

FOOD ALLERGY AND WHEEZING

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The pattern of allergy in developed countries has been changing over the last twenty years from respiratory conditions to a food-allergy epidemic. The former has stabilized while the latter has surged upwards, with most presenting as eczema.

Higher rates of food sensitization are found in more developed countries in Asia. The findings are substantiated by a study in Hong Kong and mainland China (Leung, *et al*, 2009). Significantly higher rates are detected in more 'western' environments. Up to 14% of children in Hong Kong, as compared to 6% in urban China and 2% in rural China have cow's milk-specific IgE above 0.35 ku/l. This is a so-called 'gradient' with environmental change.

Asian races are more susceptible to 'western' environmental changes. Previous studies in Australia suggested that Asian people have a higher risk of food allergies than non-Asians, and that risk of allergic disease increased with length of stay in Australia, and was higher in Australia-born Asians compared with Asian immigrants (Leung *et al*, 1994; Sicherer *et al*, 2010). This susceptibility might be related to a 'western' environment.

Risk factors associated with atopy

Research focused on the risk for developing atopy as a result of the interaction between genetic and environment (Bergmann *et al*, 1997). The results indicated that the genetic component is dominant.

A child whose mother has atopic disease has a 50% risk of allergic disease, while a father's contributes around 30%. If both parents have atopic disease, the risk for offspring can increase to 70%. With neither parents having an atopic history, the risk drops down to 14%.

Prenatal exposure is also a risk factor for developing atopy. When exposed in utero, three factors are considered, namely genetics, timing, and level of exposure (Warner *et al*, 1996). If the exposure occurs during the first trimester only, then there is no consequence. The concern begins from second trimester, when even at very low dose or very high maternal exposure then oral tolerance development in fetus is possible. So, the moderate dose exposure in mothers increases, and then primary sensitization ensues. For after birth, if this child has low dose exposure, it causes no problem but if highly exposed then allergy process is likely to develop.

The natural history of atopic diseases

Most allergies develop in the first one or two years of life, after which atopic eczema is the most common, followed by food allergy. Later in life, the initial manifestations may improve but are followed by asthma and/or rhinoconjunctivitis, as it is the so-called "Allergic March" (Fig 1).

Causes of recurrent wheeze

When considering the causes of recurrent wheeze, both cow's milk protein allergy

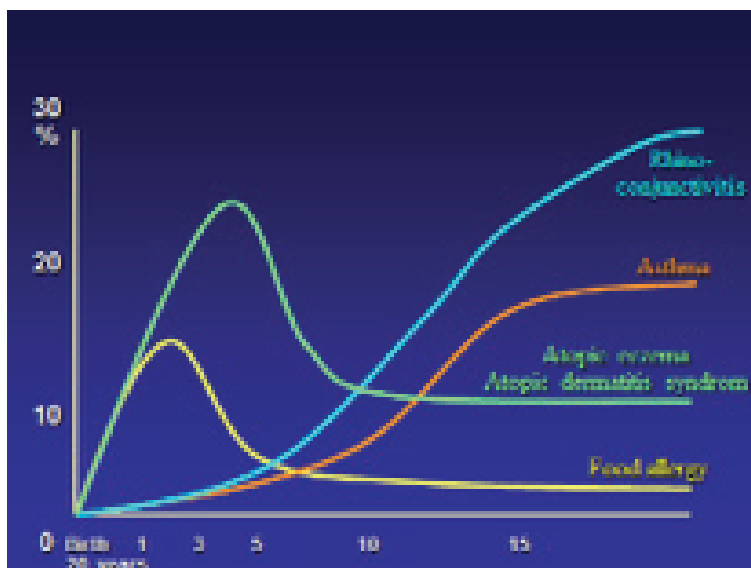


Fig 1– ‘Allergic March.’

and virus-induced wheeze may occur in the first year of life. Then, from about three years onwards, asthma and allergic rhinitis, singularly or as co-morbid, can have their onsets.

Clinical manifestations of cow’s milk protein allergy

A retrospective study of 382 children diagnosed with suspected cow’s milk protein allergy (CMPA) at King Chulalongkorn Memorial Hospital showed preponderance for males with an average age at diagnosis of 14.8 months (range 7 days to 13 years) (Ngamphaiboon *et al*, 2008). The mean duration of symptoms was 9.2 months. There was a family history of allergy in 64.2% of cases. All of the mothers had a history of high milk consumption during pregnancy. Exclusive breastfeeding was reported only in 13.2% of children in the cohort. There was an association with other food allergy, for example, egg and seafood in these children.

Positive food challenges, albeit incidentally, took place and were seen in all the children. Clinical symptoms comprised gastroenterology, dermatology, respiratory, and others. Respiratory conditions, such as recurrent wheeze, nasal blockage, and rhinitis were the most common manifestations, unlike reports from Europe and USA, where dermatological symptoms are more common. A number of gastroenteritis problems is seen, from common diarrhea and vomiting to enterocolitis. For skin manifestations, most are atopic dermatitis followed by urticaria. Other presentations observed are failure to thrive, anemia, delayed speech, and anaphylaxis.

Diagnosis of cow’s milk protein allergy

1. History taking in children who suspected of cow’s milk protein allergy include: Family history of allergic diseases; Amount of cow’s milk intake during pregnancy, for exclusive breast fed mothers, cow’s milk intake during lactation is considered; Feed-

Table 1
Atopic risk score.

Family	Type and degree of allergic symptoms						Total
	Major ^a			Minor ^b			
	Overt	Probable	Absent	Overt	Probable	Absent	
Father	2	1	0	1	0.5	0	
Mother	3	2	0	1	0.5	0	
Sibling	2	1	0	1	0.5	0	

^aMajor: Asthma, atopic dermatitis, allergic rhinitis, CMPA.

^bMinor: Urticaria, drug allergy, other food allergy, allergic conjunctivitis.

Source: Ngamphaiboon *et al* (2009a).

ing history; Onset of symptoms, usually occurring within 3-6 months after cow's milk exposure and depending on the amount of intake; Clinical symptoms, chronic and recurrent symptoms usually of more than two systems and organs involvement; and History of poor weight gain, difficult feeding, poor milk intake, and frequent change of cow's milk brands.

2. Laboratory diagnosis of cow's milk protein allergy includes: Oral challenge test is the gold standard; Radioallergosorbent test (RAST) for specific IgE has sensitivity 56% and specificity 67%; Skin prick test (SPT) for type I hypersensitivity has sensitivity 44% and specificity 67%; Eosinophile in secretions; Intestinal biopsy in patient who presents with GI symptoms; and Bronchoalveolar lavage (BAL) may find hemosiderin-laden macrophages in case of pulmonary hemosiderosis.

3. Atopic risk score: The combination of type and degree of allergic symptoms from family history can be a useful predictor for the risk of atopic development by using

this scoring system (Table 1).

Data from 3,502 children showed that the prevalence of atopy in children is varied upon feeding groups; 30.3% in breastfeeding group, 42.3% in cow's milk group and 11.3% in partial hydrolysed group (Ngamphaiboon *et al*, 2009b). When adjusted for sex and family history of atopy, children who received cow's milk had 1.66 (95% CI: 1.40-1.96) times risk of developing atopy compare to children who received breast feeding. While children who received partially hydrolysed formula had 0.23 (95% CI: 0.16-0.31) times risk of developing atopy compared to children who received breastfeeding.

Overall, positive family history carried a strong risk factor for the development of atopic disease in children. In high-risk infants who have atopic risk score ≥ 2 (Ngamphaiboon *et al*, 2009b), using partially hydrolysed formula as a breast milk substitute during the first 4 months reduces the risk of atopy during the first year of life until 4 years of age.

Mode of delivery and risk of cow's milk allergy

Mode of delivery is one of the associated factors to cow's milk allergy development in the offspring. It is hypothesized that a child who delivered by cesarean section has higher odds of developing cow's milk allergy. This might be explained by the difference in intestinal flora pathogen. Through the cesarean section the fetus does not come into contact with maternal gut microflora, which is thought to be helpful in preventing allergies.

Interventions to prevent cow's milk protein allergy and proposed mechanisms include the following: Exclusive breastfeeding for at least 4 to 6 months leads to promotion of bifidobacteria, suppression of clostridia, stimulation of TLRs and T-regulatory responses, and immune modulating compounds; For those starting complementary feeding from 4-6 months, it is likely that upregulation of T-reg responses will occur with immune bias towards tolerance; In combination with pre- and pro-biotics, bifidobacteria and lactobacilli thrive while clostridia are suppressed; TLRs, T-reg, and Th1 responses improve; With maternal fish oil supplementation, there will be increased in DHA in breast milk, reduction in Th2 cytokines, and increased TGF-beta in the cord blood.

Meta-analysis of allergy prevention showed that partial hydrolysate formula (pHF) is superior in preventing the onset on allergy over cow's milk formula up to the age of six years old (Szajewska and Horvath, 2010).

In conclusion, in the recent years, the prevalence of allergy is increasing, especially early in life. One must consider the

important role of environmental factors, including diet, in modification of immune development and predisposition to allergic diseases. A natural and complex gastrointestinal microbiota is important for growth and development of the immune system. Breastfeeding for at least six months is the best strategy to minimize the risk for allergic diseases. There is evidence to recommend use of pHF as an alternative to breastmilk for prevention of allergic diseases.

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