Annual meeting of the Tuberculosis Surveillance and Research Unit, 2008


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The Tuberculosis Surveillance and Research Unit (TSRU) held its last annual meeting in Helsinki, Finland, from 1 to 4 April 2008. Several topics of current interest for tuberculosis (TB) research and new research projects were presented and discussed in depth by 60 delegates from Europe, Africa and Asia. This paper summarises some of the highlights of the meeting which may be of interest to epidemiologists and managers active in the field of TB.

KEY WORDS: tuberculosis; research; surveillance

THE TUBERCULOSIS SURVEILLANCE and Research Unit (TSRU) was founded in 1966, with Dr Karel Styblo as Research Director.1 The main objective of the TSRU is to host a forum to discuss tuberculosis (TB) epidemiology relevant to TB control and surveillance. Planned, ongoing or finalised research projects in various countries are presented in an annual meeting. A specific feature of TSRU meetings is that there is ample time dedicated for discussion of each project. There are four thematic sessions and free presentations. All papers are compiled as the annual progress report of the TSRU meeting.

KNCV Tuberculosis Foundation hosts the secretariat of the TSRU. Members of TSRU are the World Health Organization (WHO), the International Union Against Tuberculosis and Lung Disease (The Union), KNCV Tuberculosis Foundation, and currently the following member countries: China, Germany, Finland, Japan, Korea, Malawi, the Netherlands, Switzerland, Tanzania and Vietnam. Member countries usually have good DOTS programmes and carry out high-quality scientific research on TB. This year, the following issues were presented and discussed.

HIV AND OTHER RISK FACTORS FOR TB

This session of the meeting addressed three risk factors for reactivation or relapse of TB. The discussion highlighted the need for continuous and detailed information on risk factors associated with TB for identifying possible interventions and the target groups for these interventions. The new information on human immunodeficiency virus (HIV) underscores the need for secondary prophylactic treatment regardless of HIV status.

The relation between HIV and a first episode of TB is well documented. A new study from South Africa, presented by J Glynn, demonstrated that the rate of recurrent episodes of TB is higher in HIV-positive men. As the rate slightly increased over time this was probably due to reinfection more than to relapse. Whatever makes an individual more susceptible to TB than another person, this factor continues to act as a major risk factor for another episode, particularly in environments with a high risk of exposure.

C Gunneberg presented uses of the current indirectly measured HIV prevalence in incident TB cases. This method uses country-specific HIV prevalence estimates and applies the incidence rate ratio—a best fitting ratio based on the comparison between the risk of TB among HIV-negative and HIV-positive patients from surveys in many countries.

In 2006, sufficient routine HIV testing of TB patients or national survey data allowed estimate adjustments based on direct country measurements to be made in some countries. The estimates in these 27 countries were on average three times higher than if the indirect method had been used, suggesting that the number of HIV-positive TB cases in these countries may be higher than previously thought. This

[Those interested in the papers presented can request a copy of the TSRU 2008 progress report from the TSRU secretariat at the KNCV Tuberculosis Foundation, The Hague, The Netherlands. e-mail: tsru@kncvtbc.nl]

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highlights the contribution that routine HIV testing of TB patients can make to surveillance, particularly in settings of high HIV prevalence.

A systematic review of the role of alcohol abuse as a risk factor for TB, presented by K Lonnroth, concluded that the risk did not increase significantly with moderate consumption but did so sharply with high consumption. The population attributable fraction was estimated to be globally much higher for men than for women, and could reach high values in countries where alcohol consumption is elevated.

H Rieder presented intriguing data about the seasonal variation of TB notifications in Mongolia, which show a peak in spring, combined with a variation in the male/female ratio, both of which are identical among urban and rural populations. The first observation may be due to an increased risk of transmission of TB during the winter months, but the variation in the male/female ratio remains unexplained.

**PROGRESS TOWARDS THE MILLENNIUM DEVELOPMENT GOALS: TRENDS IN PREVALENCE AND INCIDENCE OF INFECTION AND DISEASE**

The Millennium Development Goals (MDGs) include halving TB prevalence by the year 2015. Surveys of the prevalence of both disease and infection are important not only in monitoring progress with regard to achieving the MDGs but also in helping programmes to monitor the impact of their efforts to control TB.

H Ayles compared different bacteriological and screening methods for prevalence surveys of TB in four places where HIV prevalence is high, two in Zambia and two in South Africa. The methods give different estimates of the absolute as well as the relative values of TB prevalence. She concluded that the best method to diagnose TB in prevalence surveys is to perform two MGIT (Mycobacterial Growth Indicator Tube) cultures for each subject, using the Capilia test for rapid identification.

F van Leth presented a model that tried to assess the prospects for eliminating TB in the Netherlands. He showed that the number of TB patients in the next two decades will be determined largely by what happens among first-generation immigrants. The success of TB control among first-generation immigrants will largely determine the overall rate of decline in the Netherlands.

The prevalence and incidence of TB are particularly high in some African countries, mainly due to the high prevalence of HIV. A van’t Hoog presented the results of a prevalence study in Western Kenya, where the majority of TB patients are HIV-positive. Most importantly, she showed that only a minority of identified cases were currently under treatment.

N Yamada showed that, among children who are household contacts of TB patients in Cambodia, the distributions of tuberculin reaction suggest that the proportion with latent TB infection is lower in areas with good access to DOTS. It was concluded that DOTS reduces household transmission to children in Cambodia. Although it is difficult to derive precise prevalence of infection estimates, tuberculin surveys may still be useful in assessing the impact of TB control on transmission.

H Rieder discussed the potentials and limitations of tuberculin surveys. The main problem arises from the presence of environmental mycobacteria, which produce a response at smaller indurations than TB. Where environmental mycobacteria are common and the prevalence of infection is low, tuberculin surveys may not be useful; where the reverse is true, they can still provide important information. He discussed possible approaches to obtain statistically more valid estimates of the prevalence of infection than with arbitrary cut-off points.

**CHILDHOOD TB**

Consistent with the increased awareness of the importance of childhood TB, the WHO has recently revised its requirements for the reporting of childhood TB by National Tuberculosis Programmes (NTPs), coupled with the publication of a manual for the management of childhood TB for NTPs.

The emergence and increasing prevalence of drug resistance was illustrated in three serial hospital-based surveys of drug resistance amongst children with TB in South Africa by H S Schaaf. The prevalence of all drug resistance increased significantly from 1994 to 2007. These data emphasise the importance of ongoing surveillance of drug resistance using unbiased data including paediatric cases, and the need for early detection and accurate drug susceptibility data from adult index cases in settings with a high prevalence of drug resistance.

The risk of TB among HIV-infected children was illustrated by A Hesseling, who observed a much higher incidence in HIV-infected compared to non-HIV-infected South African infants, despite universal bacille Calmette-Guérin (BCG) vaccination at birth. These data underscore the need for improved TB control strategies in infants and children in settings highly endemic for TB and HIV, including the implementation of contact tracing coupled with isoniazid (INH) preventive treatment, and the need for more effective vaccine strategies.

The differences in drug dosage requirements in children compared to adults, based on the ability to absorb, metabolise and excrete drugs, and the heterogeneity across different populations, were highlighted by P Donald. Currently recommended WHO dosages of 5 mg/kg (range 4–6) for INH and 10 mg/kg (range 8–12) for rifampicin may be suboptimal in some paediatric populations; increased and weight-adjusted
Adolescents are currently targeted as a population for the study of novel anti-tuberculosis vaccines. S Verver showed that the prevalence of TB was higher than the incidence in South African adolescents, and that active surveillance resulted in more and earlier case detection compared to passive strategies in a setting with a high annual risk of *Mycobacterium tuberculosis* infection.

Despite a decline in TB incidence in the United Kingdom, I Abubakar showed that the incidence amongst children remained stable during 1999–2006, and that paediatric cases were mainly concentrated amongst African immigrant children. The rational implementation of selective BCG vaccination and TB screening in such populations was emphasised.

### DRUG RESISTANCE AND RETREATMENT PATIENTS

W Lew presented data from Korea showing that notifications from the public sector decreased from 1991 to 2006, while they increased in the private sector over the same period. The prevalence of all types of primary drug resistance in the private sector was somewhat higher than in the public sector. Multidrug resistance (MDR) slightly increased in the public sector, but decreased in the private sector, and extensive drug resistance (XDR) was seen virtually only in the private sector.

W Lew also showed that the prevalence of MDR-TB among newly diagnosed smear-positive cases slowly increased from 1994 to 2004. Compared to patients with fully drug-susceptible strains, INH-resistant patients had a two-fold increased risk of relapse and those with MDR a six-fold increased risk. Adjustment for all other factors showed that young age, male sex and drug resistance were all associated with relapse.

S Kato summarised the findings in Japan on chronic excretors, defined as TB patients who were registered as cases for >2 years and who had been bacteriologically positive within the last year. Data from the national surveillance system indicated a drop to one third from 1999 to 2006. Among those with known susceptibility patterns, the prevalence of MDR had increased from roughly one fifth to three fifths. In 2006, the main putative causes of becoming a chronic excretor were irregular drug intake by the patient and addition of a single drug by the clinician.

K Lambregts-van Wezenbeek presented a paper for discussion on the adequacy of currently recommended regimens for the retreatment of cases. Concerns about the retreatment regimen include 1) acquisition of drug resistance (one drug is added to a failing regimen), 2) high rates of drug resistance among retreatment cases, especially failures, and 3) high failure rates in patients with INH resistance or MDR-TB. The proportion of TB cases requiring retreatment has shown disturbing increases in some countries. The finding that the proportion of failures among retreatment patients also shows great variation further indicates that a single approach may not be appropriate.

E Hasker presented the design of a study in Tashkent, Uzbekistan. The DOTS strategy had been gradually implemented from 1998 to full coverage in 2005, but had to be embedded into a vertical system with active case finding, mandatory hospitalisation and a preference of radiographic over bacteriological examination of TB suspects. Although the overall treatment outcomes for the 2005 cohort were good, the failure rate in Tashkent city was twice the national average. Moreover, there are anecdotal reports of high recurrence rates after seemingly successful treatment. The retrospective study will assess both response to treatment and outcome up to 1 year after treatment completion and ascertain risk factors for an adverse outcome.

### FREE SESSION: TECHNICAL ASPECTS OF SURVEILLANCE

H Zhang showed that in China, notification rates are highest in the west and north of the country, while case detection rates are estimated to be lowest there. Most efforts to improve case detection should be directed at these provinces.

In Vietnam, the incidence of TB is decreasing in most age groups, but not in young adults. Possible explanations are rapid urbanisation and higher HIV prevalence in big cities. T N Buu presented data from a recent study showing that in a southern rural area the incidence also seemed to be increasing only in young male adults. A trend was seen towards increasing Beijing genotype with younger age.

M van der Werf presented operational research results from Indonesia. Introducing a new laboratory form for sputum collection and examination improved the completeness of acquiring sputum samples from TB suspects. Sputum quality did improve, but was still insufficient.

B Hauer had studied older TB patients in Germany in detail. Even within the elderly age group, incidence increases with older age but treatment success dropped with age, due to both non-TB- and TB-related deaths. Patient management will need to be optimised to improve outcome results in the elderly.

Studies from the Netherlands and Switzerland focused on immigrants. S Verver presented preliminary results among immigrant close contacts of TB cases in the Netherlands. These immigrants were a risk group for TB, but there was no difference in predictive value for TB by tuberculin skin test (≥15 mm) and two interferon gamma assays.
J-P Zellweger, from Switzerland, showed that it is possible to screen undocumented immigrants for TB in dedicated free care centres in a safe environment, i.e., confidential treatment without the risk of patients being reported to the police.

References


