Can we tolerate an inhaled vaccine as a way to improve BCG efficacy?

Tuberculosis continues to be a major health issue with over one-third of the global population latently infected with *Mycobacterium tuberculosis* (Mtb). Bacille Calmette-Guérin (BCG) is the only approved vaccine available for tuberculosis, however its effectiveness varies from 0-80%. BCG appears to be least effective in the tropics, and as you get closer to the equator, regions where TB is most predominant. The large variability to BCG efficacy is thought to be due to prior exposure to environmental mycobacterium (EM), thought to interfere with the effectiveness of the vaccine.

In the 6 May 2016 edition of Plos Pathogens, researchers from New Mexico, USA, studied the mechanisms and efficacy of BCG immunizations in EM-exposed mice through either the oral or intradermal route. When the researchers exposed mice to oral Mycobacterium avium (to mimic EM) and then gave BCG vaccination either intradermally (regular route) or through inhalation (pulmonary), the mice vaccinated through the intradermal route showed a substantial decrease in IFN-γ production and an increase in immunosupressive cytokine IL-10. These mice appeared to have become tolerant to the oraly adminsitered EM, which interefered with intradermal BCG efficacy. However, the mice provided with the pulmonary BCG vaccine showed protection against TB infection and there was a complete resolution of the IFN-γ response as well as T cell

recruitment to the lungs.

This study was able to show that pulmonary immunization with BCG was protective against TB infection and could overcome the tolerance-inducing effect of oral EM exposure, which is the most probable mechanism of reduced BCG efficacy. The results from this study indicate that pulmonary BCG immunizations are most effective in both exposed and non-exposed EM individuals and could pave way for future clinical trials.

Price, D. et al, 2016. Oral Tolerance to Environmental Mycobacteria Interferes with Intradermal, but Not Pulmonary, Immunization against Tuberculosis. *PLOS*.

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