

Cord blood IgE. II. Prediction of atopic disease

A follow-up at the age of 18 months

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Screening of total IgE in 2814 cord blood samples was analysed by Phadebas IgE PRIST in 2 1-year birth cohorts (1983–1984 and 1985–1986) in Denmark ($n = 1189 + 1625$). For follow-up we chose all infants with cord blood IgE ≥ 0.5 kU/l and a randomly chosen group of the same size with cord blood IgE < 0.5 kU/l. A total of 762 infants were clinically evaluated at 18 months of age. A diagnosis of definite atopy, probable atopy or no atopy, including both IgE and non-IgE mediated disease was established. Applying different cord blood IgE cut-off values (0.3, 0.5, 0.8, 1.1) we did not find an excess of atopic infants among those with elevated cord blood IgE irrespective of the chosen cut-off value. Atopic predisposition or family history of atopic disease was defined as at least one parent or older sibling with atopic disease. Significantly more infants with a family history developed atopy at 18 months. In the 2 series the positive predictive values of cord blood IgE ≥ 0.5 were 43% and 46% and the sensitivities were 17% and 15%. The predictive values of having a family history were 48% and 44% and the sensitivities were 55% and 58%.

Clinical aspects

Cord blood IgE analysed by Phadebas IgE PRIST was a poor predictor of infants developing atopic disease before the age of 18 months.

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Cord blood IgE (CB-IgE) or serum IgE measured during the first days of life, as a predictive factor of the development of atopic disease, has been evaluated in other original papers (4–9, 11, 16, 17, 18, 20, 22–28) and surveys (1, 2, 3, 10, 12, 19, 29). The exact value of these data is still controversial. The only 2 follow-up studies of 18-month-old unselected infants showed consistent results, indicating that elevated CB-IgE is a good predictive factor of atopic disease.

Croner & Kjellman (7) found that 70% of infants with elevated CB-IgE developed atopic symptoms before the age of 18 months, while 73% with atopic predisposition combined with elevated CB-IgE developed definite or probable atopic symptoms. In a similar study, Magnusson (23) found that 72% of infants with elevated CB-IgE developed atopic symptoms by 18 months. The frame of our study does not differ generally from these former studies, since we wished to establish points of comparison. In a previous paper we have reported results of a CB-IgE

screening in 2814 infants (13). A particularly sensitive PRIST method was applied.

The aim of our study was to evaluate whether knowledge of atopic predisposition combined with elevated CB-IgE could be used to detect infants at high risk of subsequent development of atopic disease. Some of these infants will be regularly examined during childhood in order to record the development of atopic disease and IgE response. The present paper deals with atopic symptoms developed during the first 18 months. Another paper describes the IgE response alone and in combination with atopic disease (14).

Material and methods

The material comprised 1189 unselected infants born at the Viborg Hospital (Vi) during the period November 1, 1983 – October 31, 1984, and correspondingly 1625 unselected infants born at the Odense Hospital (Od) during the period January 7, 1985 –

January 6, 1986. CB-IgE was analysed by a particularly sensitive Phadebas IgE PRIST (13). Of these infants 2 groups were chosen for follow up.

Group 1: All infants with CB-IgE ≥ 0.5 kU/l.

Group 2: Randomly chosen infants in numbers equal to Group 1 with CB-IgE < 0.5 kU/l.

In Viborg 176 infants (14.8%), 70 girls and 106 boys, had CB-IgE ≥ 0.5 kU/l. 162 (92.0%), 62 girls and 100 boys, were followed up. In Odense the corresponding figures were: 196 infants (12.1%), 65 girls and 131 boys, with CB-IgE ≥ 0.5 kU/l. 179 (91.3%), 61 girls and 118 boys, were followed up. The control groups were chosen as every fifth infant among those with CB-IgE < 0.5 kU/l. Thus, 179 (73 girls and 106 boys) in Viborg and 242 (138 girls and 104 boys) in Odense formed the control groups. The follow-up group was thus 341 infants (135 girls and 206 boys) in Viborg and 421 infants (199 girls and 222 boys) in Odense.

In 1983 the pediatric ward in Viborg had just adopted allergy prophylactic measures for infants at a high risk of developing atopic disease.

This high risk group was defined as infants with:

1. Biparental atopic predisposition.
2. Single severe atopic predisposition (one parent and/or one or more older siblings with perennial symptoms or symptoms from more than one organ system) and CB-IgE ≥ 0.5 kU/l.

This high risk group consisted of 37 infants (22 boys and 15 girls). Due to initial difficulties in implementing the new prophylactic measures, only 3 boys and 5 girls followed the recommendations entirely. The infants in the first 6 months were exclusively breast-fed. If breastfeeding was insufficient or not possible, a hypo-allergenic casein hydrolysate (Nutramigen) was recommended. It was recommended to delay introduction of solid foods until the age of 6 months. Cheese, fish, egg, chocolate, peas, beans, citrus, strawberry, tomato and nuts were excluded until 12 months. Avoidance of furred pets, dust-collecting materials in the bedroom, damp housing conditions and tobacco smoking at home was advised. Contrary to the policy followed in Viborg, no prophylactic measures were implemented in Odense with the exception of a general recommendation for breastfeeding. Atopic symptoms were recorded at the ages of 6 and 12 months according to questionnaires and in doubtful cases by subsequent phone interviews. The infants underwent physical examination at the age of 18 months (± 1 month), where atopic symptoms again were recorded. Blood samples were drawn to determine total and specific IgE. The pediatricians were not aware of the CB-IgE findings. Based on history and the physical examination the infants were classified into one of the 3 following groups: definite atopy, probable atopy and no atopy.

Definite atopy was defined as one or more of the following:

1. Bronchial asthma
2. Atopic dermatitis (areas of scaly, erythematous and itchy eczematous rash with atopic localisation)
3. Two or more episodes of urticaria due to specific foods
4. Two or more episodes of gastrointestinal allergy or intolerance due to specific foods

Probable atopy was defined as one or more of the following:

1. Two or more episodes of wheezy bronchitis
 2. Recurrent urticaria of unknown origin
 3. Recurrent abdominal colic of unknown origin
- No atopy was defined as none of the above mentioned conditions.

Provocation and elimination tests were carried out by a physician to establish the diagnosis of food allergy. The results were evaluated according to the initial CB-IgE cut-off value of 0.5 kU/l. Other possible cut-off values, such as 0.3 kU/l, 0.8 kU/l (Vi) and 1.1 kU/l (Od) were regarded. Positive predictive value, negative predictive value, sensitivity, specificity, efficiency and rate ratio were calculated for infants with the following characteristics:

1. Family history of atopic disease
2. CB-IgE ≥ 0.3 kU/l
3. CB-IgE ≥ 0.5 kU/l
4. CB-IgE ≥ 0.8 kU/l (Vi)/1.1 kU/l (Od)
5. Family history as well as CB-IgE ≥ 0.3 kU/l
6. Family history as well as CB-IgE ≥ 0.5 kU/l
7. Family history as well as CB-IgE ≥ 0.8 kU/l /1.1 kU/l
8. The high risk group (Vi) as described above
9. The high risk group (Vi) following prophylactic measures

Atopic disease was classified as definite or probable atopy. Calculations were made in accordance with the following diagram:

Test result	True diagnosis		
	Sick	Not sick	
Positive	a	b	a+b
Negative	c	d	c+d
	a+c	b+d	a+b+c+d

Positive predictive value (PPV): Probability that a person with positive test is sick, $a/a + b$

Negative predictive value (NPV): Probability that a person with negative test is not sick, $d/c + d$

Sensitivity: Probability of a positive test in a sick person, $a/a + c$

Specificity: Probability of a negative test in a person who is not sick, $d/b + d$

Efficiency: Probability of correct classification, $a + d / a + b + c + d$

Rate ratio: Risk of disease with positive test in relation to risk of disease with negative test, $PPV / 1 - NPV$

The calculations regarding predictive values were adjusted for the selection of the control group by increasing the number of individuals of the originally chosen control groups proportionally.

The study was approved by the human research ethics committee. Informed consent was given by the parents before entering the study.

Statistics

Statistical analyses were performed using a statistics programme, Epistat – Tracy Gustafson, 1705 Gattis School Road, Round Rock, Texas 78664, USA. Mean values (geometric mean) and standard deviations (SD) have been calculated on logarithmically (ln) transformed values, since the CB-IgE values were not normally distributed. The following statistical methods were used: chi-square test, Student's t test and variance analysis (ANOVA). P-values ≥ 0.05 were regarded as non-significant.

Results

Table 1 shows calculations of mean CB-IgE and SD among infants without atopic predisposition and without atopic symptoms at the age of 18 months. 74 (Vi) and 106 infants (Od) fulfilled these criteria. In Viborg mean CB-IgE + 2 SD was 0.8 kU/l and in

Table 1. Geometric mean CB-IgE and SD among infants without a family history and without atopic symptoms at the age of 18 months (kU/l)

	<i>n</i>	Mean	Mean+1 SD	Mean+2 SD
Viborg	74	0.11	0.29	0.76
Odense	106	0.12	0.36	1.06

Odense 1.1 kU/l. In addition to the originally chosen 0.5 kU/l, we used these values as well as 0.3 kU/l as possible cut-off values.

Table 2 (Vi) and Table 3 (Od) show the number of infants with definite, probable and no atopy according to different cut-off values. The Viborg material showed 138 (40.5%) infants with atopic symptoms, 59 (17.3%) definite and 79 (23.2%) probable atopy, 89 were boys (43.2%) and 49 girls (36.3%).

The corresponding figures from Odense showed 177 infants (42.0%) with atopic symptoms, 82 (19.5%) definite and 95 (22.6%) probable atopy, 103 were boys (46.4%) and 74 girls (37.2%). A non-significant predominance of boys with either definite or probable atopic disease was found in both materials. Atopic disease was recorded in 69 (42.6%) of infants (Vi) and in 83 (46.4%) of infants (Od) with $CB-IgE \geq 0.5$ kU/l. Among infants with $CB-IgE < 0.5$ kU/l, 69 (38.5%) in Viborg and 94 (38.8%) in Odense had definite or probable atopy. Irrespective of gender and different cut-off values (0.3, 0.5, 0.8, 1.1) no predominance of definite or probable atopy was found in infants with elevated CB-IgE.

Table 4 shows median CB-IgE, inter-quartile range (IQR) and range in infants with definite, probable and no atopy. Variance analysis showed significant differences between the groups only in Viborg ($p < 0.05$).

Table 5 shows the number of infants with different atopic manifestations. In Viborg wheezy bronchitis (17.6%) and abdominal colic (17.6%) were most common, 15.0% had atopic dermatitis, 3.8% urticaria of unknown origin, 3.5% gastrointestinal allergy, 1.5% bronchial asthma and 0.3% urticaria due to specific foods. In Odense again wheezy bronchitis (22.1%) was most common, 15.7% had or had had atopic dermatitis, 15.0% abdominal colic, 5.2% gastrointestinal allergy, 2.4% urticaria of unknown origin, 2.1% urticaria due to specific foods and 1.4% bronchial asthma. Occurrence of the individual atopic manifestations were not correlated

Table 2. Number of infants from Viborg (boys, girls, total) with definite, probable and no atopy at 18 months of age according to different CB-IgE cut-off values

CB-IgE	Boys						Girls			Total		
	Boys	Girls	Total									
				Defin.	Prob.	No	Defin.	Prob.	No	Defin.	Prob.	No
<0.3	87	59	146	13	24	50	9	10	40	22	34	90
≥0.3	119	76	195	27	25	67	10	20	46	37	45	113
<0.5	106	73	179	17	28	61	12	12	49	29	40	110
≥0.5	100	62	162	23	21	56	7	18	37	30	39	93
<0.8	150	108	258	24	38	88	18	19	71	42	57	159
≥0.8	56	27	83	16	11	29	1	11	15	17	22	44
Total	206	135	341	40	49	117	19	30	86	59	79	203

Table 3. Number of infants from Odense (boys, girls, total) with definite, probable and no atopy at 18 months of age according to different CB-IgE cut-off values

CB-IgE	Boys	Girls	Total	Boys			Girls			Total		
				Defin.	Prob.	No	Defin.	Prob.	No	Defin.	Prob.	No
<0.3	88	123	211	13	28	47	22	21	80	35	49	127
≥0.3	134	76	210	34	28	72	13	18	45	47	46	117
<0.5	104	138	242	17	30	57	23	24	91	40	54	148
≥0.5	118	61	179	30	26	62	12	15	34	42	41	96
<1.1	176	170	346	37	43	96	30	32	108	67	75	204
≥1.1	46	29	75	10	13	23	5	7	17	15	20	40
Total	222	199	421	47	56	119	35	39	125	82	95	244

Table 4. Median CB-IgE, IQR and range in the groups definite, probable and no atopy at the age of 18 months (kU/l)

	Viborg			Odense		
	Definite	Probable	No	Definite	Probable	No
<i>n</i>	59	79	203	82	95	244
Median CB-IgE	0.5	0.4	0.3	0.5	0.2	0.2
IQR	0.1–0.8	<0.1–1.0	<0.1–0.7	<0.1–0.7	<0.1–0.9	<0.1–0.7
Range	<0.1–21	<0.1–16	<0.1–5.3	<0.1–5.7	<0.1–19	<0.1–12

Table 5. Manifestations of atopic disease at the age of 18 months according to gender and CB-IgE

	Definite					Probable				No	Total
	ba	ad	u	ga	Total	wb	uu	co	Total		
Viborg											
Boys	5	33	1	8	40	48	7	39	49	117	206
Girls	0	18	0	4	19	12	6	21	30	86	135
Total	5	51	1	12	59	60	13	60	79	203	341
CB-IgE < 0.5 kU/l	1	28	1	2	29	28	6	28	40	110	179
CB-IgE ≥ 0.5 kU/l	4	23	0	10	30	32	7	32	39	93	162
Odense											
Boys	2	37	5	16	47	56	4	33	56	119	222
Girls	4	29	4	6	35	37	6	30	39	125	199
Total	6	66	9	22	82	93	10	63	95	244	421
CB-IgE < 0.5 kU/l	3	32	3	10	40	44	4	40	54	148	242
CB-IgE ≥ 0.5 kU/l	3	34	6	12	42	49	6	23	41	96	179

Atopic symptoms: ba: bronchial asthma, ad: atopic dermatitis, u: urticaria, ga: gastrointestinal allergy, wb: wheezy bronchitis, uu: unspecified urticaria, co: colic.

with elevated CB-IgE irrespective of the chosen cut-off value, but the number of infants in some of the groups was too small to draw conclusions.

In Viborg 153 (44.9%) and in Odense 164 (39.0%) infants had a family history of atopic disease. 81 (23.8%) and 90 (21.4%) of the mothers had atopic disease, while the corresponding figures for the fathers were 50 (14.7%) and 74 (17.6%) and for the siblings 58 (17.0%) and 53 (12.6%). Biparental atopic predisposition was registered in 9 (2.6%) and 24 (5.7%) in Viborg and Odense, respectively. Among infants with atopic predisposition 19.0% (Vi)

and 25.6% (Od) had definite atopy, 30.7% (Vi) and 22.6% (Od) probable atopy. Among those with biparental predisposition 44.4% (Vi) and 37.5% (Od) developed definite atopy, 22.2% (Vi) and 45.8% (Od) probable atopy. Of the infants without atopic predisposition 33.0% (Vi) and 38.1% (Od) had definite or probable atopy. 50.6% (Vi) and 55.6% (Od) of infants with maternal predisposition, and an equal proportion of 50.0% (Vi) and 55.4% (Od) with paternal predisposition developed definite or probable atopy. Mothers with atopic disease gave birth to 50 boys and 31 girls (Vi) and to 46 boys and 44 girls

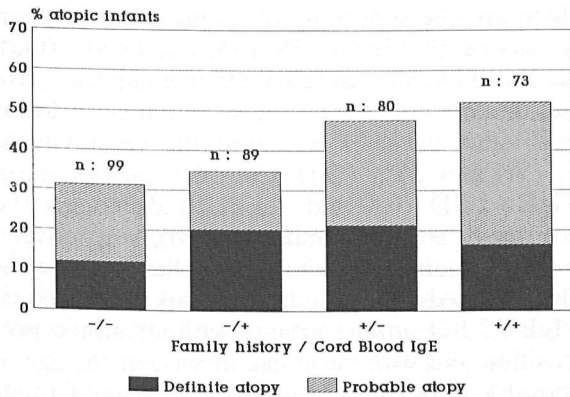


Fig. 1. Viborg: Atopy. Family history and CB-IgE (cut off 0.5 kU/l).

-/- ct +/- $p < 0.05$; -/- ct +/+ $p < 0.01$; -/+ ct +/+ $p < 0.05$; -/- and -/+ ct +/- and +/+ $p < 0.005$; -/- and +/- ct -/+ and +/+ NS; other NS.

(Od). No significant predominance of male births was found (data not shown).

Fig. 1 shows the percentage of Viborg infants with atopic disease in relation to increased CB-IgE (cut off 0.5 kU/l) and atopic predisposition. Among infants with atopic predisposition definite or probable atopy was found in 52.1% with CB-IgE ≥ 0.5 kU/l and in 47.5% with CB-IgE < 0.5 kU/l. Among infants without atopic predisposition atopic disease was found in 34.8% with CB-IgE ≥ 0.5 kU/l and in 31.3% with CB-IgE < 0.5 kU/l. Fig. 2 shows the corresponding figures from Odense 57.1%, 41.5%, 39.4% and 37.2%, respectively.

Significantly more infants with atopic predisposition developed atopic disease before the age of 18 months (Vi: $p < 0.005$. Od: $p = 0.05$). Elevated CB-IgE, on the contrary, was not associated with development of atopic disease.

Table 6 shows calculations on different predictive

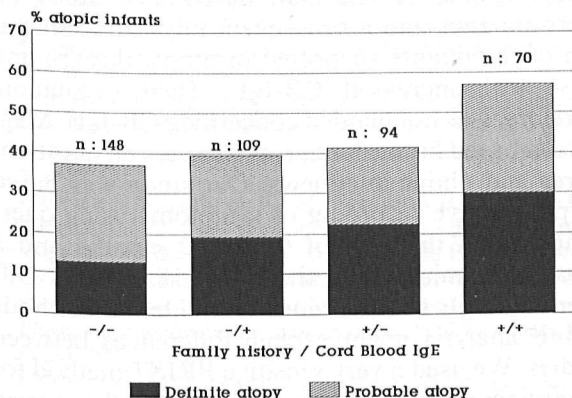


Fig. 2. Odense: Atopy. Family history and CB-IgE (cut off 0.5 kU/l).

-/- ct +/+ $p < 0.01$; -/+ ct +/+ $p < 0.05$; -/- and -/+ ct +/- and +/+ $p = 0.05$; -/- and +/- ct -/+ and +/+ NS; other NS.

Table 6. Prediction of atopic disease (definite+probable atopy) in %

Test	PPV	NPV	Sen	Spe	Eff	Rr
Viborg						
Family history	48.2	68.2	55.1	61.9	59.2	1.5
CB-IgE ≥ 0.3	41.0	61.6	32.4	70.0	55.3	1.1
CB-IgE ≥ 0.5	42.6	61.5	16.7	85.5	58.6	1.1
CB-IgE ≥ 0.8	47.0	61.5	9.4	93.2	60.4	1.2
Family history and CB-IgE ≥ 0.3	47.6	62.1	16.4	88.3	60.2	1.3
Family history and CB-IgE ≥ 0.5	52.1	61.8	9.2	94.6	61.1	1.4
Family history and CB-IgE ≥ 0.8	54.1	61.4	4.8	97.4	61.1	1.4
High-risk group	73.8	63.0	10.9	97.5	63.6	2.0
High-risk group and intervention	50.0	60.9	1.0	99.4	60.8	1.3
Odense						
Family history	43.5	62.5	57.5	63.5	55.1	1.2
CB-IgE ≥ 0.3	39.8	60.2	24.1	60.2	55.3	1.0
CB-IgE ≥ 0.5	46.4	61.2	15.0	88.5	59.3	1.2
CB-IgE ≥ 1.1	46.1	60.5	6.3	95.1	59.8	1.2
Family history and CB-IgE ≥ 0.3	52.2	61.3	10.8	93.4	60.5	1.3
Family history and CB-IgE ≥ 0.5	57.1	61.1	7.2	96.4	60.9	1.5
Family history and CB-IgE ≥ 1.1	64.3	60.7	3.3	98.8	60.8	1.6

PPV: positive predictive value; NPV: negative predictive value; Sen: sensitivity; Spe: specificity; Eff: efficiency; Rr: rate ratio.

factors of atopic disease. Applying the CB-IgE cut-off value of 0.5 kU/l we found PPV at 43% (Vi) and 46% (Od). The corresponding sensitivities were 17% (Vi) and 15% (Od). Among infants with atopic predisposition 48% (Vi) and 44% (Od) developed atopic disease (PPV), while 55% (Vi) and 58% (Od) of the infants with atopic disease had atopic predisposition (sensitivity).

Discussion

This study, conducted with an exceptionally sensitive IgE PRIST method, of unselected infants revealed divergent results as regards the predictive values of CB-IgE, compared with those obtained in similar investigations of unselected infants (7, 23). The results of our prospective observer-blinded investigation seem reliable, since the 2 parallel cohorts followed by independent pediatricians gave concordant results. In Viborg an allergy prevention programme was recommended for infants at risk of developing atopic disease. Only very few infants ($n = 8$) strictly followed this programme, hardly confounding our results. However, a recommended intervention programme in the maternity ward might also have influenced families not directly participating and risk families not closely following the programme. The study was primarily designed to assess

the predictive value of an elevated CB-IgE of 0.5 kU/l, but allowed evaluation of other cut-off values. A high rate (92%) of participation was obtained. The drop-out rate was low irrespective of CB-IgE values. The classification of the infants into "definite", "probable" and "no atopy" groups largely resemble that of Croner & Kjellman (7) and Magnusson (23). Unlike these studies, we did not include infants with solely unspecific symptoms in the group "probable atopy". In our study we have assessed the occurrence of definite and probable atopy separately, although most of the final results are given as a combined group in order to match earlier studies. The number of infants with atopic disease was rather large, probably due to an extended definition of atopic disease and the composition of our study group. This selection regarding predictive values was adjusted. Results concerning the true prevalence of atopic disease are estimated and will be published in another paper (15). The frequency of atopic disease was not significantly higher in infants with CB-IgE ≥ 0.5 kU/l, which explains the generally low predictive values.

Applying other CB-IgE cut-off values did not significantly alter the predictive values. Atopic predisposition increased the infant's risk of developing atopic disease. The presence of maternal atopy was not associated with a higher risk than paternal atopy, which agrees with the results of Croner & Kjellman (7) but not those of Magnusson (23), and we were unable to confirm Magnusson's assumption that atopic mothers gave birth to more boys than girls. The PPV of CB-IgE ≥ 0.5 kU/l were 43% (Vi) and 46% (Od) and thus were far below the PPV of 70% and 72% reported by Croner & Kjellman (7) and Magnusson (23). Sensitivity was low 17% (Vi) and 15% (Od), respectively, but specificity was high in agreement with previous reports (Table 7). Atopic predisposition showed similar PPV, 48% (Vi) and 44% (Od), as when using elevated CB-IgE.

However, the sensitivity of atopic predisposition was considerably higher 55% (Vi) and 58% (Od). Other cut-off values revealed a change in predictive values, mainly concerning the sensitivities. A lower cut-off value 0.3 kU/l increased the sensitivity to 32% (Vi) and 24% (Od). Cut-off values of mean CB-IgE + 2 SD (0.8 and 1.1 kU/l) decreased the sensitivity to 9% (Vi) and 6% (Od), respectively. The PPV remained unchanged. Kjellman (21) originally proposed CB-IgE cut-off values calculated as CB-IgE + 2 SD among infants without atopic predisposition and without atopic disease at the age of 18 months. In this way Magnusson (23) and Croner & Kjellman (7, 21) calculated their CB-IgE cut-off values 1.2 kU/l and 1.3 kU/l. The cut-off value of the latter study was later changed to 0.9 kU/l with reference to a follow-up at the age of 7 years (20). The choice of 0.3 kU/l as a cut-off value is discussed in the paper concerning IgE response by the age of 18 months (14). Our calculated cut-off values of 0.8 (Vi) and 1.1 (Od) are shown in Table 1. The combination of knowledge of atopic predisposition and CB-IgE increased the PPV and specificity but decreased the sensitivity. In the high risk group we found a high PPV (74%) and a low sensitivity (11%). PPV values were lower for the small high-risk group (8 infants) following the intervention programme (NS).

The differences in predictive values from those previously reported in similar studies may be due to several factors, such as different diagnostic criteria, regional differences, different environment, etc. The prevalence of atopic disease may vary in geographically different regions and from year to year. Our definition of atopic disease was much the same as that used by other investigators, although our's seemed less extensive than Croner & Kjellman's (7).

The method of recording data is an important factor. Croner & Kjellman based their study on questionnaires and a subsequent physical examination of the infants suspected of atopic disease and those with increased CB-IgE. Their evaluation, therefore, was not blinded concerning CB-IgE. Magnusson based his evaluation exclusively on questionnaires and phone interviews. Our study was based on prospective recording of symptoms using questionnaires at the ages of 6 and 12 months and a physical examination at the age of 18 months. Different CB-IgE cut-off values and different methods of IgE analysis might explain differences between studies. We used a very sensitive PRIST method for determining low IgE values. Croner & Kjellman used the IgE standard method and Magnusson an automatically "particle counting immunoassay" PACIA. Finally, we emphasize the difficulty in deciding whether anamnestic symptoms are atopic or not

Table 7. Comparison between studies of unselected infants at the age of 18 months

Author	Croner	Magnusson	Hansen (Vi)	Hansen (Od)
Reference	7	23	*	*
Year	1982	1988	1992	1992
Method	PRIST	PACIA	PRIST	PRIST
Cut-off kU/l	1.3	1.2	0.5	0.5
N	1701	190	1189	1625
Atopics (%)	8	20	39	40
Elevated CB-IgE (%)	5	19	15	12
PPV (%)	70	72	43	46
NPV (%)	95	92	62	61
Sensitivity (%)	44	68	17	15
Specificity (%)	98	93	86	89
Efficiency (%)	94	88	59	59

* The present study.

during early infancy. It will be easier and more reliable to diagnose atopic disease at a follow-up later in childhood, in our study planned at 5 years of age.

Conclusion

This study showed that elevated CB-IgE was not a reliable predictive factor of atopic disease at the age of 18 months. Infants with atopic predisposition developed atopic disease significantly more often. In a coming paper, we shall report CB-IgE and atopic predisposition as predictive factors for the development of IgE response and atopic symptoms, i.e. development of allergic disease.

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References

- BOUSQUET J, MENARDO J-L, VIALA J-L, MICHEL F-B. Predictive value of cord serum IgE determination in the development of "early-onset" atopy. *Ann Allergy* 1983; 51: 291-5.
- BOUSQUET J, MENARDO J-L, MICHEL F-B. Predictive capacity of cord blood IgE for the development of allergy in infancy and childhood. *Ann Allergy* 1984; 53: 692-5.
- BOUSQUET J, KJELLMAN N-IM. Childhood allergy. Predictive value of tests in childhood allergy. *J Allergy Clin Immunol* 1986; 78: 1019-22.
- BUSINCO L, MARCHETTI F, PELLEGRINI G, PERLINI R. Predictive value of cord blood IgE levels in "at-risk" newborn babies and influence of type of feeding. *Clin Allergy* 1983; 13: 503-8.
- CASIMIR G, VERMEYLEN D, DUCHATEAU J. Concentrations sériques en IgE: Prédiction des manifestations atopiques. Avantages de l'allaitement maternel. *Rev Méd Brux* 1983; 4: 323-6.
- CHANDRA RK, PURI S, CHEEMA PS. Predictive value of cord blood IgE in the development of atopic disease and role of breast-feeding in its prevention. *Clin Allergy* 1985; 15: 517-22.
- CRONER S, KJELLMAN N-IM, ERIKSSON B, ROTH A. IgE screening in 1701 newborn infants and the development of atopic disease during infancy. *Arch Dis Child* 1982; 57: 364-8.
- CRONER S, KJELLMAN N-IM. Development of atopic disease in relation to family history and cord blood IgE levels. Eleven-year follow-up in 1654 children. *Pediatr Allergy Immunol* 1990; 1: 14-20.
- DUCHATEAU J, CASIMIR G. Neonatal serum IgE concentration as predictor of atopy. *Lancet* 1983; 19: 413-4.
- FOUCARD T. Kan allergi hos spädbarn förebyggas eller förutsägas? *Läkartidningen* 1986; 83: 190-1.
- FURUKAWA S, NAKACHI S, MATSUBARA T, YABUTA K, TAKEUCHI T, BABA M. Neonate blood IgE levels on filter paper as indicators of atopic disease. *Allergy* 1990; 45: 375-81.
- HAMBURGER RN. The immunogenetics of IgE provides predictive value for the development of allergy. *Ann Allergy* 1982; 49: 9-11.
- HANSEN LG, HØST A, HALKEN S, et al. Cord blood IgE. I. IgE screening in 2814 newborn children. *Allergy* 1992; 47: 391-6.
- HANSEN LG, HØST A, HALKEN S, et al. Cord blood IgE. III. Prediction of IgE high-response and allergy. A follow up at the age of 18 months. *Allergy* 1992; 47: 404-10.
- HANSEN LG, HALKEN S, HØST A, ØSTERBALLE O. Prevalence of atopic disease. A follow-up at the age of 18 months and 5 years. A prospective and controlled study. *Cord blood IgE. V.* (in manuscript).
- HATTEVIG G. Sensitization and type I allergy in infants and children. Linköping University Medical Dissertations No. 285, 1989.
- HAUS M, HEESSE H DE V, WEINBERG EG, POTTER PC, MALHERBE, D, HALL JM. Genetic and environmental influences on cord blood serum IgE and on atopic sensitization in infancy. *S Afr Med J* 1990; 77: 7-13.
- KJELLMAN N-IM, JOHANSSON SGO. IgE and atopic allergy in newborns and infants with a family history of atopic disease. *Acta Paediatr Scand* 1976; 65: 601-7.
- KJELLMAN N-IM. Prediction and prevention of atopic allergy. *Allergy* 1982; 37: 463-73.
- KJELLMAN N-IM, CRONER S. Cord blood IgE determination for allergy prediction - a follow up to seven years of age in 1651 children. *Ann Allergy* 1984; 53: 167-71.
- KJELLMAN N-IM, JOHANSSON SGO, ROTH A. Serum IgE levels in healthy children quantified by a sandwich technique (PRIST). *Clin Allergy* 1976; 6: 51-9.
- LILJA G. Development of atopy during infancy in relation to food allergen intake. Stockholm University Medical Dissertations, 1990.
- MAGNUSSON CGM. Cord serum IgE in relation to family history and as predictor of atopic disease in early infancy. *Allergy* 1988; 43: 241-51.
- MICHEL FB, BOUSQUET J, GREILLIER P, ROBINET-LEVY M, COULOMB Y. Comparison of cord blood immunoglobulin E concentrations and maternal allergy for the prediction of atopic diseases in infancy. *J Allergy Clin Immunol* 1980; 65: 422-30.
- STORM K, HAAHR J, KJELLMAN N-IM, ØSTERBALLE O. Allergiprævalens, prædiktation og profylakse. En efterundersøgelse af en årgang danske børn ved 7 års alderen. *Ugeskr Laeger* 1986; 148: 3295-9.
- STRIMAS JH, CHI DS. Significance of IgE level in amniotic fluid and cord blood for the prediction of allergy. *Ann Allergy* 1988; 61: 133-6.
- VANDENPLAS Y, SACRE L. Influences of neonatal serum IgE concentration, family history and diet on the incidence of cow's milk allergy. *Eur J Pediatr* 1986; 145: 493-5.
- ZEIGER RS, HELLER S, MELLON MH, et al. Effect of combined maternal and infant food-allergen avoidance on development of atopy in early infancy: A randomized study. *J Allergy Clin Immunol* 1989; 84: 72-89.
- ZEIGER RS. Prevention of food allergy in infancy. *Ann Allergy* 1990; 65: 430-41.

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