# Correction

**LETTER (ONLINE ONLY)**

Correction for "Parameters that influence the prediction of epidemiological benefits of more-effective tuberculosis vaccines, drugs, and diagnosis," by Janakiraman Vani, Mohan S. Maddur, Sébastien Lacroix-Desmazes, Srini V. Kaveri, and Jagadeesh Bayry, which appeared in issue 46, November 17, 2009, of *Proc Natl Acad Sci USA* (106:E129; first published October 26, 2009; 10.1073/pnas.0911020106).

The authors note that on page E129, right column, first full paragraph, second line, "One of the reports suggests that >80% of current smokers or ex-smokers are positive for tuberculin skin test as compared to <3% in nonsmokers (5)" should instead appear as "One of the reports suggests that >80% of current smokers or ex-smokers are positive for tuberculin skin test and this was significantly higher than for nonsmokers (5)."

www.pnas.org/cgi/doi/10.1073/pnas.0913611107

LETTER

# Parameters that influence the prediction of epidemiological benefits of more-effective tuberculosis vaccines, drugs, and diagnosis

*Mycobacterium tuberculosis*, the etiologic agent of tuberculosis, is a leading cause of death worldwide, killing an estimated 3 million people annually. An estimate of one-third of world's population is infected with tuberculosis bacilli. By using an age-structured mathematical model of tuberculosis, Abu-Raddad et al. (1) recently explored the potential benefits of novel interventions under development and those not yet in the portfolio, focusing on the WHO Southeast Asia region. Their model predicts that a triple combination of a portfolio vaccine, drug regimen, and diagnostics reduces the incidence of tuberculosis by 71%. Although we agree that novel regimens are expected to reduce tuberculosis incidence in the future, for the reasons discussed below, we believe that the proposed reductions in tuberculosis incidence is overestimated. The major drawback with the model is that the authors have considered only the latent infections as a parameter that may determine the sensitivity and uncertainty of the predictions. However, tuberculosis is a very complex disease and, in addition to host–pathogen parameters, one has to consider several socio-economic factors for modeling tuberculosis.

In most developing countries, it is not uncommon to be concurrently infected with more than one infectious disease. According to WHO report, 74% people in countries with high incidence of neglected diseases are battling with two or more diseases such as tuberculosis, HIV, dengue, helminthiasis, leishmaniasis, and malaria and 19% with six or more (2). The genetic background of the population, polymorphisms in immune protective genes, the chronic nature of pathogenesis, and treatments of these coinfections can block or deviate efficient immune response to *M. tuberculosis*. Therefore, it is important to consider the immune system that is affected by coinfections, past therapeutic history, and age.

Most tuberculosis patients are in developing countries, and it is well known that nutrition deficiencies and intestinal parasite burden (such as ascaris, trichuris, and schistosomiasis) can weaken the immune response and reduce vaccine efficacy. Further, the above two factors significantly bias the type of immune response to vaccines towards Th2 type whereas the desired protective immune response for tuberculosis is Th1 type (3, 4).

Association between smoking and tuberculosis has also been documented. One of the reports suggests that >80% of current smokers or ex-smokers are positive for tuberculin skin test as compared to <3% in nonsmokers (5). Smoking reduces the innate and adaptive immune compartment's ability to mount protective immune response to tuberculosis and to vaccines.

Socio-economic factors such as poverty rate, education status, the efficiency of the health care system of a country, and a population's ability to follow the therapeutic regimes can further influence the tuberculosis control measures. Therefore, caution should be exercised while predicting the reduction in the incidence of tuberculosis due to triple combination of a portfolio vaccine, drug regimen, and diagnostics. We suggest including some of these parameters in the analysis to forecast the reduction of the incidence of tuberculosis.

**ACKNOWLEDGMENTS.** This work was supported by grants from Institut National de la Santé et de la Recherche Médicale (INSERM), Centre National de la Recherche Scientifique (CNRS), UPMC-Paris VI, Paris V, and Coopération INSERM-ICMR-AO 2009/2010.

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1. Abu-Raddad LJ, et al. (2009) Epidemiological benefits of more-effective tuberculosis vaccines, drugs, and diagnostics. *Proc Natl Acad Sci USA* 106:13980–13985.
2. World Health Organization. (2006) *Neglected Tropical Diseases: Hidden Successes, Emerging Opportunities* (WHO, Geneva).
3. Ferreira AP, et al. (2002) Can the efficacy of bacille calmette-guerin tuberculosis vaccine be affected by intestinal parasitic infections?. *J Infect Dis* 186:441–442.
4. McDade TW, Beck MA, Kuzawa C, Adair LS (2001) Prenatal undernutrition, postnatal environments, and antibody response to vaccination in adolescence. *Am J Clin Nutr* 74:543–548.
5. den Boon S, et al. (2005) Association between smoking and tuberculosis infection: A population survey in a high tuberculosis incidence area. *Thorax* 60:555–557.

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The authors declare no conflict of interest.

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