

Correlation between atopy and tuberculin/*Candida* skin test reactivity in a bacillus Calmette-Guérin-vaccinated cohort

H.-C. Kuo, C.-A. Liu, C.-Y. Ou, T.-Y. Hsu, K. D. Yang*

Keywords: atopy; *Candida* skin test; tuberculin skin test.

The prevalence of atopy including asthma, atopic dermatitis, and allergic rhinitis has increased in recent years all over the world, mainly in developed countries. Bacillus Calmette-Guérin (BCG) is among the group of vaccines capable of eliciting strong Th1 immune response and therefore decreasing risk of Th2-associated atopy. Shirakawa et al. (1) reported an inverse association between tuberculin response and atopic disorders. Some studies found conflicting results to support the inverse correlation between the tuberculin skin test (TST) and atopy. There were some diseases such as Kawasaki disease with enhanced Th2 expression but like an infectious disease clinically (2). The balance between Th1/Th2 responses seems to be more complex so as the relationship between the delayed-type hypersensitivity (DTH) and atopy.

Tuberculin skin test reactivity negatively correlates with atopic dermatitis/allergic rhinitis but not asthma.

We conducted to investigate the relationship between the DTH (including tuberculin and *Candida albicans* antigen) response and atopy at the age of 6 in a nonselected birth cohort infants who were all BCG vaccinated at birth (3). A total of 530 children were followed including physical examination, allergen test, and questionnaire at 6 years of age. Purified protein of tuberculin was administered by the Mantoux method using 0.1 ml (two tuberculin units) of purified protein derivative RT23 (Statens Serum Institut, Copenhagen, Denmark) and 0.1 ml *Candida albicans* (Green Laboratories, Lenoir, NC, USA) at 6 years of age by injecting intradermally on the volar surface of the forearm. The diameter of the indurated area was measured at 72 h. Atopy were defined as clinical diagnosis of asthma, allergic rhinitis, or atopic dermatitis, together with detectable serum-specific IgE levels (>0.7 KU/l in one or more allergens). The specific IgE directly against the common allergens in Taiwan, including *Dermatophagoides pteronyssinus*, cockroach, dog dander, seafood, or pollen mixture, was measured by using the PharmaciaCap

system, as previously described (4). Questionnaires were asked on previous and recent (<6 months) symptoms of asthma, allergic rhinitis, or atopic dermatitis. Ever atopy was defined as atopy noted before but acquired remission at 6 years of age. Persistent atopy was referred to ever atopy before and still with atopy when studied. During the follow-up period, no patient had active tuberculosis disease or *Candida albicans* infection detected.

A significantly inverse correlation was found between TST and persistent allergic rhinitis ($P = 0.023$)/persistent atopic dermatitis ($P = 0.002$) but not in asthma (Table 1). There were no significant correlations between TST and ever allergic rhinitis, atopic dermatitis or asthma. There were no significant association between *Candida* skin test (CST) and ever/persistent atopy. No significant association was found between TST/CST and rate of positive specific IgE test ($P > 0.05$). There was no significant correlation between TST and log-transformed IgE levels at the age of six ($P = 0.59$). There was no significant correlation between TST and CST reactivity ($P = 0.69$).

Table 1 Correlation of tuberculin skin test reactivity and atopy

	Tuberculin skin test (TST)	P
Atopic dermatitis		
Persistent	0.43 $\pm$ 0.03 vs 0.21 $\pm$ 0.06 cm (530/44)	0.002*
Ever	0.43 $\pm$ 0.03 vs 0.35 $\pm$ 0.07 cm (470/104)	0.32
Allergic rhinitis		
Persistent	0.45 $\pm$ 0.04 vs 0.32 $\pm$ 0.04 cm (418/156)	0.023*
Ever	0.43 $\pm$ 0.04 vs 0.38 $\pm$ 0.05 cm (367/207)	0.37
Asthma		
Persistent	0.42 $\pm$ 0.03 vs 0.31 $\pm$ 0.08 cm (521/53)	0.16
Ever	0.44 $\pm$ 0.03 vs 0.32 $\pm$ 0.06 cm (456/118)	0.10

Data were presented as mean with SE. *P*-values were assessed by the Student's *t*-test. Ever atopy was defined as ever allergic rhinitis, asthma or atopic dermatitis before, but acquired remission during the 6 years of life. * $P < 0.05$.

The objective methods as CAP allergen test and the validated questionnaire were used to identify ever/persistent atopy. A significant inverse correlation was found between TST reactivity and persistent allergic rhinitis/persistent atopic dermatitis but not in ever atopy or asthma. This suggests that TST may be useful for evaluating different types of atopic disorders in various severities. Most of the animal studies have shown that BCG infection was capable to reduce the allergic response, but as for humans, correlation between TST reactivity and atopy provided conflicting results (1, 5). The definition of positive TST showed great variation between studies and might lead to conflict results with atopic disorders. TST reaction positive rate (> 5 mm in diameter) was low in this study (32.1%) and similar to a previous study in Taiwan that vaccinated children with BCG at birth (6). In conclusion, child with positive TST reactivity has an inverse association with persistent atopic dermatitis, and allergic rhinitis but not found in asthma

or ever atopy. CST skin test did not have significant association with atopy.

*Department of Pediatric Allergy
Immunology and Rheumatology
Chang Gung Memorial Hospital-Kaohsiung
Medical Center
Graduate Institute of Clinical Medical Science
Chang Gung University
123 Ta-Pei Road
Niaosung Hsiang
Kaohsiung
Taiwan
Tel.: +886 7 7317123 ext. 2031
Fax: +886 7 7312867
E-mail: yangkd@adm.cgmh.org.tw

Accepted for publication 12 May 2010
Allergy 2010
© 2010 John Wiley & Sons A/S
DOI: 10.1111/j.1398-9995.2010.02427.x

References

1. Shirakawa T, Enomoto T, Shimazu S, Hopkin JM. The inverse association between tuberculin responses and atopic disorder. *Science* 1997;**275**:77–79.
2. Kuo HC, Wang CL, Liang CD, Yu HR, Huang CF, Wang L et al. Association of lower eosinophil-related T helper 2 (Th2) cytokines with coronary artery lesions in Kawasaki disease. *Pediatr Allergy Immunol* 2009;**20**:266–272.
3. Yang KD, Ou CY, Chang JC, Chen RF, Liu CA, Liang HM et al. Infant frequent wheezing correlated to Clara cell protein 10 (CC10) polymorphism and concentration, but not allergy sensitization, in a perinatal cohort study. *J Allergy Clin Immunol* 2007;**120**:842–848.
4. Yang KD, Chang JC, Chuang H, Liang HM, Kuo HC, Lee YS et al. Gene-gene and gene-environment interactions on IgE production in prenatal stage. *Allergy* 2009;**65**:731–739.
5. Marks GB, Ng K, Zhou J, Toelle BG, Xuan W, Belousova EG et al. The effect of neonatal BCG vaccination on atopy and asthma at age 7 to 14 years: an historical cohort study in a community with a very low prevalence of tuberculosis infection and a high prevalence of atopic disease. *J Allergy Clin Immunol* 2003;**111**:541–549.
6. Chan PC, Chang LY, Wu YC, Lu CY, Kuo HS, Lee CY et al. Age-specific cut-offs for the tuberculin skin test to detect latent tuberculosis in BCG-vaccinated children. *Int J Tuberc Lung Dis* 2008;**12**:1401–1406.