

**IgE**

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**MEASUREMENTS IN  
SMALL  
CHILDREN**

# **IgE MEASUREMENTS IN SMALL CHILDREN**

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## IgE MEASUREMENTS IN SMALL CHILDREN

Foetal IgE synthesis has been reported in the liver and lungs as early as the 11th week of pregnancy (1). Initially, elevated cord-blood IgE was identified as a predictive marker of later atopic disease (2). Unfortunately, this has not proved to be a useful marker of subsequent disease development as was previously hoped. The observation indicates, however, that foetal priming occurs in utero. Allergen-specific reactivity with skin and blood antibodies at birth has been demonstrated to a range of common allergens, both of food and inhalant origin (3,4).

Subsequent studies have confirmed the association between high IgE levels and the development of atopic disease, and that IgE antibodies are measurable in a child's circulatory system at an early age.

Presence of IgE antibodies to ingested and inhaled allergens were followed by Hattevig et al. in a longitudinal study from birth to 12 years of age in 86 girls, unselected with regard to family history of allergy (5,6). Total serum IgE was significantly higher in the 13 children with obvious atopy/allergy at 7 years than in the 55 children without such symptoms. This was observed already at 8 months and at 2 and 4 years (Table 1). Specific IgE to egg white and cow's milk reached a peak at 8 months with high concentrations only in atopics (Fig. 1). An elevated level of IgE antibodies to egg white during infancy was found to predict future appearance of antibodies to inhalants. Furthermore, serum IgE antibodies to both egg white and inhalants were often elevated before the allergic symptoms.

**TABLE 1**

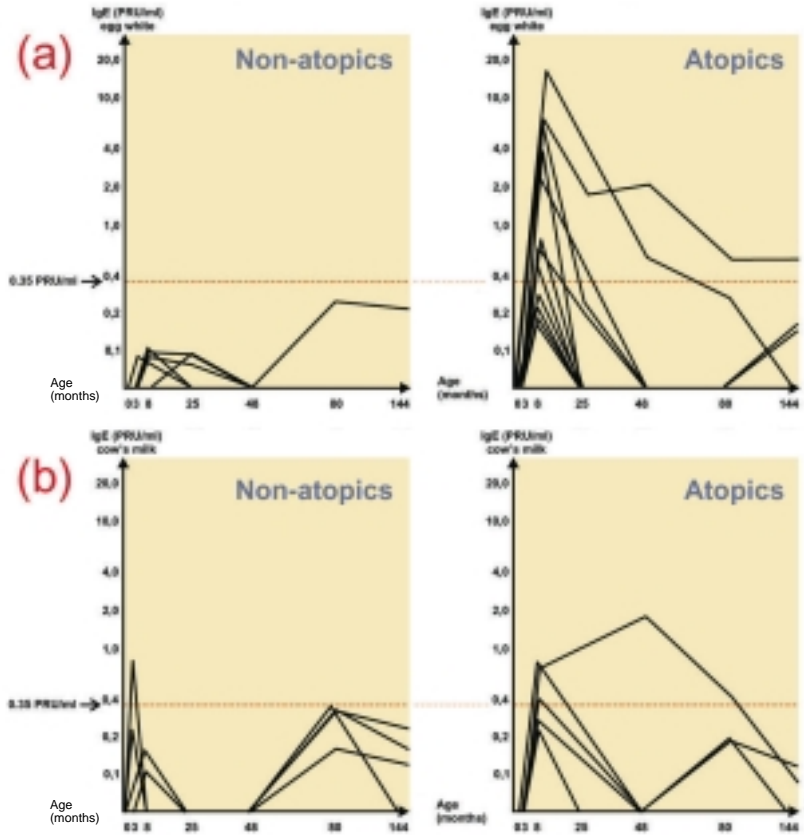
**Development of total IgE (kU/L) in children with current atopy/allergy at 7 years compared to values in children without previous or current atopy/allergy**

Age (months)	Number		Geometric mean		P
	Atopics	Healthy	Atopics	Healthy	
0	12	51	0.3	0.2	n.s.
3	12	46	2.8	1.5	n.s.
8	13	51	6.4	3.1	0.035
25	9	38	18	6.1	0.040
48	13	55	23	8.8	0.023
80	13	55	54	19	0.036

*Adapted from: Hattevig G et al.  
Clinical Symptoms and IgE responses  
to common food proteins and inhalants  
in the first 7 years of life.  
Clin Allergy 1987;17:571-78*

FIGURE 1

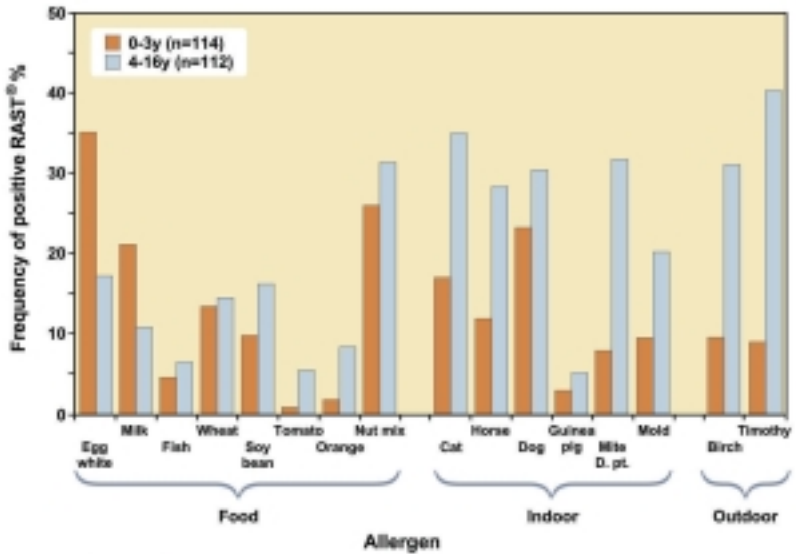
Specific IgE antibodies to egg white (a) and cow's milk (b) at various ages in children developing or not developing atopic symptoms during the first 12 years of life



Adapted from:  
Hattveig, G., et al. Appearance of IgE antibodies to ingested and inhaled allergens during the first 12 years of life in atopic and non-atopic children. *Pediatr Allergy Immunol* 1993; 4: 182-86

FIGURE 2

Specific IgE antibodies in atopic children



Adapted from:  
 Sigurs, N. et al. Sensitization in childhood atopic disease identified by Phadebas RAST<sup>®</sup> serum IgE and Phadiatop<sup>®</sup>  
*Pediatr Allergy Immunol* 1990; 1: 74-78

Similar results were presented by Sigurs et al. in two other studies (7,8). The distribution of specific IgE in 224 children, age 1 to 15 years and with atopic manifestation, showed that IgE antibodies to foods dominated in young children and reactions against inhalants became important from the second year of life (Fig.2).

In a longitudinal study 324 children were followed from birth for 4, 12 and 15 years respectively. The appearance of IgE antibodies followed the previously described pattern with food antibodies (especially to egg white) being the most common in infancy and antibodies to inhalant allergens beginning to be more important from 18 months of age. IgE antibodies to the individual food and inhalant allergens often appeared before the allergic symptoms, as observed by others.

Bruno et al. (9) followed 174 newborns at risk for atopic disease due to positive family history, from birth up to 4 years of age. The study includes detailed history, as well as signs and symptoms of atopic disease. Total IgE and specific IgE were determined at 6 and 12 months and every year thereafter. The children with atopic disease had significantly higher levels of total IgE (Table 2) and more positive specific IgE than the asymptomatic children. Specific IgE antibodies could only be detected in 2% of the asymptomatic children.

**TABLE 2**

**Development of total IgE (kU/L) by age in atopic and healthy children**

Age (months)	Geometric mean + 2 SD	
	Atopics*	Healthy*
Birth	0.30 + 4	0.25 + 7
6	29 + 135	7 + 63
12	37 + 240	16 + 217
24	48 + 299	25 + 123
36	48 + 235	28 + 120
48	51 + 307	30 + 130

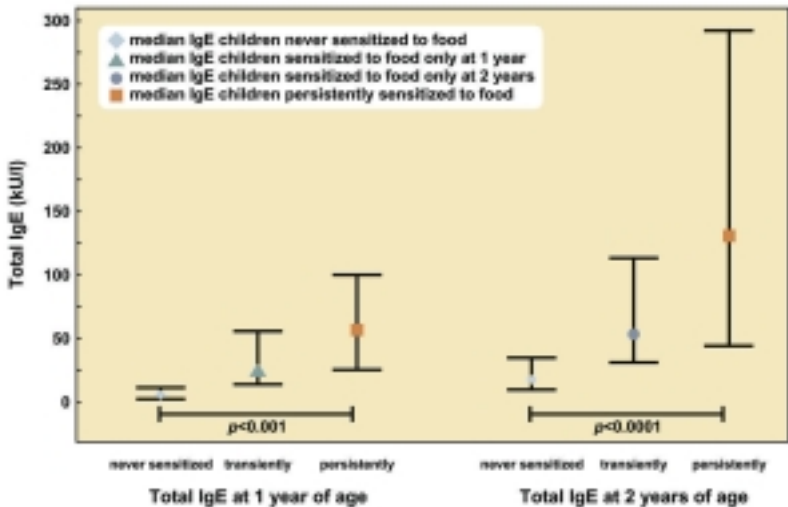
\* P < .01

*Adapted from: Bruno G et al. Natural history of IgE antibodies in children at risk for atopy. Ann Allergy Asthma Immunol 1995;74:431-36*

In a Japanese study (10) specific IgE was determined in 111 infants at the age of 6 months and followed to 5 years of age. A positive reaction to egg white in infants at 6 months proved to be a significant predictor for the development of allergic disease to common inhalant allergens during the 5 first years.

FIGURE 3

Total IgE in never, transiently and persistently food-sensitized children at 1 and 2 years of age (median, 25<sup>th</sup> and 75<sup>th</sup> percentile)

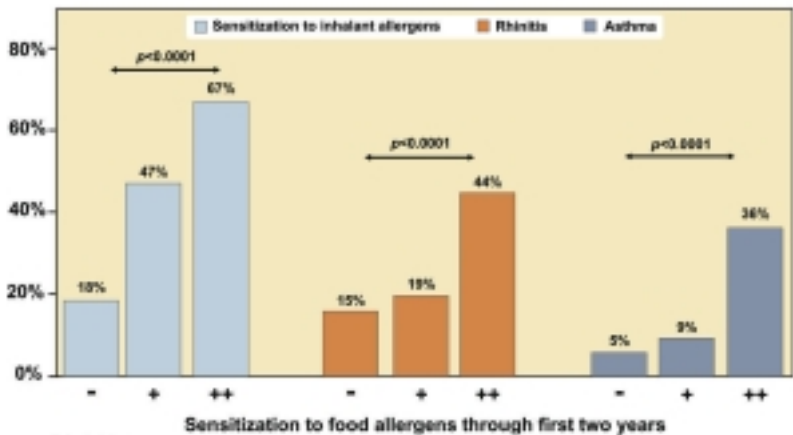


Adapted from:  
Kulig, M. et al. Long-lasting sensitization to food during the first two years precedes allergic airway disease. *Pediatr Allergy Immunol* 1996; 9: 61-67

The large Multicenter Atopy Study (MAS) study in Germany followed a cohort of children from birth to 1,3,6,12, and 18 months, and thereafter to 2, 3, 4, and 5 years of age (11,12). Total serum IgE and specific IgE were analysed at 1, 2 and 5 years. Children with a long-lasting and early sensitization to food allergens produced significantly higher total IgE and specific IgE levels to hen's egg than children not or only transiently food-sensitized (Fig.3). Those children with av long-lasting sensitization to food allergens also had a 3.4 fold greater risk of developing allergic rhinitis and a 5.5 fold greater risk of developing asthma than only transiently food-sensitized children (Fig.4).

FIGURE 4

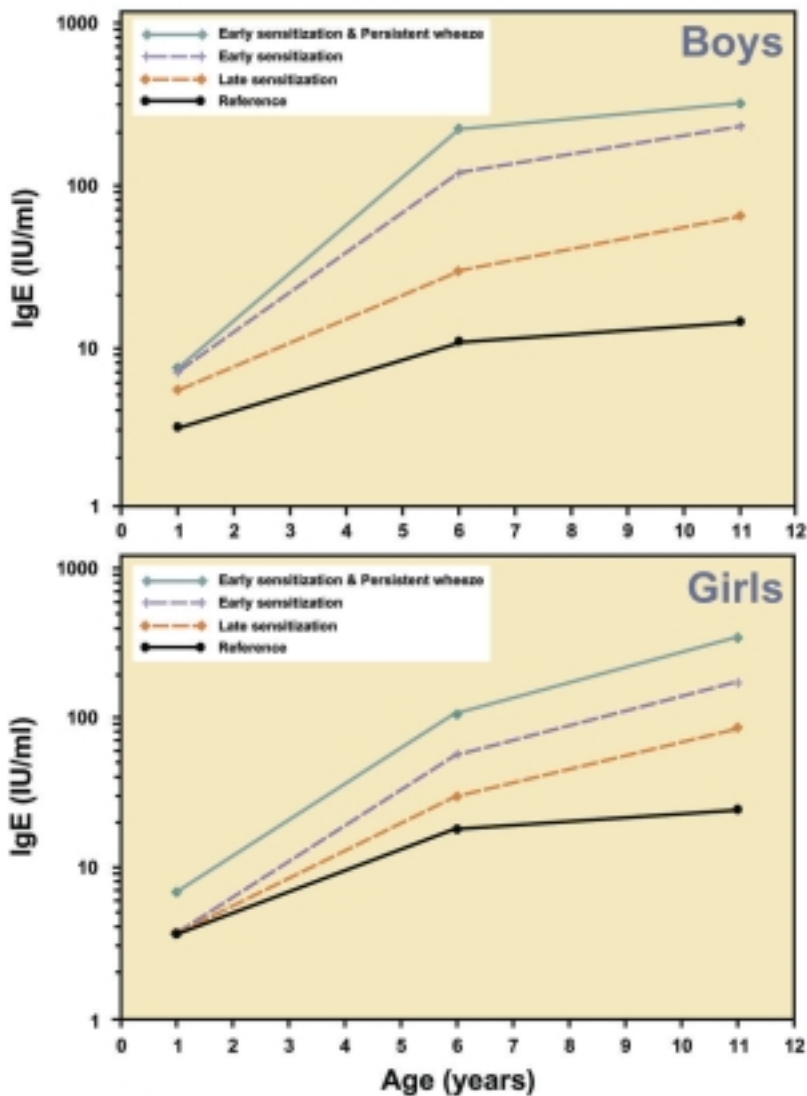
Prevalences of sensitization to inhalant allergens, allergic rhinitis and asthma at 5 years of age in never (-), transiently (+) and persistently (++) food-sensitized children



Adapted from:  
Kulig, M. et al. Long-lasting sensitization to food during the first two years precedes allergic airway diseases. *Pediatr Allergy Immunol* 1998; 9: 61-67

FIGURE 5

Association of total IgE, wheezing and sensitization in children followed from 9 months to the age of 11 years



Adapted from:  
Sheriff, D.L., et al. Total IgE and its association with asthma symptoms and allergic sensitization among children. *J Allergy Clin Immunol* 1999; 104: 28-36

Total IgE and its association with wheezing and allergic sensitization in children was reported by Sherrill et al. (13). The 540 children were participants in the Tucson Children's Respiratory Study and underwent IgE measurements at 9 months, 6 and 11 years and allergy skin tests at 6 and 11 years. Children less than 1 year old with elevated serum IgE levels continued to have high levels at ages 6 and 11 years. Both persistent wheezing and early sensitization were associated with high IgE at all ages (Fig.5). Early wheezers i.e., children wheezing only during the first years of life, had serum levels that were not different from those of non-wheezing children. From these findings the authors conclude that children who are predisposed to persistent wheezing and early sensitization already have high levels of IgE at age 9 months.

A study in the Netherlands regarding the development of atopic diseases during the two first years of life in 133 newborns at high risk of atopy (14) was recently published in the Netherlands. Specific IgE in plasma at 12 months was only found against food allergens, whereas specific IgE against both food and inhaled allergens was observed at 24 months of age.

Wever-Hess et al (15) studied 419 children aged 0 to 4 years with possible asthma. The addition of laboratory data to patient history showed that total serum IgE had a prognostic value, and specific IgE against inhalant allergens was a strong predisposing factor, especially in the 2 to 4 year group (Table 3).

The studies discussed above and others (see Reference list: Further reading) confirm that total IgE and specific IgE can be detected early in life. Specific IgE could be a valuable tool, used in combination with other information, to predict the progression of atopic disease and thus provide an opportunity for early intervention.

**TABLE 3****Total and specific IgE in children with diagnosed asthma or non-asthma**

<b>Age 0-2 years</b>	<b>All n=231(%)</b>	<b>Asthma n=113(%)</b>	<b>Non-asthma n=118(%)</b>	<b>p-value</b>
Total IgE				
elevated	90 (42)	58 (55)	32 (30)	<0.001
geometric mean (kU/l)	11.1	18.1	6.78	<0.001
Phadiatop positive	17 (8)	15 (14)	2 (2)	0.001
Food mix (fx5) positive	43 (20)	29 (28)	14 (13)	0.008
Phadiatop + fx5 positive	10 (5)	10 (10)	0	0.001
<hr/>				
<b>Age 2-4 years</b>	<b>All n=188(%)</b>	<b>Asthma n=144(%)</b>	<b>Non-asthma n=44(%)</b>	<b>p-value</b>
Total IgE				
elevated	119 (65)	107 (75)	12 (29)	<0.001
geometric mean (kU/l)	66.8	105	14.7	<0.001
Phadiatop positive	88 (47)	86 (60)	2 (5)	<0.001
Food mix (fx5) positive	70 (38)	64 (46)	6 (14)	<0.001
Phadiatop + fx5 positive	53 (29)	51 (36)	2 (5)	<0.001

*Adapted from: Wever-Hess J et al.  
Prognostic characteristics of asthma diagnosis  
in early childhood in clinical practice.  
Acta Paediatr 1999;88:827-34*

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