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## A Single Dose of Vitamin D Enhances Immunity to Mycobacteria

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**Rationale:** Vitamin D was used to treat tuberculosis in the pre-antibiotic era. Prospective studies to evaluate the effect of vitamin D supplementation on antimycobacterial immunity have not previously been performed. **Objectives:** To determine the effect of vitamin D supplementation on antimycobacterial immunity and vitamin D status. **Methods:** A double-blind randomized controlled trial was conducted in 192 healthy adult tuberculosis contacts in London, UK. Participants were randomized to receive a single oral dose of 2.5 mg vitamin D or placebo and followed up at 6 weeks. **Measurements and Main Results:** The primary outcome measure was assessed with a functional whole blood assay (BCG-*lux* assay) that measures the ability of whole blood to restrict luminescence, and thus growth, of recombinant reporter mycobacteria *in vitro*; the read-out is expressed as a luminescence ratio (luminescence post-infection/baseline luminescence). Interferon-gamma responses to the *M. tuberculosis* antigens early secretory antigenic target-6 and culture filtrate protein 10 were determined with a second whole blood assay. Vitamin D supplementation significantly enhanced the ability of participants' whole blood to restrict BCG-*lux* luminescence *in vitro* compared to placebo (mean luminescence ratio at follow-up 0.57 vs. 0.71 respectively, 95% CI for difference 0.01 to 0.25; P=0.03) but did not affect antigen-stimulated Interferon-gamma secretion. **Conclusions:** A single oral dose of 2.5 mg vitamin D significantly enhanced the ability of participants' whole blood to restrict BCG-*lux* luminescence *in vitro* without affecting antigen-stimulated Interferon-gamma responses. Clinical trials should be performed to determine whether vitamin D supplementation prevents reactivation of latent tuberculosis infection.

**Key words:** Human, Vitamin D, Innate Immunity, Mycobacteria

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