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# LETTERS

BCG VACCINATION AND TB IN CHILDREN

## No proof that BCG protects against infection with *Mycobacterium tuberculosis*

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BCG protects against primary tuberculosis, but evidence for protection against infection with *Mycobacterium tuberculosis* remains controversial. Roy and colleagues merely showed that previous BCG vaccination is associated with a reduced frequency of positive interferon γ release assay (IGRA) results in children recently exposed to *M tuberculosis*.[1]

A positive IGRA response indicates a previous interaction with *M tuberculosis* sufficient to lead to an adaptive immune response. For BCG to prevent infection it must limit this interaction, either by preventing entry of bacilli to alveoli or by strengthening the innate immune system. The authors do not propose how this might occur. Furthermore, it is difficult to see how a vaccine could protect against active disease, through the adaptive immune system, while simultaneously preventing the interaction with T cells on initial exposure that is necessary for immunity.

An alternative explanation for these findings is that BCG alters rather than prevents interaction between *M tuberculosis* and the adaptive immune system. With BCG vaccination, T cells gain memory for most mycobacterial antigens shared with *M tuberculosis*. This excludes the RD1 antigens ESAT-6, CFP10, and TB7.7, which are present in *M tuberculosis* but absent from BCG. Thus, when BCG vaccinated people meet *M tuberculosis*, the secondary and larger immune response is against previously recognised antigens, and a primary response to the three new antigens is either not mounted or is too small to elicit an IGRA response. This "original antigenic sin" is well demonstrated for serial immune responses to strains of influenza[2] and also occurs in other mycobacterial infections.[3 4]

Only if there is the additional argument that infection with *M tuberculosis* always leads to a response to RD1 antigens might BCG be considered to "prevent infection." The logic of this argument is unlikely if BCG provides any immunity against tuberculosis.

Competing interests: None declared.

Full response at: www.bmj.com/content/349/bmj.g4643/rr/762333.

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