

Histamine release from cord blood basophils is influenced by plasma IgE concentration, osmolarity, gestational age at birth and atopic disposition

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To characterize the normal values of histamine release from basophil leucocytes in cord blood after stimulation with both IgE-mediating and non-IgE-mediating secretagogues, a population of 1,684 newborn infants was studied using a microfiber-based method for detecting histamine release. A wide variation in anti-IgE and Concanavalin A-induced histamine release in the population was found. An increase in osmolarity in the release media selectively enhanced the maximal IgE-mediated histamine release, in addition to an increase in sensitivity in the dose response for anti-IgE and Concanavalin A. Both anti-IgE and Concanavalin A mediated histamine release were found to be significantly associated with the concentration of IgE in cord blood. Furthermore, an increased sensitivity to the IgE-mediated response and a close correlation between anti-IgE and Concanavalin A histamine release were found in the group of newborns with high IgE levels. Gestational age at birth and histamine release after stimulation with both IgE-mediating, and non-IgE mediating secretagogues were found to be significantly related, thus suggesting a continuing maturation of the human basophil leucocytes in the last weeks of gestation. Parental atopic disposition also affected basophil releasability in cord blood.

**T. Bjerke¹, M. Hedegaard¹,
T. B. Henriksen², B. W. Nielsen¹,
P. O. Schiøtz¹**

¹Allergy Research Laboratory, ²Perinatal Research Unit, University Hospital, Aarhus, Denmark

Torbjørn Bjerke, Allergy Research Laboratory, Department of Pediatrics, University Hospital of Aarhus, DK-8000 Aarhus C, Denmark

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Several investigations have shown that histamine release (HR) from blood basophils is a valuable diagnostic tool for detecting hypersensitivity reactions in children (1, 2). Few studies, however, have evaluated the HR patterns from basophils in non-allergic individuals and in newborns. Cord blood (CB) basophils have previously been found to show maximal HR and an HR sensitivity to anti-IgE which was dependent on the total plasma IgE concentration (3). These studies were carried out in hyperosmolar medium, and the results were not in accordance with other studies (4–7).

In the present study, we therefore further investigated basophil reactivity in a large population of newborn infants using both physiological and hyperosmolar release media. Normal values of HR were established and the relation between CB plasma IgE and the HR was elucidated. Furthermore, we in-

vestigated whether gestational age at birth influenced basophil HR. Finally, an evaluation of the possible effect of parental atopic disposition on CB basophil HR was performed.

Material and methods

Study population

The study design is outlined in Fig. 1. CB was collected from infants born at the Department of Obstetrics at the University Hospital of Aarhus during the period March 1, 1990 to April 31, 1991. Women living in a well-defined geographical area with about 250,000 inhabitants are referred to the department, which is the only maternity ward in the city. The number of CB samples taken were 2,638, corresponding to 47% of the total number of infants born during this period. HR was analyzed in 1,684

STUDY DESIGN

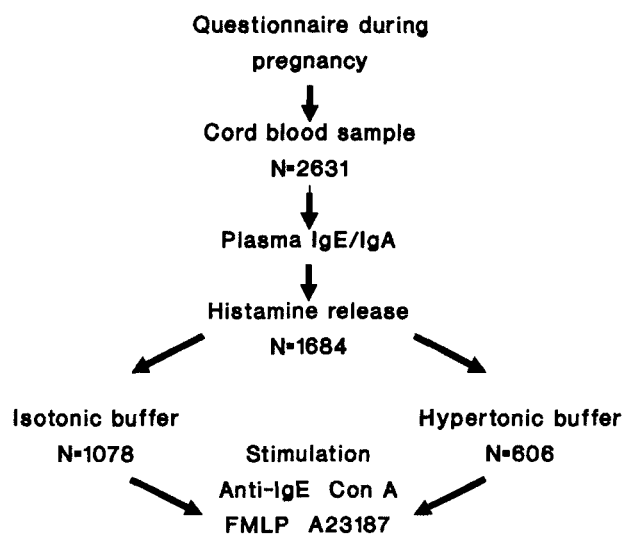


Fig. 1. Schematic presentation of the study design.

cord blood samples. Pregnant women who planned to deliver at the hospital were recruited by their midwives during routine prenatal visits. During these visits, a detailed description of the planned project was given to the women who agreed to participate. During the 28th week of gestation, the women received a questionnaire (Q₃₀) which was returned to their midwives during the 30th week of gestation. This questionnaire contained detailed questions on atopic diseases of the pregnant women and the fathers. The parental atopic diseases were subdivided into seasonal rhinitis, perennial rhinitis, allergic/atopic dermatitis, urticaria and bronchial asthma for each of the parents. A reminder was mailed once to non-responders.

Immediately after delivery, the attending midwife secured a sample of CB, as well as a specific registration form for the baby (gestational age, weight, length, Apgar score, CB pH). The gestational age at delivery was based on measurement of the fetal biparietal diameter by ultrasound before the 21st week of gestation (8).

Blood sampling

Cord blood was collected immediately after birth by direct needle aspiration of the cord vein. The samples were anticoagulated with 10 mM EDTA (pH = 7.2) and stored at 4°C pending analysis. To assure cell viability, basophil histamine release was determined as soon as possible and not later than 24 h after blood sampling.

Histamine release assay

HR was measured by a glass fiber based fluorometric method first described by Stahl Skov et al. (9). The glass fibers have been shown to bind histamine with a high degree of specificity and affinity (9). In several studies the conventional histamine methods were found to qualitatively correlate very well (i.e. correlation coefficients of >0.9) with the glass fiber technique when comparing the results of patients responding to antigen challenge, cell sensitivity and dose response curves (1, 10, 11). These studies confirm that the glass fiber assay measures similar histamine responses compared with the conventional assays. In addition, when the same histamine standards were measured by the glass fiber method and Immunotech, RIA histamine, a correlation coefficient of 0.996 was found (Hendrik Nolte, pers. comm.). Furthermore, the glass fiber technique is fast and requires only small amounts of blood (5 ml blood for 96 analyses). Therefore, this technique is convenient when HR is measured in a large population of newborns.

Briefly, after removal of plasma, the blood cells were washed four times in the release medium which consisted of ((piperazine-N,N'-bis(2-ethanesulfonic acid)) (PIPES)-buffered Na-K acetate (PAH). As hypertonic acetate buffer has been shown to enhance HR from human basophils (12), two different PAH buffers were employed in the first part of the present study:

1. An isotonic (305 mOsm) containing PIPES 10 mM, Na-acetate 140 mM, K-acetate 5 mM, CaCl 0.6 mM, MgCl 1.1 mM adjusted to pH 7.40 with Tris(hydroxymethyl)aminomethane as well as heparin 7.5 IE/ml, glucose 2.8 mM and human serum albumin 0.16 g/l (1,078 CB samples).
2. A hypertonic (500 mOsm) PAH buffer differing from the isoosmolar buffer only in Na-acetate concentration (230 mM Na-acetate) (606 CB samples).

50 µl PAH/well was added to microfiber-coated microtiter plates (96 wells/plate) (Referencelaboratoriet, Copenhagen, Denmark).

Aliquots of washed blood cells (50 µl/well) were added, prior to the secretagogue dissolved in 20 µl PAH. After incubation for 60 min at 37°C, the plates were washed in purified water. In order to remove interfering substances and protein residues, the plates were incubated with a detergent/enzyme mixture (Renafix, Referencelaboratoriet, Copenhagen, Denmark) for 30 min at 37°C, and finally the plates were washed in purified water. HR was determined by fluorescence of the histamine-ophthaldehyde

Table 1. Histamine release from cord blood basophils following stimulation with different concentrations of anti-IgE, Con A, FMLP and A23187 in the normotonic buffer. N = 1,078

Secretagogue	Histamine release (ng/ml blood)		Responders*
	Median	Range	
Anti-IgE (U/ml)			
0.4	0.0	(0.0–14.5)	92%
4.0	0.7	(0.0–68.0)	
40.0	6.6	(0.0–134.6)	
400.0	11.3	(0.0–115.3)	
Con A (µg/ml)			
10.4	1.7	(0.0–29.8)	79%
20.8	5.0	(0.0–46.0)	
41.6	8.3	(0.0–66.8)	
83.2	12.0	(0.0–96.9)	
FMLP (M)			
10 ⁻⁸	1.0	(0.0–54.5)	58%
10 ⁻⁶	4.5	(0.0–77.1)	
10 ⁻⁴	4.8	(0.0–79.9)	
A23187 (µM)			
1.0	8.6	(0.0–55.4)	98%
2.0	17.0	(0.0–122.5)	

*Maximum histamine release exceeding 1.65XSD of triple measurements on unstimulated blood (see Methods)

complex, and all histamine measurements were performed in triplicate.

To quantitate the HR (HR/ml blood), four sequential histamine standards corresponding to 6.25, 12.5, 25.0 and 50.0 ng histamine/ml blood were added to unstimulated blood cells from each cord blood sample. A linear standard curve was generated by simple regression analysis, and slope and intercept were used when calculating the fluorometric response. A significant cell HR response was defined for each secretagogue based on the median spontaneous histamine release + 1.65 × SD in wells of unstimulated blood cells. The microplates were designed with three wells of unstimulated blood cells, followed by wells of cells stimulated with increasing concentration of the secretagogue studied.

Secretagogues

All secretagogues studied were diluted in PAH buffer on the day of testing to ensure maximum response. Rabbit anti-human IgE (anti-IgE; Behringwerke, Marburg, FRG) was used at final concentrations of 0.4, 4.0, 40.0 and 400.0 U/ml (U corresponds to 2.5 ng protein), Concanavalin A (Con A; Pharmacia, Uppsala, Sweden) 10.4, 20.8, 41.6 and 83.2 µg/ml, N-formyl-methionyl-leucyl-phenylalanine (FMLP; Sigma, St. Louis, USA) 10⁻⁸, 10⁻⁶, 10⁻⁴ M, and the calcium ionophore A23187 (Sigma, St. Louis, USA) 0.5, 1.0 and 2.0 µM were used.

Total plasma IgE and IgA measurements

The concentration of IgE in plasma was quantitated with an enzyme-linked immunoassay (ELISA) with a detection limit of 0.2 IU/ml. In the statistical analyses, IgE below 0.2 IU/ml was arbitrarily chosen as 0.1 IU/ml. In order to evaluate possible contamination of the cord blood samples with maternal blood, total plasma IgA was determined in samples with CB-IgE ≥ 0.5 IU/ml. The IgA was assayed in an ELISA with a detection limit of 60 µg/ml, and values exceeding 60 µg/ml were considered potentially contaminated and excluded from further analyses (13).

Statistical methods

HR values were found not to be normally distributed. Therefore, non-parametric statistical methods were used. Wilcoxon's test was employed for paired comparisons. To detect the influence on HR of variables with more than two groups, Kruskal-Wallis one-way analysis of variance (ANOVA) test was used for the comparison of the sum of group ranks. Spearman's method was employed for regression analysis (the regression coefficient is denoted as r_s).

The statistical analyses were carried out using the statistical package SPSS/PC + TMV4.0 (SPSS Inc. Chicago, Illinois 60611). P values < 0.05 were considered significant. All HR values are presented as medians (ranges).

Ethical considerations

The Committee for Scientific Ethics in the county of Aarhus approved the present study as fully compatible with Helsinki Declaration II.

Results

Study group characteristics

Of the 2,638 cord blood samples taken, HR was analyzed in 1,687 samples (63.8%). The loss of samples was due to limited volume of blood, microcoagulation in samples and storage time exceeding 24 h. Contamination with maternal blood was suspected in 3 samples (CB-IgA ≥ 60 µg/ml) and these samples were excluded from further processing, yielding a total sample size of 1,684. The median IgE concentration in the cord blood samples utilizing the isotonic buffer was 0.20 IU/ml (range; < 0.10 to 7.00 IU/ml, N = 1,078). When a hypertonic buffer was applied (N = 606), the median value of CB-IgE was 0.10 IU/ml (range; < 0.10 to 4.90 IU/ml).

Table 2. Effect of osmolarity on maximum histamine release

Secretagogue	Histamine release (ng/ml blood)	
	Isotonic N = 1,078	Hypertonic N = 606
Anti-IgE*	11.3 (0.0–115.3)	20.2 (0.0–192.4)
Con A*	12.0 (0.0–96.0)	26.7 (0.0–228.5)
FMP**	4.8 (0.0–79.9)	4.8 (0.0–52.4)

All HR values are median (range)

* $p < 0.00001$ (Wilcoxon's test)

** $p > 0.05$

Normal values of histamine release in cord blood

Cord blood basophils were stimulated with secretagogues acting via FcεRI (anti-IgE and Con A), in addition to FMLP and the calcium ionophore A23187, which bypasses the high affinity IgE receptor. The histamine release responses following challenge with the different concentrations of the secretagogues using the physiological buffer are given in Table 1.

Effects of osmolarity on histamine release

In previous studies, it has been suggested that hyperosmolarity increases the histamine response from human basophils and mast cells (12, 14–16). However, the extent to which basophils from the newborn respond to different osmolarities has not been extensively studied (12). The influence of osmolarity on the median values of maximum HR after stimulating the cord blood basophils with anti-IgE, Con A and FMLP in the present study is shown in Table 2. Both anti-IgE and Con A mediated HR were significantly enhanced in the hypertonic PAH-buffer ($p < 0.00001$), whereas the FMLP response was not changed by the increase in osmolarity. Furthermore, the anti-IgE dose response, as well as the Con A dose response, showed an increased releasability in the hypertonic buffer (Fig. 2A, B).

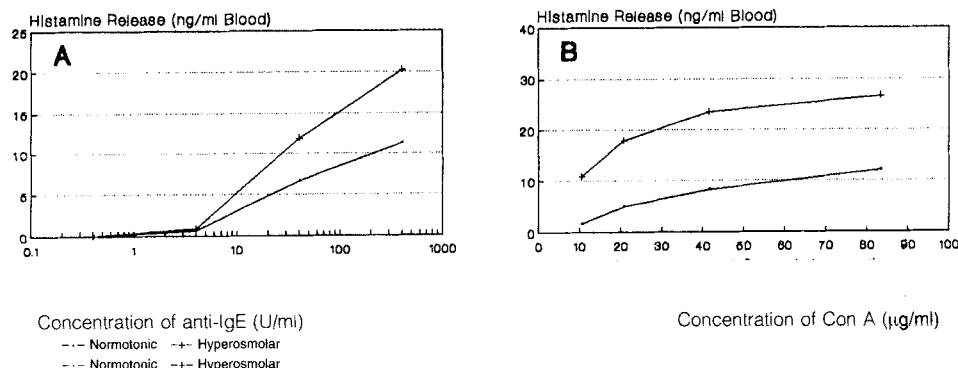


Fig. 2. Anti-IgE (A) and Con A (B) histamine release dose responses in the isoosmolar and hyperosmolar buffer. Both dose responses reveal an increased releasability in the hyperosmolar buffer compared to the normotonic buffer.

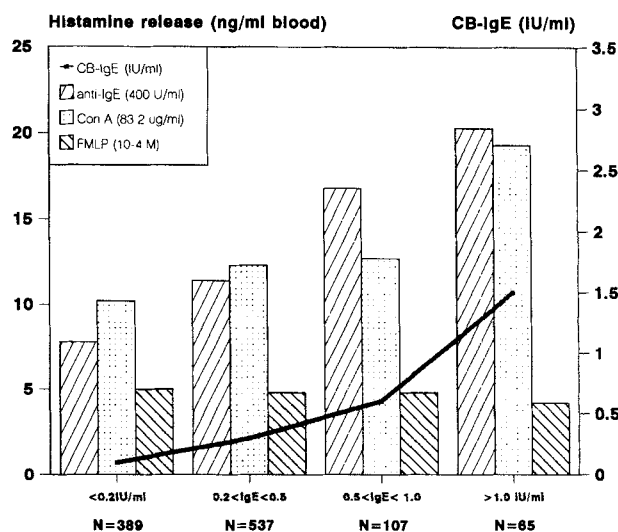


Fig. 3. The influence of plasma IgE concentration on maximum histamine release in the physiological buffer. The difference in histamine response between the increasing IgE levels was highly significant after both anti-IgE and Con A stimulation ($p < 0.00001$ and $p < 0.0007$, respectively, Kruskal-Wallis). Histamine release after challenge with the secretagogues which bypasses the high affinity IgE receptor was unaffected by the concentration of IgE in plasma.

Influence of plasma IgE concentration on histamine release

As shown in Figs 3 and 4, anti-IgE and Con A mediated HR was significantly associated with the concentration of IgE in CB in both buffers. Using the isotonic buffer (Fig. 3), the difference in maximum HR between the increasing IgE levels was highly significant after both anti-IgE and Con A stimulation ($p < 0.00001$ and $p < 0.0007$ respectively). In the hypertonic release media, however, only anti-IgE mediated HR differed significantly between the IgE levels ($p < 0.00001$) (Fig. 4). In contrast, neither the concentration of CB-IgE, nor the calcium ionophore mediated HR in the isotonic buffer (Fig. 3) influenced the FMLP response in any of the buffers (Figs. 3, 4). We also evaluated the basophil cell sensitivity to the four different anti-IgE concentrations and total plasma IgE concentration.

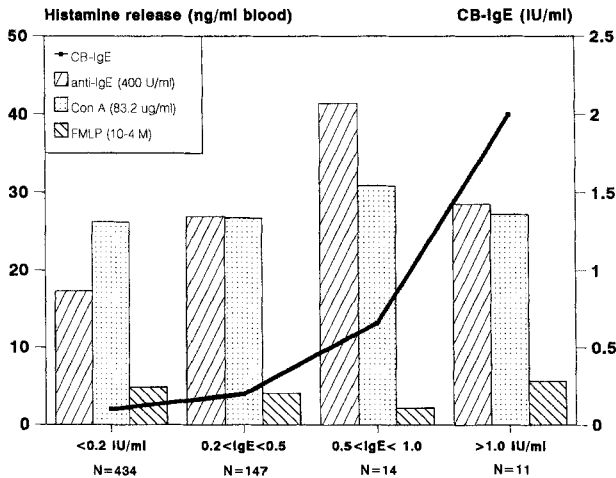


Fig. 4. The influence of plasma IgE concentration on maximum histamine release in the hyperosmolar buffer. Only anti-IgE mediated histamine release was found to be significantly different between the IgE levels ($p < 0.00001$, Kruskal-Wallis test).

This approach revealed results similar to when we compared maximum HR and total plasma IgE concentration ($p < 0.00001$, Kruskal Wallis, data not shown), indicating that different methodological approaches to the specific correlations gives the same results.

Dose responses for anti-IgE and Con A in the buffers according to plasma IgE concentration are given in Figs 5 and 6. In both buffers, an increased sensitivity to the two IgE-mediated responses was seen in the group of newborns with high CB-IgE levels. As illustrated in Figs 5A, B, a shift in the dose response curve for anti-IgE resembling the bell shape seen in adult blood occurred in the group of infants with CB-IgE exceeding 1.0 IU/ml. The doses response for Con A induced HR was likewise influenced by the CB-IgE concentration (Figs. 6A, B).

We found a progressive increase in the correlation between anti-IgE and Con A induced maximum HR which was most prominent in the hypertonic buffer ($pIgE < 0.2$, $r_s = 0.67$ and $pIgE > 1.0$, $r_s = 0.91$, $p < 0.001$). However, also in the isotonic buffer, a significant correlation between the two IgE-mediated

ated secretagogues was seen ($pIgE < 0.2$, $r_s = 0.30$ and $pIgE > 3.0$, $r_s = 0.90$, $p < 0.001$, respectively).

Gestational age at birth and histamine release

In order to test the possible association between gestational age at birth and cord blood basophil releasability, the durations of the pregnancies were divided into weeks, starting with 36 and ending with 42 gestational weeks. As illustrated in Table 3, highly significant differences were found between the groups after anti-IgE and Con A mediated stimulation. In addition, the FMLP response was found to differ significantly between the gestational groups as well, although somewhat weaker.

Parental atopic disposition and basophil histamine release

Detailed information on parental atopic disposition was gathered from questionnaire Q₃₀. Sixty three percent of the parents ($N = 689$) answered the questions. Anti-IgE mediated histamine release was found to be significantly influenced by atopic disposition if the mothers suffered from seasonal rhinitis, and if the fathers had perennial rhinitis (Table 4). As also shown in Table 4, fathers atopy and anti-IgE mediated CB histamine release were negatively associated. The presence of atopic disposition also affected FMLP mediated HR if fathers suffered from perennial rhinitis.

Discussion

This paper describes CB basophil reactivity with regard to HR in a large population of newborns. Both isotonic and hypertonic release media were tested.

Our results show that anti-IgE and Con A mediated HR from cord blood basophils are significantly influenced by osmolarity. These findings are consistent with previous studies on adult basophils and mast cells (12, 14–16). Moreover, cord blood basophils seem to respond in a manner similar to adult basophils upon the change in osmolarity (12). The

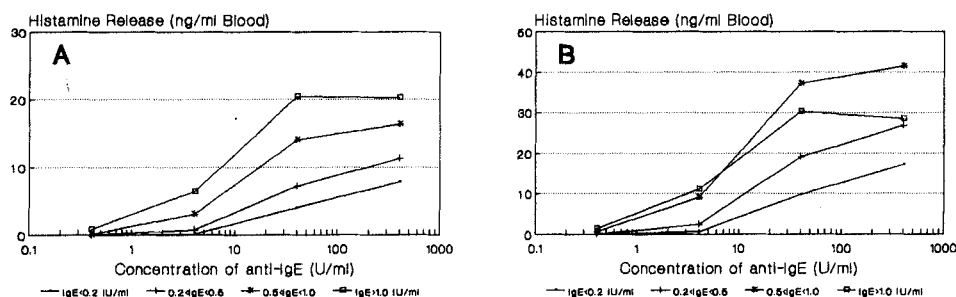


Fig. 5. Dose responses for anti-IgE induced histamine release in the isoosmolar buffer (A), and in the hyperosmolar buffer (B) according to plasma IgE concentration. An increased sensitivity to the anti-IgE response was seen in both buffers in the groups of newborns with high IgE levels. Furthermore, a shift in the curve resembling the bell shape seen in adult blood was seen if the IgE concentration exceeded 1.0 IU/ml in both buffers. Error bars are omitted for clarity.

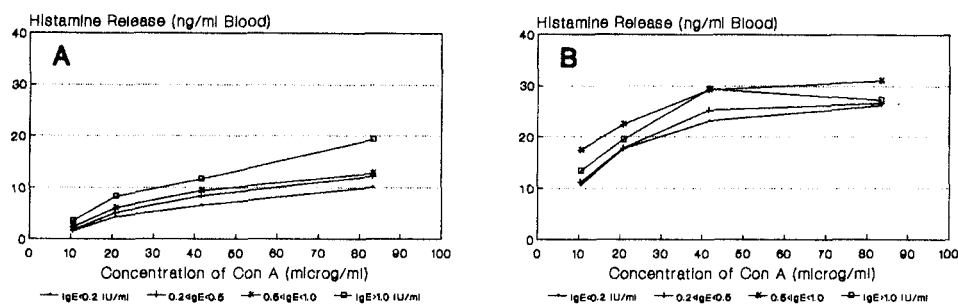


Fig. 6. Dose responses for Con A induced basophil histamine release in the two different buffers. The sensitivity of the cell response is influenced by the plasma IgE concentration in both the isoosmolar buffer (A), and the hyperosmolar buffer (B). Error bars are omitted for clarity.

results from the present study confirm our previous conclusion that the increase in osmolarity selectively magnifies the IgE-mediated HR, as shown by the constant FMLP response in the two different buffers. The obvious selectivity in the enhancement of HR suggests that the biological mechanism includes FcεRI interactions, perhaps due to receptor immobilization which has been suggested as being important for D₂O upon basophil mediator release (17), or to changes in the spatial arrangement of the FcεRI receptor due to a possible decrease in the size of the basophils in the hyperosmolar media.

We observed wide variation in anti-IgE and Con A induced HR in our population of newborns. In a previous study including 97 CB samples, we found that when using a hypertonic release medium, both the maximum HR and the sensitivity to anti-IgE, but not to Con A, were dependent on total plasma IgE concentration (3). Prior studies had failed to show the positive correlation between CB-IgE and histamine release after anti-IgE stimulation utilizing an isotonic buffer (4–7). In the present study, we confirmed our previous findings with respect to the anti-IgE response. However, we also found a highly significant difference between HR induced by Con A in the physiological buffer and with the different CB-IgE concentrations. Thus, these data suggest that histamine release from CB basophils after stimulation with both anti-IgE and ConA is dependent on the total CB-IgE concentration in both hypertonic and isotonic buffers.

Passive sensitization of CB basophils with IgE has been shown to enhance the anti-IgE mediated HR (3–5, 7), in addition to an increase in sensitivity (3, 5). In the present study, the anti-IgE dose responses showed a progressively increasing sensitivity to the secretagogue with increasing CB-IgE concentration. Furthermore, we observed a shift in the shape of the dose response curve towards that seen in adult blood (3) with maximum histamine release occurring at a tenfold lower concentration of anti-IgE. The latter result indicates that normal untreated basophils from CB show mature releasability patterns to anti-IgE. Moreover, our data suggests that the postulated reduced CB basophil releasability to anti-IgE observed in previous studies (4, 5, 7) is due to a reduced CB-IgE concentration when compared to the present study. In a previous study, we found no difference in IgE-mediated maximum HR between cord and adult blood (3). In agreement, results from Miadonna et al. (7) revealed similar histamine content in the two sources of blood.

The HR induced by Con A from adult basophils has been shown to share great similarities with immunological activation of the cell (18). Both Con A and anti-IgE react with sites on the Fc portion of the IgE molecule bound to the FcεRI receptor on the surface of the basophils (18). Several reports have found a strong correlation between Con A and anti-IgE induced histamine release in adult blood (18–20). However, in the previous paper we did not observe a close correlation in the HR between the

Table 3. Maximum histamine release and gestational age at birth. Isotonic buffer, N=948

Secretagogue	Gestational age (weeks)						
	36 N=31	37 N=33	38 N=79	39 N=197	40 N=290	41 N=217	42 N=101
Anti-OgE*	3.2	3.2	9.8	10.6	11.5	13.0	15.8
Con **	6.5	7.7	9.1	12.2	13.2	12.9	14.9
FMLP***	3.2	2.9	3.9	5.3	5.4	5.4	4.9
IgE (IU/ml)****	0.2	0.2	0.2	0.2	0.2	0.2	0.2

All histamine release values are median values

*p<0.00001, **p<0.006, ***p<0.04, ****p>0.05 (Kruskal-Wallis)

Table 4. Influence of parental atopic disposition on cord blood basophil histamine release

Atopy	Anti-IgE HR		Con A HR		FMLP HR	
	Mother	Father	Mother	Father	Mother	Father
Rhinitis, seasonal						
Yes	15.9* (N = 86)	11.0 (N = 107)	16.8	14.5	5.0	5.0
No	11.2 (N = 603)	11.6 (N = 574)	14.4	12.6	5.0	5.1
Rhinitis, perennial						
Yes	10.5 (N = 42)	7.2** (N = 42)	14.4	10.2	4.0	2.5***
No	11.4 (N = 635)	11.5 (N = 605)	12.7	12.7	5.0	5.0
Allergic/atopic eczema						
Yes	11.8 (N = 111)	9.1 (N = 75)	12.4	10.8	4.9	5.3
No	11.4 (N = 572)	11.4 (N = 579)	12.7	12.7	5.0	4.9
Urticaria						
Yes	11.6 (N = 50)	8.9 (N = 18)	15.2	10.3	3.9	3.5
No	11.4 (N = 622)	11.5 (N = 620)	12.4	12.7	5.1	4.9
Bronchial asthma						
Yes	13.8 (N = 32)	8.7 (N = 38)	13.7	12.0	5.1	5.0
No	11.3 (N = 642)	11.6 (N = 610)	12.6	12.7	5.0	4.9

All histamine release values are median

* $p < 0.0004$, ** $p < 0.03$, *** $p < 0.01$, Mann-Whitney U-test

two secretagogues in cord blood, indicating that Con A may activate cord blood basophils by a non-IgE-dependent mechanism (3). In the present paper, we demonstrate a close and significant correlation between Con A and anti-IgE response in both buffers. It is evident that the critical factor in this respect is the concentration of IgE in plasma, as the correlation increases progressively with elevation of CB-IgE, and therefore probably the number of occupied high affinity IgE receptors on the basophil cells. These results indicate that HR induced by Con A from newborn basophils, as in adult basophils, shares great similarities with activation of the cell if there is an elevation of the IgE concentration in plasma (> 1.0 IU/ml). In contrast, if the CB plasma IgE level is low (< 0.2 IU/ml), the correlation between the two secretagogues is rather weak ($r_s = 0.2$). Thus, as indicated previously (3), an additional non-IgE mediated mechanism could take place in this group of basophils. Con A could interact with carbohydrate groups on the plasma membrane and/or on the FcεRI receptor, causing HR.

In the second part of the present study, we found that gestational age at birth and HR after stimulation with both anti-IgE, Con A, and FMLP were significantly associated (Table 3). The biological mechanisms behind the progressive increase in HR could be explained by a complementary increase in the level of cord blood IgE during the last weeks of gestation. However, we and others (22, 23) did not find any association between gestational age and CB-IgE concentration. Another explanation is a gen-

eral maturation of the basophil cell during the last weeks of gestation, resulting in an increased releasability. The maturation of the cell could include both 1) the number of receptors on the plasma membrane, and 2) the content of histamine in the basophil granules (increasing synthesis). Both Mendoza et al. (4) and Miadonna et al. (5) found a significantly lower amount of IgE receptors on basophils from newborns compared to adults. The association between the histamine release and gestational age could also be due to an increase in the number of basophil cells from the 36th to 42th week of gestation. Finally, a possibility could be a hampered signal transduction pathway in basophils from premature newborns. The effects of acetylsalicylic acid on the cyclooxygenase pathway in cord blood basophils have been shown to differ from observations in adult blood (3, 19). This might indicate a maturational phenomenon.

Croner & Kjellman concluded in a recent study that a detailed questionnaire for establishing the prevalence of atopic disease provides adequate information and can be used in epidemiological investigations (24). In the present study, we used information on parental atopic diseases gathered from questionnaires given to the mothers in the 30th. week of pregnancy. Concerning the mothers' atopy, we found a significant association between atopy and elevation of anti-IgE induced HR if the mothers suffered from seasonal rhinitis (Table 4). Ebbesen et al. (32 cord blood samples) (6) and our previous study (93 cord blood samples) (3) did not detect any relationship between histamine release in cord blood

and a family history of atopic diseases. In contrast, Miadonna et al. (25) found that cord blood basophils from infants with atopic parents produced more histamine compared to a non-atopic group. They concluded that newborns from atopic parents probably carry more fixed IgE on the basophils than newborns from healthy parents. In the present paper we were able to distinguish between several different atopic diseases. Another cause of the discrepancy in results could be the large difference in the size of study populations between the present study and the previous investigations (3, 6). Surprisingly, fathers' atopy and anti-IgE mediated histamine release were found to be negatively associated (Table 4). We observed a significant decrease in histamine release if the fathers suffered from perennial rhinitis, whereas the other groups of atopy showed the same tendency, although not statistically significant. It is difficult to speculate on the biological mechanisms behind these observations. In our recent paper evaluating IgE in cord blood, we found a positive association between cord blood IgE concentration and fathers perennial rhinitis (22). Miadonna et al. (25) considered whether basophil releasability at birth could be regarded as a predictive marker for allergy. The possible relation between basophil releasability at birth and appearance of allergic diseases in childhood is a very interesting issue, and our group is now completing a large study in which we have been following 400 infants from birth until one year of age. This group of infants has been evaluated every third month with both HR, IgE measurements and clinical examination.

We conclude that histamine release from cord blood basophils is dependent on a variety of factors, of which the IgE concentration in plasma plays a significant role indicating free FcεRI receptors in the groups with low IgE levels. Furthermore, increased osmolarity in the release media selectively enhances the IgE-mediated histamine release. Gestational age at birth is also important when evaluating cord blood basophil releasability, suggesting a continuing maturation of the cell during the last weeks of gestation. Finally, parental atopic disposition seems to be related to CB basophil HR.

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