



Published in final edited form as:

Clin Infect Dis. 2009 February 15; 48(4): 496–497. doi:10.1086/596550.

Tuberculosis Transmission From Patients With Smear-Negative Pulmonary Tuberculosis in Sub-Saharan Africa

Stephen D. Lawn^{a,b}, David J. Edwards^a, and Robin Wood^a

^aThe Desmond Tutu HIV Centre, Institute for Infectious Disease and Molecular Medicine, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa

^bClinical Research Unit, Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, UK

Keywords

HIV; antiretroviral; tuberculosis; smear-negative; transmission; nosocomial

SIR-We read with interest the report by Tostmann *et al.* of a national study of tuberculosis (TB) transmission in The Netherlands between 1996 and 2004 [1]. The relative TB transmission rate among patients with smear-negative, culture-positive pulmonary disease compared with patients with smear-positive disease was found to be 0.24. Overall, 13% of tuberculosis (TB) transmission events were attributable to source patients with sputum smear-negative, culture-positive disease. These important findings are in close agreement with similar studies from San Francisco, USA, and Vancouver, Canada [2,3], collectively showing that at in high-income countries 10–20% of TB transmission a population level is due to source cases with smear-negative pulmonary TB. The authors speculated on the relevance of these data for countries where HIV is endemic and rates of smear-negative disease are high.

In sub-Saharan Africa HIV infection has had a devastating impact on TB control [4,5]. In a study community in a township in Cape Town, South Africa, for example, the antenatal HIV seroprevalence rate is approximately 30% and the annual TB notification rate has increased to over 1,500/100,000 [5] – almost 200-fold higher than TB rates in The Netherlands [4]. This has been associated with a major and disproportionate increase in the rate of smear-negative disease among HIV-infected individuals [5]. Moreover, the prevalence of undiagnosed TB (a key determinant of transmission) among HIV-infected patients in this community is very high and disease duration prior to diagnosis is prolonged [6]. In view of these observations, transmission attributable to smear-negative pulmonary TB cases at the community level may be important.

Antiretroviral treatment (ART) services continue to expand in sub-Saharan Africa [7]. The high burden of TB in these clinical settings presents a great challenge with regard to morbidity, mortality and TB transmission risk [8,9]. Nosocomial outbreaks of both drug sensitive and drug resistant TB constitute a major threat [10]. In a recent study in an ART service in Gugulethu township, Cape Town, we did routine microbiological screening for TB in all newly referred ART-naive patients who did not already have a diagnosis of TB. Using automated MGIT 960 liquid culture (Becton Dickinson, Sparks, MD) of sputum, we

found that over one quarter of patients had culture-confirmed pulmonary TB [11]. In this highly immunocompromised patient group, however, more than 80% of this disease was sputum smear-negative despite use of fluorescence microscopy; culture-based diagnosis took over 3 weeks on average. Recurrent attendance of patients at these overcrowded facilities over a period of several weeks while their TB remains undiagnosed represents an unacceptable hazard. These data have important implications for screening for TB among patients entering HIV care and treatment services in Africa. Rapid and appropriate diagnostic tests that are able to detect smear-negative pulmonary TB are urgently needed to reduce risks of transmission in these clinical environments.

In summary, we suspect that TB transmission associated with smear-negative culture-positive TB in communities in Africa with high HIV prevalence may be important and especially in the context of ART services where this is the predominant form of TB.

Acknowledgments

SDL is funded by the Wellcome Trust, London, UK. RW is funded in part by the National Institutes of Health, USA, RO1 grant (A1058736-01A1) and a CIPRA grant 1U19AI53217-01.

References

1. Tostmann A, Kik SV, Kalisvaart NA, et al. Tuberculosis transmission by patients with smear-negative pulmonary tuberculosis in a large cohort in the Netherlands. *Clin Infect Dis*. 2008; 47:1135–1142. [PubMed: 18823268]
2. Behr MA, Warren SA, Salamon H, et al. Transmission of *Mycobacterium tuberculosis* from patients smear-negative for acid-fast bacilli. *Lancet*. 1999; 353:444–449. [PubMed: 9989714]
3. Hernandez-Garduno E, Cook V, Kunimoto D, Elwood RK, Black WA, FitzGerald JM. Transmission of tuberculosis from smear negative patients: a molecular epidemiology study. *Thorax*. 2004; 59:286–290. [PubMed: 15047946]
4. World Health Organization. WHO report. Geneva: World Health Organization; 2008. Global tuberculosis control: surveillance, planning, financing. (WHO/HTM/TB/2008.393).
5. Lawn SD, Bekker LG, Middelkoop K, Myer L, Wood R. Impact of HIV Infection on the Epidemiology of Tuberculosis in a Peri-Urban Community in South Africa: The Need for Age-Specific Interventions. *Clin Infect Dis*. 2006; 42:1040–1047. [PubMed: 16511773]
6. Wood R, Middelkoop K, Myer L, et al. Undiagnosed tuberculosis in a community with high HIV prevalence: implications for tuberculosis control. *Am J Respir Crit Care Med*. 2007; 175:87–93. [PubMed: 16973982]
7. World Health Organization. Towards universal access: scaling up priority HIV/AIDS interventions in the health sector: progress report, April 2007. 2007. http://www.who.int/hiv/mediacentre/universal_access_progress_report_en.pdf.
8. Lawn SD, Myer L, Bekker LG, Wood R. Burden of tuberculosis in an antiretroviral treatment programme in sub-Saharan Africa: impact on treatment outcomes and implications for tuberculosis control. *AIDS*. 2006; 20:1605–1612. [PubMed: 16868441]
9. Lawn SD, Harries AD, Anglaret X, Myer L, Wood R. Early mortality among adults accessing antiretroviral treatment programmes in sub-Saharan Africa. *AIDS*. 2008; 22:1897–1908. [PubMed: 18784453]
10. Gandhi NR, Moll A, Sturm AW, et al. Extensively drug-resistant tuberculosis as a cause of death in patients co-infected with tuberculosis and HIV in a rural area of South Africa. *Lancet*. 2006; 368:1575–1580. [PubMed: 17084757]
11. Lawn, SD. TB and HIV: report from the front line of delivering HIV care and treatment. Abstracts of the 39th Union World Conference on Lung Health; International Union Against Tuberculosis & Lung Disease; October 2008; Paris, France. Abstract #