

edema, cough, and dyspnea developed. The youth's pre-event meal 2 h earlier had included Parmesan, a cow's milk cheese. Referred to our clinic, the patient and his parents gave their informed consent to challenges. Fresh-food SPT were negative for cow's milk lactalbumin, beef, and lamb, but positive (wheal diameter 5 mm) for fresh cow's milk casein and ewe's milk (wheal diameter 6 mm). Positive RAST for cow's milk casein (3.44 IU/ml) and elevated total IgE (195 IU/ml) were then found. During double-blind, placebo-controlled, food-exercise challenge (DBPCFEC) with four planned doubling doses (5, 10, 20, 40 ml) of cow's milk masked in soybean formula, a reaction to cow's milk was confirmed when symptoms developed with the 20-ml dose. At immunoblotting (following methods described elsewhere), however, serum IgE reacted strongly to ewe's and weakly to cow's milk proteins (Fig. 1).

This patient, who had been allergic to ewe's milk since childhood, was observed to develop allergy to cow's milk at food-exercise challenge. Cow's milk and cow's milk products had been tolerated from birth until severe anaphylactic reactions were triggered by ingestion (with other foods) after exercise during adolescence. To the best of our knowledge, this is the second case of food-dependent, exercise-induced anaphylaxis diagnosed at DBPCFEC (6). Although ewe's milk allergy is usually coexistent with cow's milk allergy, it can also occur in isolation. The same phenomenon applies in the case of allergies to the milk of the goat, the mare, and other animals (7, 8). Common allergenic epitopes can be shared by ewe's and cow's milk protein; therefore, cow's milk allergy may be associated.

Caseins are held responsible for this cross-reaction, justifying caution regarding the consumption of dairy products by children who are allergic to the milk of nonbovine species. Weak food sensitization, which appears only after strenuous exercise, could trigger more severe allergic symptoms (9).

Furthermore, there is a compelling need for accurate labeling of all dairy products as to the nature and origin of the milk from which they are made. We conclude that hypersensitivity reaction to ewe's milk may be viewed as a forerunner of cow's milk intolerance when a fresh-food workup and carefully conducted DBPCFEC establish sensitization.

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Asthma and TNF variants in Chinese and Malays

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Key words: alleles; asthma; haplotypes; lymphotoxin; tumor necrosis factor.

● MOFATT & Cookson (1) reported an association of specific haplotypes of tumor necrosis factor (TNF) with asthma, the TNF- α -308*2 and LT α NcoI*1 allelic variants being found more commonly in asthmatics. Albuquerque et al. (2) also found an association of TNF haplotypes with childhood asthma, but identified the at-risk alleles as TNF- α -308*1 and LT α NcoI*2. We

compared the frequency of each of the two alleles of each cytokine in asthmatics and nonasthmatic controls in two ethnic groups in the Singapore population. Genotyping of lymphotoxin- α with the NcoI restriction fragment-length polymorphism (RFLP) was carried out as described previously (1). For the -308 promoter variant of TNF- α , we developed an allele-specific polymerase chain reaction (AS-PCR) assay. The sequence of the allele-specific primer used for G was 5'-AATAGGTTTGTAGGGGCAAGG-3'; for A, it was 5'-AATAGGTTTGTAGGGGCATGA-

We found no association of TNF haplotypes or alleles with asthma in two main racial groups in Singapore.

3'. The antisense primer was 5'-AGGGAGCGTCTGCTGGCTG-3' for both alleles. The reaction volume was 10 µl, comprising 100 µM dNTP, 67 mM Tris-Cl, 16 mM (NH₄)₂SO₄, 0.01% Tween 20, 10% glycerol, 20 ng genomic DNA, 50 ng of each primer, and 1 U Taq polymerase. Cycling conditions were as follows: initial denaturation at 94°C for 5 min, 35 cycles at 94°C for 1 min, 63°C for 30 s, and 72°C for 30 s, followed by 72°C for 10 min. The accuracy of the AS-PCR typing was confirmed by sequencing 25 of the samples.

A total of 219 southern Chinese (Cantonese, Hokkien, and Teochew) and 73 Malay unrelated subjects were studied with informed consent. We found no association of the at-risk alleles, as defined by Mofatt & Cookson (1) (Fisher's statistic of between 0.20 and 2.35 and *P* values of between 0.354 and 0.902) with the asthma phenotype (Table 1). There was no association of TNF-308*2/LTα NcoI*1 haplotype with asthma in either race. For Malays, the frequency of TNF-308*2 was extremely low although the incidence and severity of asthma in Malays is comparable to Chinese (3). Comparison showed both the at-

risk allele frequencies between asthmatics and controls in both race groups not to be significantly different (Z scores between 0.274 and 1.484, *P* values of >0.05).

In summary, we found no evidence of association of TNF haplotypes or alleles with asthma in the two main racial groups in our population. The failure to confirm the findings of Mofatt & Cookson (1) indicates that the susceptibility genes for asthma are probably different in our population. Another possible factor is the difference in recruitment, as their 413 subjects were from 88 nuclear families while all our subjects were unrelated. It should also be noted that another study on Caucasians by Albuquerque et al. (2) not only failed to confirm the association, but identified different at-risk alleles for each of the biallelic polymorphisms.

The TNF-308*2 genetic variant has been linked with susceptibility to cerebral malaria (4) and worse outcome in patients with severe sepsis (5) and may therefore be a useful clinical marker. The AS-PCR assay we have developed for genotyping the TNF-α polymorphism is simpler and quicker than conventional allele-specific hybridization using TMAC (4), and

should be useful for studying individuals at risk of infectious or autoimmune diseases associated with TNF-α promoter variants and increased TNF-α secretion.

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Table 1. Association of tumor necrosis factor genotypes with asthma

Genotypes	1.1	1.2	2.2	<i>P</i> value
TNF-308				
<i>Malays</i>				0.358
Asthmatics (38)*	34	4	0	
Controls (36)	35	1	0	
<i>Chinese</i>				0.734
Asthmatics (67)	49	18	0	
Controls (151)	115	36	0	
LT α				
<i>Malays</i>				0.354
Asthmatics (38)	7	20	11	
Controls (35)	4	15	16	
<i>Chinese</i>				0.902
Asthmatics (66)	13	38	15	
Controls (153)	30	84	39	

*Number in parenthesis indicates total number of subjects studied. At-risk alleles according to Mofatt & Cookson (1) are allele 2 for TNF-308 and allele 1 for LTα.

Vacuum cleaners and airborne dog allergen

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Key words: asthma; Can f 1; dog allergen; HEPA; vacuum cleaner.

● EFFECTIVE allergen avoidance carried out for a sufficiently long period may improve asthma control in sensitized individuals. Complete avoidance of dog allergens is all but impossible in areas with a high proportion of pet ownership, because the exposure may occur not only in homes with dogs, but also in homes without dogs