RESEARCH LETTER

BCG protects against tuberculosis irrespective of HIV status: a matched case-control study in Mwanza, Tanzania

While BCG vaccine protects against severe tuberculosis (TB) in children, its effect against adult TB is questionable. Furthermore, it is not known if HIV co-infection modifies the effect of BCG. Among 352 pairs of Tanzanian TB cases and matched controls, the BCG scar was associated with a reduced risk of TB (OR 0.3, 95% CI 0.2 to 0.7, p=0.005), irrespective of HIV status (interaction, p=0.623). BCG vaccination considerably reduced the risk of TB, both among individuals with and without HIV infection.

BCG vaccination is used in most tuberculosis (TB)-endemic countries, and from 1980 to 2008, the coverage of BCG vaccination in Africa increased from 11% to 84%.[1] However, the data on protection from childhood vaccine against adult TB are inconsistent,[2] and its role in HIV infection is unclear.[3] We conducted an age- and sex-matched case-control study in Tanzania, to assess the protective effect of BCG vaccination and other risk factors for pulmonary TB.

Data were available for 352 pairs of TB patients and non-TB controls (n=704). A majority of cases lived alone and worked as farmers or fishermen (see online supplementary table). Fewer cases than controls had a visible BCG scar (78.9 vs 93.1%, p<0.001, χ^2), but more cases were HIV co-infected (46.3 vs 9.9%, p<0.001, χ^2). The associations between TB and BCG, HIV, smoking and alcohol intake were assessed in a multivariable conditional logistic regression model adjusted for age, diabetes status and sociodemographic factors (table 1). A BCG scar was associated with a considerable reduction in risk of TB (OR 0.3, 95% CI 0.2 to 0.7, p=0.005), and this association was not confounded or modified by any of the other covariates (ie, BCG-HIV interaction test, p=0.623). In stratified analysis by HIV status and adjusted for age, diabetes and sociodemographic factors, the BCG scar was associated with TB among both HIV-negative (0.3, 0.1;0.5, p<0.001) and HIV-positive (0.1, 0.02;0.95, p=0.045) participants. There was a similar effect across all age groups (data not shown), indicating a long-term BCG effect.

The BCG efficacy in 14 prospective trials and 12 case-control studies was 50%, ranging from a zero effect to 80%,[4] and a recent case-control study from India among 412 pairs of cases and controls reported a protective effect of BCG vaccination (OR 0.47, 95% CI 0.35 to 0.63).[5] The variations in the observed protective efficacy have been explained as potential differences in the BCG vaccine strains used, the application methods, preexisting immunity induced by environmental non-tuberculous mycobacteria, or latent TB infection. Our study was not a vaccine efficacy study, but aimed to examine the association between the presence of a BCG scar and developing active TB disease, but the OR of 0.3 does reflect a high efficacy. Since not all BCG-vaccinated individuals develop a BCG scar, the presence of a BCG scar, rather than information on BCG vaccination, might better predict protection, since this indicates that an immunological reaction has actually taken place.

This is the first study providing evidence strongly suggesting that BCG vaccination may prevent TB among both HIV-infected and uninfected participants. We do not have data on the time of HIV infection in the current population, but due to the inclusion criteria (age >15 years), and since most patients were antiretroviral-treatment naïve, the majority of the HIV infected must have contracted the infection in adulthood.

In conclusion, BCG vaccination seems to have an overall protective effect on the risk of developing active TB, and importantly, the effect is similar among HIV-uninfected and HIV-infected adults.

Daniel Faurholt-Jepsen,[1] Nyagosya Range,[2] George PrayGod,[3] Kidola Jeremiah,[3] Maria Faurholt-Jepsen,[1] Martine G Aabye,[4] Harleen M S Grewal,[5] John Changalucha,[3] Daniel R Witte,[6] Aase B Andersen,[7] Henrik Friis[1]

[1]Department of Human Nutrition, University of Copenhagen, Frederiksberg, Denmark
[2]Muhimbili Research Centre, National Institute for Medical Research, Dar es Salaam, Tanzania
[3]Mwanza Research Centre, National Institute for Medical Research, Mwanza, Tanzania
[4]Clinical Research Centre, University of Copenhagen, Hvidovre Hospital, Hvidovre, Denmark
[5]Section for Microbiology and Immunology, University of Bergen and Department of Microbiology and Immunology, The Gade Institute, Haukeland University Hospital, Bergen, Norway
[6]Steno Diabetes Center, Gentofte, Denmark
[7]Department of Infectious Diseases, Odense University Hospital, University of Southern Denmark, Odense, Denmark

Correspondence to Dr Daniel Faurholt-Jepsen, Department of Human Nutrition, Faculty of Life Sciences, University of Copenhagen, Rolighedsvej 30, Frederiksberg C 1958, Denmark; dfa@life.ku.dk

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Table 1 Predictors of pulmonary tuberculosis with OR and 95% CI based on 352 pulmonary tuberculosis cases and 352 controls (n=704)

	Crude* OR (95% CI)	p	Multivariable† OR (95% CI)	p
BCG scar	0.3 (0.2 to 0.5)	<0.001	0.3 (0.2 to 0.7)	0.005
HIV infection	9.0 (5.4 to 15.1)	<0.001	9.6 (4.7 to 19.5)	<0.001
Smoking	3.0 (1.9 to 4.8)	<0.001	2.4 (1.2 to 4.8)	0.017
Alcohol	3.0 (2.1 to 4.3)	<0.001	2.8 (1.6 to 5.2)	0.001

*Univariate conditional logistic regression for matched case-control groups.
†Multivariable conditional logistic regression for matched case-control groups including all covariates from table and adjusted for age, tribe, marital status, occupation, religion and diabetes status.

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