

Letter to the editor

The inverse relationship between tuberculin responses and atopic disorder

Studies from different countries on the same populations, years to decades apart, have provided good evidence of the increase in prevalence of atopy in children and young adults over the last two decades (1). Various environmental factors, including air pollution, cigarette smoking, allergen exposure, diet, infections, and general living standards, have been cited to explain the changes in prevalence of atopic diseases (2). It has also been suggested that some factors which had protected children from atopic diseases might have been lost; in particular, the changing patterns of childhood infection have been considered to be related to the rise in allergic diseases (3). In this regard, Shirakawa et al. (4) recently reported a negative association between tuberculin responses and atopic disorders in Japan, concluding that a decline in tuberculosis infection is a factor underlying the rising severity and prevalence of atopic disorders in developed countries.

While one factor temporally associated with the rise of atopic disorders is the decline of many infectious diseases as the result of improved living standards and immunization programs, it is possible, in this case, that the protection against atopy was provided by tuberculosis immunization (a strongly immunogenic BCG vaccine was administered to all tuberculin-negative subjects after birth, at 6 years, and at 12 years of age). In their study, Shirakawa et al. considered intermediate reactions (5-9 mm) to tuberculin skin testing a response to nontuberculous environmental mycobacteria or BCG, while they considered a positive response (≥ 10 mm diameter of skin induration) to be caused by infection with *Mycobacterium tuberculosis*. However, with a history of BCG vaccination, the presence of active tuberculosis is suggested by a reaction to the Mantoux tuberculin skin test equal to or larger than 15 mm (5, 6).

The 5-14-mm induration of a Mantoux tuberculin skin test in a subject who previously received BCG vaccine may suggest the occurrence of active tuberculosis if risk factors (7), such as clinical or radiographic changes indicative of tuberculosis, recent close contact with a person smear-positive for tuberculosis, cellular immunodeficiency, or

treatment with high doses of corticosteroids, are present. Although children born in a high prevalence area of tuberculosis represent a moderate risk category, it seems unlikely that 577 (group 2 plus group 3 plus group 4 in Woolcock et al.'s study [1]) of 867 children had developed active infections. Shirakawa et al. themselves note that some of the conversions to tuberculin positivity (induration ≥ 10 mm) after 6 years of age might be attributable to a second immunization with BCG. However, this may be the case also in children younger than 6 years, particularly in the absence of risk factors for tuberculosis infection or disease. Although BCG vaccine has a 0-80% efficacy for prevention of tuberculosis and only 38-75% protection against pulmonary tuberculosis (5), none of the children studied by Shirakawa et al. suffered clinical tuberculous disease. Thus, it is possible not only that a decline in infection by *M. tuberculosis* is a factor associated with the rising prevalence of atopic disorders, but also that immunization with a potent bacterial vaccine - in this case, BCG - is associated with the growth of TH1 cells, which secrete interleukin-2 and interferon-gamma and may prevent the development of atopy. Therefore, we may already have the suggested potential vaccine strategy for prevention of asthma and allied atopic disorders during early childhood (8). Is the prevalence of atopy increased in countries which have stopped the BCG vaccination campaign?

References

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