

Natural history of cow's milk allergy

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Cow's milk allergy is the most common food allergy in children, with rates estimated at 2% to 3%.¹ An article in 2007 from investigators from Johns Hopkins speculated that the natural history of food allergy is changing, with longer time to resolution and lower rate of resolution.² As part of the National Institutes of Health–sponsored Consortium on Food Allergy Research, Wood et al³ examined the natural history of milk allergy in one of the larger cohorts studied.

Their cohort consisted of 293 children with cow's milk allergy (part of their cohort of 512 children with cow's milk allergy and egg allergy). One hundred fifty-four (53%) children outgrew their cow's milk allergy by 66 months of age. In addition, another 21% of the children were tolerating cow's milk in baked goods, indicating that they will probably tolerate "raw" cow's milk in the near future. These data suggest that approximately 75% of children outgrow their cow's milk allergy at approximately 5 years of age or later. Their results fall in between those of previous studies, most likely because of differences in the study design and population involved.^{2,4-10} For example, the study of the tertiary referral population at Johns Hopkins had a resolution rate of 19% at 4 years of age and 42% at 8 years of age.² This compares with 78% seen at 5 years of age in the original study by Bishop et al⁴ of general pediatrics from 1990 and with 57% by 5 years of age in 54 infants with cow's milk allergy from a general birth cohort of 13,000 infants in Israel (Table I).^{2,4,6-11} Other potential reasons for the study differences that require exploration include the genetics of the study population, the details of the cow's milk exposure history (eg, age of introduction, preparation of the cow's milk, and amount and regularity of milk ingestion), the severity of the initial allergic reaction, and the association of other atopic

features. For patients with peanut allergy, we have found that the more severe the presenting allergic reaction, the less likely the patient is to outgrow food allergy, which raises the question of whether this is true for cow's milk allergy.¹² Combining the previous studies with the current data allows the creation of a survival curve for the development of tolerance to cow's milk (Fig 1). These combined data (Table I and Fig 1) suggest that 50% of the children have tolerance to cow's milk by 5 years and 75% by the early teenage years, which is consistent with the recent data from Wood et al.³

A concern in the article by Wood et al³ is that some of the children might not have food allergy to cow's milk because they were included in the study based on specific IgE levels (>5 kU_A/L) to cow's milk in children with atopic dermatitis. Fleischer et al⁵ found that specific IgE levels in children with atopic dermatitis have a high rate of false positivity, indicating that many of these children might not have food allergies. However, Wood et al³ report no difference in their results if this population were excluded, suggesting that in the current article patients with atopic dermatitis and specific IgE do have food allergies.

The authors examined various factors to predict the development of tolerance or "outgrowing" food allergy. These factors include cytokines, transcription factors involved in the development of regulatory T cells, skin test reactivity, and specific IgE to cow's milk. Wood et al³ report that assessing skin test reactivity or specific IgE levels to milk is superior to molecular techniques. In particular, patients with a wheal of 5 to 10 mm to cow's milk extract had a 52% chance of achieving tolerance compared with 72% for the subjects with a wheal of less than 5 mm and 37% for those with a wheal of greater than 10 mm. Subjects with an enrollment specific IgE level to cow's milk of less than 2 kU_A/L had a 72% chance of achieving tolerance compared with 52% for a specific IgE level of between 2 and 10 kU_A/L and 23% for a specific IgE level of greater than 10 kU_A/L. These results confirm previous finding by several other groups.^{6,7,11} Another risk factor for the persistence of cow's milk allergy was the severity of atopic dermatitis because patients with moderate-to-severe atopic dermatitis had a hazard ratio of 2 compared with those having mild or no atopic dermatitis. Using these values, Wood et al³ extended their results to develop an online calculator (www.cofargroup.org) to predict the natural history of cow's milk allergy. This novel tool might help physicians and families with important clinical questions, such as "Will I outgrow my food allergy?" or "When will I outgrow my food allergy?" It is a very practical tool available for the practicing allergist without the use of more expansive laboratory techniques.

The data in this issue suggest that milk allergy resolves by 5 years of age in 50% of subjects, which is more slowly than previously reported. The ability of the initial skin test result and specific IgE level to predict the natural history of cow's milk allergy is an important finding for the practicing allergist because this information is readily available in the clinic. However, additional investigation is needed to compare these data with

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TABLE I. Natural history of IgE-mediated cow's milk allergy

Authors	No.	Population	Age at enrollment	Tolerance rate
Ahrens et al ⁶	52	Referral	(3-114 mo)	61.5% (3.7 y later)
Bishop et al ⁴	97	Referral	16 mo	28% at 2 y, 56% at 4 y, and 78% at 6 y
Elizur et al ¹¹	54	General pediatrics	Birth	57% by 5 y
Fiocchi et al ⁷	112	Referral	Median, 14 mo	53%; median age, 2 y; age range, 0.75-4.9 y
Host et al ⁸	39	General pediatrics	Birth*	56% at 1 y, 77% at 2 y, 87% at 3 y, 92% at 5 y and 10 y, and 97% at 15 y
Saarinen et al ⁹	75	General pediatrics	7 mo	74% at 5 y and 85% at 8.6 y
Skripak et al ²	807	Referral	13 mo, Retrospective	19% at 4 y, 42% at 8 y, 64% at 12 y, and 79% at 16 y
Vanto et al ¹⁰	95	Referral	<12 mo	31% at 2 y, 53% at 3 y, and 63% at 4 y
Wood et al ³	293	Current study	3-15 mo	53% at 5.3 y

*Mixture of IgE-mediated and non-IgE-mediated reactions.



FIG 1. Natural history of cow's milk allergy: survival curve for the development of cow's milk allergy. The survival curve is based on equal representation from each study listed in Table I.

information from other populations and with additional foods to determine whether the findings are generalizable.

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