. For example, it has been demonstrated that poor nutrition, drinking alcohol to excess, and having lungs already damaged because of indoor pollution, smoking or inhaling dust that contains glass-like particles (silicosis)—common among those who have worked in the mines—all increase the risk of active TB.

## What is the lifetime risk of developing active TB?

Some illnesses also increase the risk of developing active TB, such as cancers and diabetes. HIV is far and away the most dangerous illness for someone with latent TB. It increases the risk of active TB dramatically.

|   | Risk of TB   |
|---|--|
| <b>HIV-negative persons</b>   | 1 in 10 <b>lifetime</b> risk of developing TB  |
| <b>HIV-positive persons</b>   | 1 in 10 <b>annual</b> risk of developing TB<br>20-37 times higher risk than HIV negative persons<br>Higher risk if skin-test positive (i.e. latent TB infection) |
| <i>Excerpted from: <b>The Basics of TB for TB counselors and GXP counselors, a powerpoint presentation from the WRHI (Wits Reproductive Health and HIV Institute)</b></i> |  |

So how do we prevent HIV from triggering cases of active TB? The best strategy depends on how the person has been affected by HIV, because the risk of TB varies over the course of the disease — and some tools seem to work better at some stages of disease than others.

Without a doubt, the greatest risk of TB is in people with low CD4 cell counts when the body's defences are too weak to control either HIV or M.TB. But even early in the course of HIV infection, while CD4 cells are still high, the risk of active TB is much greater in people living with HIV than in HIV-negative people. Something needs to be done to reduce it.

For instance, a large international study called CASCADE, [presented at the International AIDS Society conference](#) in 2011 found that the risk of TB changes depending on how long someone has been HIV-infected, with falling CD4 cell counts, and the use of ART.

## Risks for TB in people living with HIV

### TB risk and CD4 cell count

*There is no CD4 cell count where a person living with HIV is safe from developing active TB.*

The risk of TB in people with CD4 cell counts above 500 is dramatically higher than in the general public. In the Cascade Study at least, the risk of TB increased a little more, but not significantly, for people with CD4 cell counts between 350-500.

*The risk of TB grows much greater when CD4 cell counts fall below 350 and especially below 200 CD4 cells.* In the CASCADE study, the risk of TB doubled at CD4 cell counts between 350 and 200, then it shot through the roof when CD4 cell counts fell below 200. But the CD4 cell count does not appear to be the only factor increasing the risk of TB in people living with HIV.

### Time since HIV infection

*The risk of TB jumps very soon after becoming HIV-infected and continues climbing sharply over the next year, according to the CASCADE study.*

After that, though the risk in the HIV-infected participants of the CASCADE study fell by about half and stayed more or less the same for two or three years. Then it began to grow again, with TB becoming more and more common the longer someone had been infected – until starting antiretroviral treatment.

Notably, this mirrors how the level of HIV in the blood is very high soon after infection, and then a massive response from the body's immune system knocks it down and keeps it low for a few years in many people. Then, viral load begins to rise again – and at that point, CD4 cell counts begin declining.

That doesn't mean that TB prevention becomes less important during this stage, because the risk of TB is still far greater than when someone is not HIV-infected. But it may tell us something about TB and HIV – either the high HIV levels, or the immune system reaction to it, are partly responsible for the high risk of TB in people living with HIV.

HIV infection seems to enable TB to break free from the places where it is walled up in the lungs. When someone is infected by HIV, their immune system tries to mount a defence against it, and some of the weapons the immune system uses accidentally break down the granuloma prison walls, wake up the sleeping TB bacilli, which then escape, and while HIV keeps the immune system busy or distracted, TB colonies spring up in lungs, and the bacteria may be free to spread to other parts of the body, causing extrapulmonary TB.

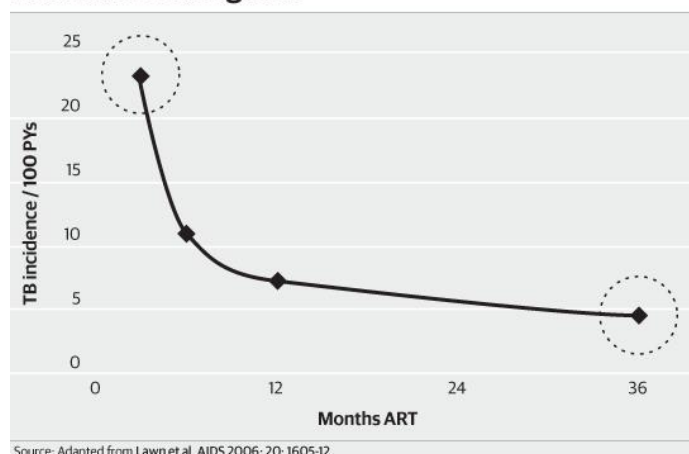
Another way of looking at it is that when a person has latent TB, the immune system can't wipe the TB out, but it can contain it – there is a sort of balance. HIV disturbs the balance. This might also explain the gradual decline in the risk of TB when someone living with HIV is put on ART.

### The risk of TB on ART

ART dramatically reduces the risk of TB in people living with HIV in people who qualify for treatment (with CD4 cell counts below 350) according to data from CASCADE and several other studies.

However, during the early weeks after starting treatment, there is a **jump** in TB diagnoses shortly after starting ART in people, especially those who come to the clinic with very low CD4 cell counts (below 50).

## Incident TB during ART



These TB cases are most common in the first three to six months after going onto ART. Some of the cases are due to the immune system belatedly recognising previously undetected TB, and reacting quite violently. However, other cases may actually be triggered by changes in the balance of the immune system, now that it no longer has to contend with so much HIV. The first several months on ART are a time to monitor patients very closely.

### People on ART continue to have a significantly higher risk of TB than the general population

In the CASCADE study, after people had been on effective ART for about two years, and from then onward, the risk of TB was lower than at any point since HIV infection – but it was still higher than among the general population.

This could be because the immune system never fully recovers after HIV – or takes years to do so.

Another possibility is that people living with HIV are at greater risk of being exposed to TB, either in their communities, or their health facilities or other congregate settings.

### Starting ART earlier, when CD4 cell counts are above 350, has not been shown to have much effect upon the risk of TB

Many researchers believe that earlier treatment, at CD4 counts above 350, could be expected to reduce the risk of TB – and indeed this makes sense if it prevents people's CD4 cell counts from falling to where they are at greater risk of TB.

However, findings from a randomised study of earlier treatment in couples where one partner has HIV and the other does not – this was the famous study that showed ART could prevent HIV transmission between these couples – also looked at whether earlier treatment reduced the risk of pulmonary TB. It did not reduce the risk of TB over the relatively limited course of follow-up in the study, though there was some change reported in extrapulmonary TB, mostly at sites in India.

Other studies have shown that sustaining CD4 cell counts above 500 is associated with less risk of TB. People who start treatment with higher CD4 cell counts have a better chance of keeping them high. So over the long run, this may be a good strategy.

Nevertheless, when someone starts to take ART, reducing the amount of HIV in the body could temporarily disturb the balance in the immune system, and activate TB, or, people attending the clinic routinely to receive ART might also be exposed to TB in the health facility.

## Preventing HIV-related TB

### HIV prevention IS TB prevention

In high-burden settings, there are high rates of M.TB exposure and latent infection just as people enter early adulthood. At this time they become more sexually active, so increasing their risk of HIV, and HIV infection increases their risk of developing active TB too.

So the best way to prevent the increased risk of active TB in young people and adults is to keep them from ever becoming HIV-infected — controlling TB in these settings may depend upon it.

### Scale-up HIV testing and counselling to find people living with HIV as soon as possible

Identifying HIV-positive people earlier in the course of infection may provide an opportunity to prevent TB before the risk grows too high. Too many people living with HIV are only diagnosed *AFTER* they have been diagnosed with TB.

### Screen for TB using the WHO 4-symptom screening tool

Screen for TB using the WHO 4-symptom screening tool during HIV testing and counselling, and routinely in all people living with HIV, at all CD4 cell counts and regardless of whether they are on ART or not, because they continue to be at risk of TB.

Those with symptoms of TB should be provided with diagnostic services, and those without should be put on isoniazid preventive therapy, unless it is contra-indicated. Note however, that...

### ART is the most important TB prevention tool in people with CD4 cell counts below 350

Getting people who qualify for treatment onto ART is the first priority, because they are at risk of other opportunistic infections and malignancies — and the reduction in risk of TB is profound.

### Screen intensively and monitor closely for TB or TB IRIS during the first six months of initiating ART

The risk of TB or TB IRIS is particularly great in people with very low CD4 cell counts. In people with CD4 cell counts below 50, having access to new diagnostic tools like the LAM lateral flow test or the Xpert MTB/Rif test may increase the ability to diagnose TB in these patients.

Engaging expert patients and community health workers to keep closer track of these patients may be another strategy to detect TB before it is too late.

| Impact of ART and INH on TB incidence according to tuberculin skin test (TST) status: the BOTUSA study |                          |                          |
|--|--------------------------|--------------------------|
|  | TST negative             | TST positive             |
|  | HR (% reduction in risk) | HR (% reduction in risk) |
| ART alone  | 0.44 (56%)               | 0.44 (56%)               |
| 36 months INH alone  | 0.92 ( 8%)*              | 0.07 (93%)               |
| ART & INH  | 0.40 (60%)*              | 0.03 (97%)               |
| * non-significant reductions in risk of TB   |                          |                          |
| Adapted from: Samandari, Lancet, 2011.   |                          |                          |

### Isoniazid preventive therapy (IPT) can prevent TB in people with high CD4 counts and low CD4 cell counts

Isoniazid preventive therapy can prevent TB in people with high CD4 counts and low CD4 cell counts, when there are signs of immune response to TB, as measured by a positive tuberculin skin test (TST).

TSTs can be difficult to perform in some settings and given the high risk of TB in people living with HIV, WHO guidelines emphasise that TSTs are not a requirement for initiating IPT.

### Providing IPT may further reduce the risk of TB when it is given to people on ART

Several studies have shown that co-administering IPT to people taking ART results in fewer cases of TB. In the BOTUSA study, the effect on TB was not great for the population overall, but was dramatic in those who were tuberculin skin test positive.

### Good infection control in facilities where people on ART congregate is essential.

ART cannot prevent exposure to infectious TB but good infection control practices can. A future bulletin will look at TB infection control more closely.

| IPT or ART?   |  |
|---|--|
| High CD4 count?   | IPT  |
| Low CD4 count   | ART<br>- If the patient on IPT is ready for ART, do not delay ART  |
| Patient on ART  | - ART reduces the risk of TB<br>- But PLHIV still at risk compared to HIV negative people<br>- There should be increased vigilance for TB with systematic TB screening before initiating and during ART<br>- During the first 6 months after start ART there is a risk for TB IRIS |
| Patient on ART and IPT  | - There may be an increased risk of peripheral neuropathy when d4T is part of the ART regimen<br>- Watch for liver toxicity in those taking nevirapine   |
| <b>BUT EXCLUDE ACTIVE TB FIRST!</b>   |  |
| Adapted from: from: 'Kick TB Out..... Using Isoniazid Prophylactic Therapy (IPT)', Training slides provided by Wits Reproductive Health and HIV Institute, and from: 'TB and HIV Control'. Republic of South Africa 14 October 2011 Department of Health, Republic of South Africa. |  |

## Further resources

`Kick out TB using isoniazid prophylactic therapy` : Training slides developed by Wits Reproductive Health and HIV Institute, South Africa, supported by PEPFAR. ([Download pdf of slide set, 448kb](#)).

`The basics of TB for TB counselors and GXP counselors` : Training slides developed by Wits Reproductive Health and HIV Institute, South Africa, supported by PEPFAR. ([Download pdf of slide set, 298kb](#)).

ARASA Three I's HIV/TB Advocacy and Communication Toolkit: Training materials on HIV and TB for advocates and the community

sector, designed to be used at grassroots level. ([Download pdf part 1](#), 3.04mb); ([Download pdf part 2](#), 2.19mb).

## about HATiP

A regular electronic newsletter for health care workers and community-based organisations on HIV treatment in resource-limited settings.

The newsletter is edited by Theo Smart (Cape Town) and Keith Alcorn, NAM's Senior Editor (London).

For further information please visit the HATIP section of [aidsmap.com](http://aidsmap.com)