

IgE levels in cord and capillary blood at 5 days of age

Hansen D, Hornnes P, Poulsen LK. IgE levels in cord and capillary blood at 5 days of age.

We have determined the correlation between IgE in cord blood and capillary serum from 98 mature children at 5 days of age. Sixty-six per cent had no family history of atopy, 29% had a single and 5% a double disposition. The study showed a good correlation, $\rho = 0.75$, $p < 10^{-5}$, between IgE levels in cord blood and capillary blood samples drawn on the 5th day of life in children both with and without a heredity of atopic diseases. There was no correlation between the concentrations of cord blood IgE and IgA.

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In recent years, the prevalence of atopic diseases in the Western part of the world has been increasing (1). With the purpose of minimizing by means of allergen avoidance regimens the risk of developing atopic disease, many investigators have pursued methods predicting high-risk children. For many years an increased IgE level in cord blood has been assumed to be a good predictor for development of atopic symptoms in childhood (2,3). However, this has been questioned, since positive predictive values between 20% (4) and 80% (2) have been observed. Even so, many obstetric departments still measure the IgE concentration in cord blood. The cord blood is however not always collected at birth. Another opportunity to measure IgE could be at 4–6 days of age, when by a capillary blood sample infants are tested for phenylketonuria and hypothyroidism. Others studies have demonstrated a good correlation between cord and capillary blood samples from neonates with a maternal (5) and double family history of atopy (6). This has however never been studied in a general population.

The aim of the present study was to determine the correlation between IgE in cord blood and capillary serum from mature children at 4–6 days of age with and without a family history of atopy.

Material and methods

At the National University Hospital, Rigshospitalet, Copenhagen, cord blood was sampled from newborns during a 6-month period. Among all children born between 15th August, 1990 and 14th February 1991, 125 were randomly selected for this study. The following inclusion criteria were applied: 1) the child had to be mature and healthy, 2) the parents had to accept participation in the study and to speak Danish, in order to make certain that the histories of familial disposition were qualified.

The sole exclusion criterion was that the capillary blood sample for IgE had not been taken. Acceptance was obtained from all parents asked to participate in the study. Twenty-seven children (22%) dropped out because, for logistical reasons, the capillary blood samples had not been drawn, leaving 98 children. The study was approved by the Human Research Ethics Committee, Copenhagen. A family history was defined as presence of atopic diseases: atopic eczema, bronchial asthma, rhinoconjunctivitis and urticaria in the first degree of family, e.g. parents and siblings. Two of the investigators interviewed the parents. In half the cases both parents were interviewed, and in the other half, only the mothers.

Sixty-five children had no family history of atopy, 28 had a single and five a double history of atopy. There were no differences between the fam-

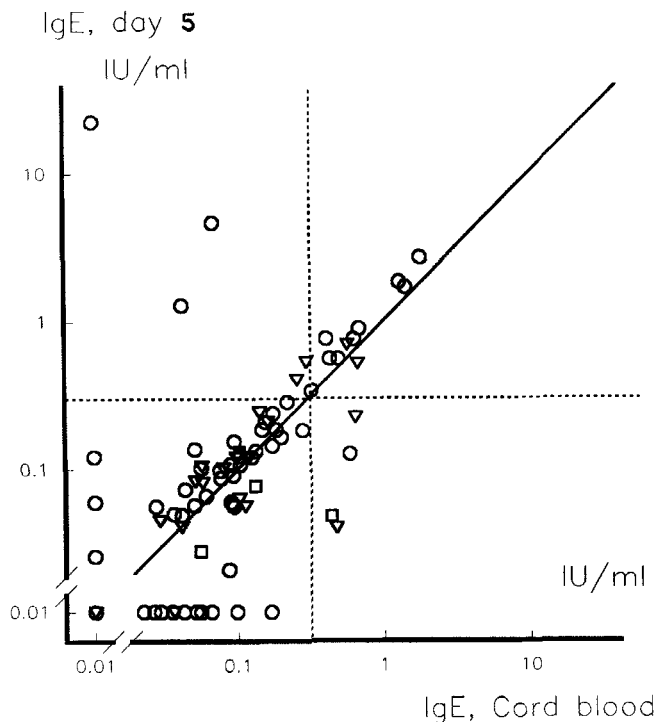


Fig. 1. Shows the IgE levels of cord blood compared with capillary blood on the 5th day of life. ○ = none, ▽ = single, ◻ = double disposition of atopy. — $X = Y$, - - - - IgE = 0.3 kU/l.

ily history of atopy in those participating and those from whom capillary blood samples were not drawn.

Cord blood sampling was performed either by needle aspiration from the cord or allowing the blood to run freely from the cord into the tube.

The capillary blood sample was drawn on 4th–10th day of life, median 5th day of life and lower and upper quartiles 5th–6th of life. Drawing of capillary blood samples was performed by heel puncture, when a routine blood sample for phenylketonuria and hypothyroidism was drawn from the child. The sera were stored at -20°C until analysed.

Laboratory investigations

IgE was determined using a modification of the radioimmunometric assay previously described (7). Briefly, 150 μl of the sample were incubated in polystyrene tubes ("Maxisorp", NUNC, Roskilde, Denmark), onto which anti-IgE (Behringwerke) had been adsorbed. I^{125} -labelled anti-IgE (Pharmacia, Uppsala, Sweden) was used for detection. The sensitivity of the assay was 50 pg/ml equivalent to 0.02 kU/l.

IgA was determined by radioimmunometric assay similarly to the IgE-assay (8). The standard or

the samples to be tested were diluted 1:10, and 500 μl were incubated in tubes precoated with rabbit anti-human IgA antibody (Code No. A262, Dakopatts, Copenhagen, Denmark, diluted 10^3 times in PBS). For detection, mouse anti-human IgA monoclonal antibody (Code M 12011 from Oxoid, Basingstoke, Hampshire, England) was incubated at 37°C for 2 h followed by overnight incubation (room temperature) with iodine-labelled rabbit anti-mouse IgG.

The measurement range was 4 to 500 ng IgA/ml. When the control serum diluted to 26 ng/ml was repeatedly tested in quadruplicate on 4 different days, the intra- and interassay variations were 5% and 12%, respectively.

Statistical analysis

Spearman rank correlation test was used in correlation studies. Wilcoxon's paired test and Mann-Whitney test were used to test intergroup differences. $P = 0.05$ was chosen as level of significance.

Results

The median IgE value in all the cord blood samples was 0.08 kU/l, range <0.01 –1.81. The medians for none, single and double atopic familial disposition were 0.08 kU/l (range <0.01 –1.81), 0.07 kU/l (range <0.01 –0.67) and 0.12 kU/l (range 0.06–0.43), respectively. No significant difference was found in cord blood from the children with and without a family history of atopy.

In the 19 children with a maternal history of atopy, the median IgE level of the cord blood was higher, however not significantly: 0.11 kU/l, range <0.01 –0.64.

The Allergy Committee of the Danish Paediatric Society recommends a cut-off limit of 0.3 kU/l (9). Among the 18 children with an IgE-level exceeding 0.3, five had a maternal history, two a paternal, one a double, and 10 no history of allergy.

IgE-capillary blood sample

The median IgE value in the capillary samples was 0.1 kU/l, range <0.01 –1.70. Some children had a much higher IgE level in the capillary than in the cord blood sample. These results were verified by a second determination.

The correlation between the IgE level in cord and capillary blood samples is given in Fig. 1. There was a good correlation between the two samples: $\rho = 0.75$, $p < 10^{-5}$. In some infants, however, the capillary IgE values rose or dropped compared to the cord IgE values of 0.3 kU/l.

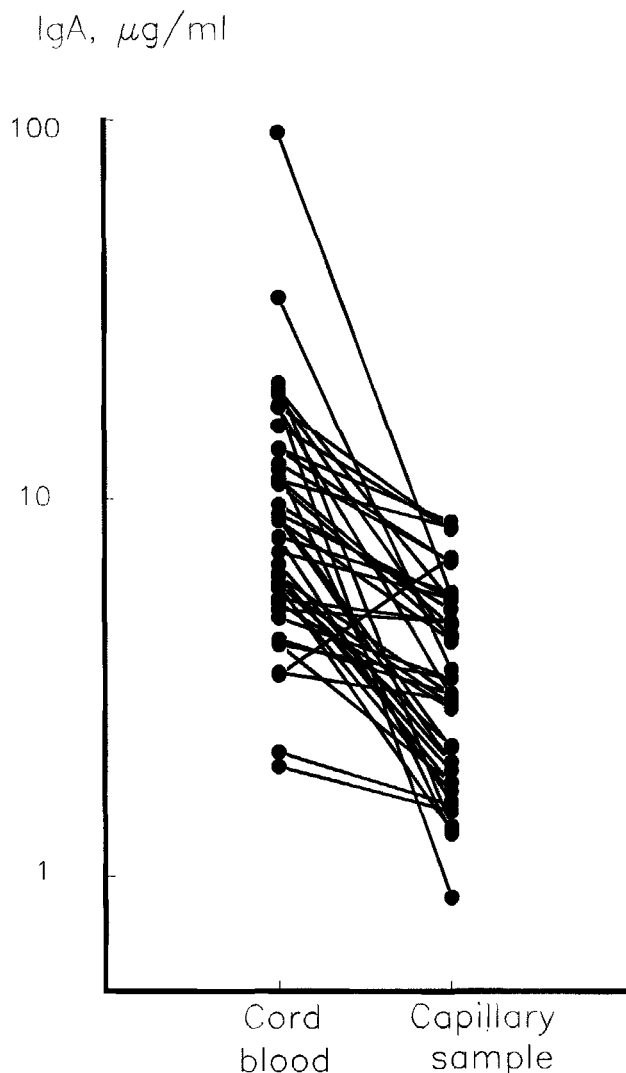


Fig. 2. Shows the IgA level of cord blood compared with capillary blood on the 5th day of life.

Of the four children whose capillary IgE levels dropped below 0.3 kU/l, one child had no pre-disposition, two had a single and one had a double familial pre-disposition to atopy. Only two of the four also had large drops in capillary IgA levels compared with cord blood.

None of the three children whose IgE levels exceeded 0.3 kU/l had a family history of atopy. These IgE capillary samples had been drawn on Days 5, 6 and 7 of life. From only one of these children is the capillary IgA value available. It showed an approx. 50% drop in capillary blood IgA level compared with cord blood.

IgA could be detected in all cord samples. The median value for the cord blood was 6.52 $\mu\text{g/ml}$, range 1.88–92.70. The medians for none, single and double familial pre-disposition of atopy were 6.43 (range 1.88–33.80), 6.83 (range 1.96–92.70) and 6.28 (range 3.44–20). There were no signif-

icant differences between the groups with and without a family history of atopy.

IgA was measured in 44 of 98 capillary samples leaving sufficient sera. IgA level in these cord and capillary blood samples is shown in Fig. 2. In all but one, drawn on Day 5 of life, there was a drop in IgA concentration in capillary blood compared with cord blood. The IgA drop was significant, $p < 0.001$, and the median drop was 52.6%. The only capillary sample which showed a rise in IgA compared to cord blood had been drawn on the 5 day of life. There was no correlation between the IgE and IgA levels in the blood cord samples, Fig. 3.

Discussion

Our data which have been obtained from a group of infants unselected for family history of allergy, confirm the results from other studies (5,6) demonstrating a good correlation between cord and capillary blood samples from neonates.

In a small number of children, however, the IgE level in cord blood was either significantly higher or lower than that of the capillary samples. This was independent of any family history of atopy.

When the IgE level in cord blood is higher than in capillary blood, the most likely explanation is maternal contamination of cord blood. Other reasons might be materno-foetal passage of IgE (11),

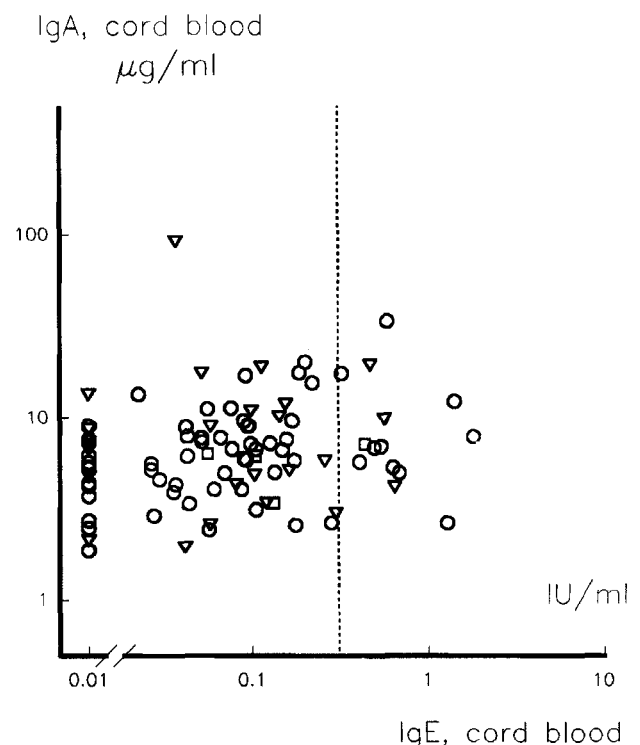


Fig. 3. Shows the IgE level compared with IgA level in cord blood. ○ = none, ▽ = single, □ = double disposition of atopy. ----- IgE = 0.3 kU/l.

or that mothers with high IgE levels at delivery are "high IgE producers", stimulating the foetus in a non-specific way, to produce IgE during the pregnancy, such that there is a drop in IgE concentration in the newborn baby (5).

The cord blood sampling was performed either by needle aspiration or by allowing the blood to run freely from the cord. We did not instruct the staff how to sample the cord blood, nor did we prescribe cleansing of the cord for maternal blood before sampling, which might diminish the risk of maternal contamination. High IgA levels or positive RAST for inhalant allergens in cord blood have been used to determine the degree of maternal contamination (12–14). Recently Lilja et al. (5) concluded that IgA determinations are of no value in determining maternal contamination of cord blood as no correlation was found between the IgE and IgA levels. Our results confirm that there is no correlation at all between levels of IgE and IgA in cord blood. We need better methods to determine a possible maternal contamination of cord blood.

Only 6 of 18 children with IgE levels above 0.3 kU/l had a history of maternal atopy. Our data do not support the hypothesis that the mother induces an IgE synthesis in the foetus, however the number of children with a maternal history of atopy is small, and we did not measure the IgE level in any of the parents.

Since the IgE level in cord blood is lower than in capillary blood, a possible explanation might be that these children are "high responders" at high risk of developing atopic disease. However, none of these children had any family history of atopy. We do not have any follow-up data, but this calls for further investigation.

Since, in general, there is good correlation between IgE in cord and capillary blood samples on the 5th day of life, one might hypothesize that capillary blood should be preferred to cord blood because there is no contamination risk from maternal blood, and children with a quick rise in IgE would also be identifiable. However there are arguments against this. The positive predictive cord blood IgE value for developing atopic disease within the first 18 months of life is 42% (5), and in capillary samples from the 5th day of life between 25–38%, with an IgE cut-off limit between 0.5–1.3 kU/l (5) for children with a maternal history of atopy. For children with a double history of atopy the positive value of capillary IgE is 60% and the negative predictive value 52% with a cut-off limit of 0.7 kU/l (6). The extra amount blood drawn is negligible, but the procedure might injure the child.

We conclude that there is good correlation between the IgE concentration in cord and capillary blood samples drawn on the 5th day of life. IgA analysis of cord blood is of no value in determining the maternal contamination of cord blood.

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