

## **HIV/TB meeting report at 15th conference on retroviruses and opportunistic infections**

*February 3, 2008, Boston, USA.*

The Stop TB and HIV/AIDS Departments of the World Health Organization (WHO) in collaboration with the Consortium to Respond Effectively to the AIDS TB Epidemic (CREATE) organized an HIV/TB meeting as an affiliated event to the 15<sup>th</sup> Conference on retroviruses and opportunistic infections (CROI 2008) on behalf of the TB/HIV Working Group of the Stop TB Partnership. The meeting was held on Sunday February 3, 2008 at Westin Copley Place Hotel in Boston, USA and was attended by more than 50 leading HIV researchers, policy makers and representatives from funding agencies. The main objectives of the meeting were to review ongoing research efforts, promote interchange of scientific ideas on unmet research needs and discuss priorities around the prevention of TB (isoniazid preventive therapy) and enhanced TB case finding (TB screening) among people living with HIV (PLHIV). The meeting was chaired by Dr Diane Havlir from the University of California at San Francisco as chairperson of the Global TB/HIV Working Group of the Stop TB Partnership. She began by stating that the meeting is part of a series of efforts that the TB/HIV Working Group and WHO are conducting in conjunction with the main HIV conferences in order to promote basic and operational research around HIV/TB and to enhance interchange of experiences and ideas among HIV researchers and funding agencies.

Dr Haileyesus Getahun of the Stop TB Department of WHO presented the current level of global implementation of TB prevention and intensified TB case finding among PLHIV. Although there are limitations in the global monitoring system that may lead to underestimating the level of activity, the reported rate of implementation of IPT and TB screening among PLHIV is very low. By the end of 2006, only 0.08% and 0.96% of PLHIV were put on IPT and screened for TB respectively. Most of the data is coming from very few countries, despite the existence of national policies to offer these interventions in many more. For example, 82 countries stated that they have national policies that allow the provision of IPT for PLHIV by end of 2006. However, only 24 countries actually reported the provision of IPT to PLHIV and 70% of these cases were reported from a single country (Botswana). Likewise, 109 countries reported having a policy promoting TB screening among PLHIV but only 44 countries actually reported the activity. ([http://www.stoptb.org/wg/tb\\_hiv/assets/documents/Getahun\\_CROI\\_2008.pdf](http://www.stoptb.org/wg/tb_hiv/assets/documents/Getahun_CROI_2008.pdf)). This disconnect between policy and practice is a clear reflection of the operational difficulties in scaling up these two important interventions. During the discussion, on top of the absence of a rapid, simple and accurate diagnostic tool for TB, the lack of a standard evidence-based diagnostic algorithm and poorly developed laboratory systems were cited as the main bottle necks for implementation. The perceived risk of drug resistance following use of IPT and the overall control and authority of National TB Control Programmes over the purchase and distribution of isoniazid were cited as challenges for the scale-up. It was also suggested to systematically document the experiences of co-trimoxazole prophylaxis expansion programmes and draw lessons, if any, for the scale-up of IPT.

Dr Kevin Cain of CDC gave an overview of published, unpublished and ongoing research findings around intensified case finding among PLHIV. His presentation was jointly prepared with Dr Jay Varma also from CDC. It was noted that there is a dearth of published literature on the topic and most of those studies reported did not use culture as a gold standard to confirm the diagnosis of TB. Nonetheless, most studies suggested that chronic cough may be insufficiently sensitive as a diagnostic indicator for TB among PLHIV, and a combination of symptoms and

signs may be needed. Dr Cain shared preliminary data from their multi-country study in South East Asia including a recalculation and comparison of the sensitivity and specificity of symptoms and signs used in previous studies to diagnose TB among PLHIV, applying the results found in their study. Their newly calculated specificity and sensitivity figures are, by and large, inconsistent with the reported figures in the published studies. They also reported stratified analysis of their data using CD4 count of 250 as a cut off of point to explore the role of symptoms and signs as tool to diagnose TB. The draft IPT Consensus Statement of the TB/HIV Working Group (which is still under development) emphasized symptom screening to diagnose TB before the start of IPT at CD4 count > 250. Their preliminary findings suggested that symptom screening may not be able to rule out TB at a higher CD4 count ([http://www.stoptb.org/wg/tb\\_hiv/assets/documents/Cain\\_CROI\\_2008.pdf](http://www.stoptb.org/wg/tb_hiv/assets/documents/Cain_CROI_2008.pdf)). Dr Stephen Lawn from the Desmond Tutu HIV Centre in South Africa briefly shared preliminary findings from their ongoing study where 31% of referred adult PLHIV for ART have culture proven TB with a higher rate of drug resistant TB ([http://www.stoptb.org/wg/tb\\_hiv/assets/documents/Lawn\\_CROI\\_2008.pdf](http://www.stoptb.org/wg/tb_hiv/assets/documents/Lawn_CROI_2008.pdf)). The extraordinarily high rates of TB in their study area, as has been illustrated in previous publications, was noted in discussion to be unique, and further exploration to define the causes was suggested. Non-TB mycobacteria (NTM) were not much of a problem in this African setting in contrast to the report by Dr Cain from the Asian settings where high rates of NTM were reported. During the discussions, defining the best clinical approach (and symptom and sign complexes) to rule-in and rule-out TB among PLHIV, as confidently and expeditiously as possible, was underlined as an urgent research priority. The importance of replicating the reported multi-country study of CDC in sub-Saharan Africa was also mentioned.

The other important topic that was discussed during the meeting were the options available for the prevention of TB among PLHIV beyond IPT. Dr Richard Chaisson of the John Hopkins University and CREATE gave a general overview ([http://www.stoptb.org/wg/tb\\_hiv/assets/documents/Chaisson\\_CROI\\_2008.pdf](http://www.stoptb.org/wg/tb_hiv/assets/documents/Chaisson_CROI_2008.pdf)). He started his presentation by mentioning the limitations of IPT which include operational difficulties in its implementation, limited duration of protection, and high breakthrough rates of TB even when combined with ART. He summarized ongoing studies that are intended to explore better options, including the use of isoniazid in different combinations with other drugs (e.g. rifampicin and rifapentine), different durations, and other drugs (e.g. PA 824, moxifloxacin ). He also discussed the role of secondary IPT for PLHIV to prevent recurrence of TB and underlined the importance of TB infection control and intensified case finding as part of a TB prevention strategy. During the discussion the role of IPT in settings which are badly affected by both TB and HIV was debated, as the possibility of missing cases with TB (and hence mono-treatment) is high. In such settings, exploring the role of short-duration (e.g. 1-3 months) TB treatment with full drug regimen drugs as a means of TB prevention among PLHIV was suggested. While advocating for greater implementation of IPT, as it is the only evidence based tool available for TB prevention among PLHIV, concomitant intensification of research efforts (and identification of funding streams) was recommended to identify better TB prevention tools, mainly for PLHIV.

It was noted that children are generally neglected in most of the research efforts around HIV/TB. More emphasis was suggested on studies that look at the interaction of anti-TB drugs, including those in the pipeline, with new ART drugs. The role of new ART drugs in TB prevention should also be studied.

It was agreed to continue this series of meetings and promote the exchange of ideas and experience among HIV researchers and funding agencies in conjunction with major HIV conferences.