Limited Tuberculosis Progression in Guinea Pigs Naturally Exposed to Human Multidrug Resistant Strains.

A. S. Dharmadhikari, MD[1], R. Basaraba, DVM[2], G. Palanisamy, DVM[2], K. Venter[3], M. Mphahlele, MSc[3], P. Jensen, PhD[4], M. First, ScD[5], S. Parsons, PhD[6], K. Weyer, ScD[3] and E. A. Nardell, MD[1]. Email: adharmadhikari@partners.org

[1]Brigham and Women's Hospital, Boston, MA; [2]Colorado State University, Fort Collins, CO; [3]Medical Research Council of South Africa, Pretoria, South Africa; [4]Centers for Disease Control and Prevention, Atlanta, GA; [5]Harvard School of Public Health, Boston, MA and [6]Center for Scientific and Industrial Research, Pretoria, South Africa.

Rationale: Multidrug resistant *M. tuberculosis* (MDR–TB) infections are a major source of morbidity and mortality worldwide. Some laboratory and epidemiologic studies, however, suggest that MDR–TB strains display heterogeneous fitness. Animal models of TB have been used to study MDR–TB pathogenesis, but these studies have used cultivated MDR–TB strains that are aerosolized in relatively high concentrations compared to natural infection. Little is known about whether MDR–TB aerosols generated directly from humans propagate differently in sentinel animals.
Methods: Using a unique airborne infections research facility in South Africa, we exposed 362 guinea pigs (GP) to exhaust air from a 6–bed MDR–TB hospital ward over a 4 month period and performed monthly tuberculin skin tests (TST) on them. To accelerate disease progression and enhance microbial recovery rate, we pharmacologically immunosuppressed half the TST positive animals after MDR–TB exposure and examined and scored lung and spleen tissues for pathology.
Results: Although 74% of GPs acquired infection (e.g. had positive TST), only 15% of TST positive GPs had pathologic evidence of TB. We also noted TST reversions in more than 20% of TST positive GPs. Less pathology was found in GPs with TST reactions of the longest duration. Steroid immunosuppression did not alter disease prevalence or severity.
Conclusions: Even in the highly vulnerable GP model, most (but not all) MDR–TB strains naturally generated by our patients failed to progress to disease, suggesting reduced fitness.

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