

Is thrombopenia in cord blood indicative of intra-uterine sensitization?

C. G. M. MAGNUSSON & A. L. DE WECK

Department of Clinical Immunology, Karolinska Institute and Hospital, Stockholm, Sweden and
Institute of Clinical Immunology, Inselspital, Bern, Switzerland

The relation between platelet counts (PCT) and IgE was studied in cord blood from 136 European newborns. PCT was significantly lower ($P = 0.0014$) when cord-IgE was superior to 1.20 IU/ml ($n = 29$; 245,000/ μ l) than when it was inferior to this value ($n = 107$; 284,080/ μ l) which resulted in a significant negative Spearman rank correlation between PCT and cord-IgE ($P = 0.002$; $r_s = -0.25$). A follow-up by questionnaire in 97 of the newborns revealed that those newborns who had developed definite atopy within 18 months of age had significantly ($P = 0.002$) lower PCT at birth ($n = 8$; 196,000/ μ l) than those free of atopic symptoms ($n = 61$; 286,000/ μ l). Further newborns to atopic mothers ($n = 23$; 245,000/ μ l) had significantly ($P = 0.014$) lower PCT than newborns to non-atopic mothers ($n = 74$; 286,000/ μ l). The lowest PCT was recorded when both the mother was atopic and the newborn had developed definite or probable atopy by the age of 18 months ($n = 7$; 175,000/ μ l) as compared to atopy alone in mothers ($n = 16$; 276,000/ μ l; $P = 0.005$), to atopy alone in infants ($n = 9$; 281,000/ μ l; $P = 0.005$) and to non-atopic infants of non-atopic mothers ($n = 65$; 286,000/ μ l; $P = 0.0007$). Significantly ($P = 0.03$) lower PCT amongst boys ($n = 49$; 259,000/ μ l) compared with girls ($n = 48$; 294,000/ μ l) was attributed to the higher incidence of elevated cord-IgE and infant atopy among boys. These findings were limited to PCT, since the erythrocyte count, hematocrit and hemoglobin concentration in cord blood did not significantly ($P > 0.10$) differ in any of these groups. Paternal atopy and atopy in siblings did not influence PCT, neither did maternal smoking or drug intake (progesterone and β -mimetics) during pregnancy. These data as a whole are compatible with a direct or indirect role for platelets and their mediators in immediate hypersensitivity reactions. We speculate that a low PCT in cord blood of newborns reflects an on-going intra-uterine sensitization and therefore it might be a complementary parameter to family history and cord-IgE in predicting newborns at high risk of developing atopy.

Key words: atopy; cord blood; IgE; infant; *in utero*; platelets; sensitization.

Accepted for publication 2 October 1988

It is well known that immediate hypersensitivity reactions are due to the bridging of receptor-bound IgE by allergen and a subsequent release of a variety of inflammatory mediators (8). The cells involved are mainly basophils and mast cells which have high-affinity receptors for IgE (8), and a number of mediators are presently known, e.g. histamine, prostaglandins, leukotrienes, eosinophil and neutrophil chemotactic factors (43). However, other types of cells have also been shown to bear surface receptors for IgE, though of lower affinity, e.g. lymphocytes, monocytes, eosinophils and macrophages (36).

Recently, platelets were added to the latter list and it was shown that an IgE-Fc $_{\epsilon}$ -platelet mediated interaction was protective against schistosomula infections in rats (11).

It has been known for a long time that anaphylactic shock (15, 16) and drug-associated allergies (1, 10, 38) are accompanied by a decrease in the number of circulating platelets. Further possible associations between the atopic state and low platelet counts have been proposed for patients allergic to food (2, 10, 28, 30, 32, 37), cat dander (10) and pollen allergens (10, 40). However, these studies were con-

ducted when IgE was still not discovered, and very few data concerning the relationship between IgE and platelets in atopic individuals are available. More recent reports have dealt with a defective serotonin transport (23) and a possible dysfunction of the second phase of platelet aggregation in asthmatics compared with controls, though with conflicting results (9, 25, 34, 35). However, it seems that a dysfunction in aggregation exists that correlates with elevated serum IgE levels and the presence of specific IgE (19). Moreover, evidence exists that the platelet release reaction (4, 31, 41) may be the cause of bronchoconstriction, and increased levels of plasma PF4 occur during antigen-induced bronchoconstriction in human asthmatic subjects (13). Human platelet derived factors were also shown to enhance IgE-mediated histamine release from human basophils and mast cells (14). Recent findings further strengthen the implication of platelets in both parasitic and allergic diseases (4, 5, 27).

Because of these direct and indirect relations between IgE and platelets, we thought it interesting to investigate the relationship between platelet counts (PCT) and IgE in cord blood of newborns, for whom a follow-up study of atopic symptoms had been performed at 18 months of age (20, 22). The influence of family history and of some other parameters on PCT were also evaluated.

SUBJECTS AND METHODS

We have recently reported on the assay of cord serum IgE in 288 un-selected European newborns (21) and in 190 of those have studied the predictive value of cord serum IgE above 1.20 IU/ml for subsequent development of atopy in early infancy (22). The newborns studied in this paper are an unselected part of the previous material (21, 22) and comprise all those for whom relevant parameters were available from medical records.

The platelet count in cord blood was available in a total of 136 newborns. Of these, 97 had been involved in the follow-up study at 18 months of age, performed by using a questionnaire, as described elsewhere (20, 22).

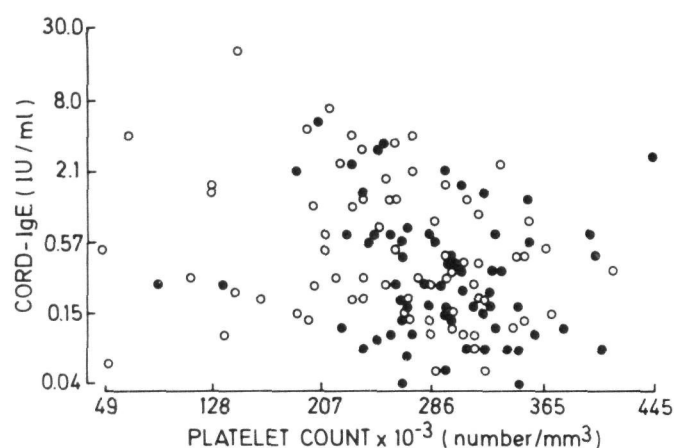


Fig. 1. Correlation between cord-IgE and platelet count in cord blood (boys = $\circ$, girls = $\bullet$). Spearman rank correlation ($n = 136$; $r_s = -0.25$; $P = 0.002$).

Briefly, the infants were classified into: A. *Definite atopics* ($n = 8$), only when very strong cumulative evidence of atopic disease was present, e.g. multiple evident atopic symptoms of eczema, urticaria, bronchial asthma or food allergy. B. *Probable atopics* ($n = 8$), if they had had at least one probable atopic sign and/or presented with recurrent infections (≥ 3 times). C. Those having *doubtful symptoms* ($n = 20$) if they had experienced occasional (≤ 2 times) isolated symptoms of doubtful etiology. D. Those having *no symptoms* of atopy ($n = 61$). Data concerning the family history of allergy and smoking, and some other parameters were also obtained in the questionnaire. Mothers and fathers were considered atopic if they reported symptoms of asthma, allergic rhinitis, eczema, urticaria or an etiology strongly suggesting a food allergy. Further details on the study population with respect to infant classification, family history, cord-IgE and its predictive value (≥ 1.20 IU/ml) are described in detail elsewhere (20, 22).

IgE and IgD in cord serum (IU/ml) was assayed in duplicate by particle counting immunoassay (PACIA) as described (21; Magnusson, in preparation). The hematological parameters in cord blood (EDTA-tubes) were obtained in a Haemalog Total (Technicon, U.S.A.) and included data obtained over an 18 months' period, which should give a random spread of possible technical errors. The platelet count (PCT) was expressed in $1000/\mu\text{l}$ of cord

Table 2

Platelet count (1000/ μ l) in cord blood of newborns followed-up at 18 months of age for atopic symptoms

Atopic symptoms	Boys			Girls			Total		
	<i>n</i>	MIFH ^a (%)	Mean ($\pm$ 1 SD)	<i>n</i>	MIFH ^a (%)	Mean ($\pm$ 1 SD)	<i>n</i>	MIFH ^a (%)	Mean ($\pm$ 1 SD)
A Definite	6	83.3	185 (84)	2	0	230 (34)	8	62.5	196 (75)
B Probable	6	16.7	281 (70)	2	50.0	251 (83)	8	25.0	273 (68)
C Doubtful	12	41.7	257 (46)	8	37.5	313 (48)	20	40.0	280 (53)
D None	25	28.0	271 (87)	36	2.8	296 (57)	61	13.1	286 (71)
A + B (Atopic)	12	50.0	233 (89)	4	25.0	241 (53)	16	43.8	235 (80)
C + D (Non-atopic)	37	32.4	267 (76)	44	9.1	299 (55)	81	19.8	284 (67)
Total	49	36.7	259* (80)	48	10.4	294* (57)	97	23.7	276 (71)
Mann-Whitney U-test:									
A vs. D			<i>P</i> = 0.021			<i>P</i> = 0.058			<i>P</i> = 0.002
A + B vs. C + D			<i>P</i> = 0.22			<i>P</i> = 0.042			<i>P</i> = 0.014
A vs. C + D			<i>P</i> = 0.030			<i>P</i> = 0.046			<i>P</i> = 0.0025

^a Incidence of positive maternal atopy. * *P* = 0.030.

PCT in cord blood and subsequent infant atopy

The differences between PCT in the four groups of infants followed up at 18 months of age for atopic symptoms (Fig. 2 and Table 2) were statistically significant by Kruskal-Wallis test (*P* = 0.008). The lowest PCT were found in cord blood of those infants who developed definite atopy (*n* = 8; 196) and the highest in those who had not developed any atopic symptoms at all (*n* = 61; 286) at the time of control follow-up (*P* = 0.002). Comparing the definite and probable atopy groups (*n* = 16; 235) to the doubtful and negative groups (*n* = 81; 284), PCT was still significantly different (*P* = 0.014). We also analysed each sex separately in the four groups (Fig. 2 and Table 2), even if the number of cases available was limited. A significant difference in PCT between Groups A and D was present for boys (*P* = 0.021) and tended to be so for girls (*P* = 0.058), whereas the significance was lost for boys when Groups A + B and C + D were compared (*P* = 0.22) but became valid for girls (*P* = 0.042). These latter relations may be related to that only two (33.3%) probable atopic boys but both probable atopic girls (100%) had elevated cord-IgE. Further, positive maternal history among boys was com-

paratively high (41.7%) in the doubtful group and low (16.7%) in the probable group, perhaps indicating that the former group hides some atopy-prone infants and the latter group some “misclassified” infants.

PCT in relation to infant and maternal atopy

Since maternal atopy appeared to influence PCT, we wondered whether mere “atopic heredity” was responsible and could explain low PCT observed in infants who developed atopy. Therefore, we compared newborns from the atopic (A + B) and non-atopic (C + D) groups and their family history of maternal atopy (Fig. 3). There was no significant difference in PCT between atopic and non-atopic infants of non-atopic mothers or between non-atopic children of atopic and non-atopic mothers (Fig. 3). However, when the mother was atopic and the newborn developed definite or probable atopy before 18 months of age, there was a significant decrease in PCT (*n* = 7; 175) compared with the other three groups (*n* = 16; 276; *P* = 0.005), (*n* = 9; 281; *P* = 0.005) and (*n* = 65; 286; *P* = 0.0007). The same pattern was observed when boys were considered alone, i.e. PCT was significantly lower (*P* < 0.025) when both the newborn

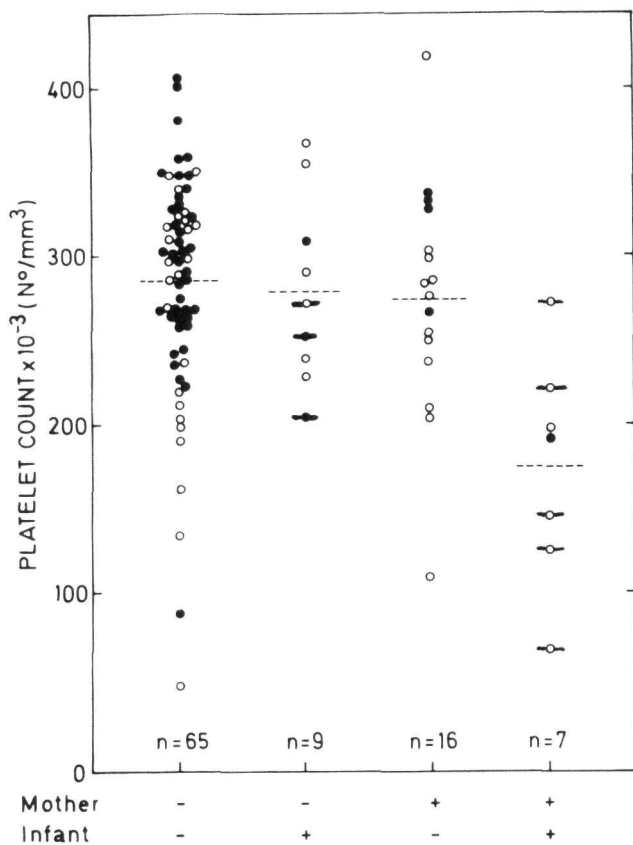


Fig. 3. Platelet count in cord blood of atopic (+) and non-atopic (-) infants to atopic (+) and non-atopic (-) mothers (boys = $\circ$, girls = $\bullet$). Those infants who developed definite atopy are also indicated (boys = $\circ$ - $\circ$, girls = $\bullet$ - $\bullet$). The horizontal bars indicate the arithmetic means.

developed atopy and the mother was atopic, compared with the other three groups (Fig. 3). The uneven distribution of girls in the four groups was not appropriate for a meaningful statistical evaluation.

Influence of gender on PCT at birth

A significant influence of gender on PCT was observed ($P = 0.007$) on the total population ($n = 136$) with boys having lower PCT ($n = 71$; 258) than girls ($n = 65$; 294). Considering only the infants for which a questionnaire was completed ($n = 97$), the gender difference ($P = 0.03$) was less pronounced (Table 2). Since we suspected this difference to be caused by the accumulation of atopic infants, we also calculated PCT for the two sexes in infants who were free of atopic symptoms at 18 month's follow-up (negative Group D; Fig. 2), in order to exclude the influence of the predominance of atopic boys. Indeed, the significance was lost ($P = 0.47$), even if boys still tended to have lower PCT ($n = 25$; 271) than girls ($n = 36$; 296). Moreover, in this study, boys had a higher incidence of maternal atopy (18/49; 36.7%) than girls (5/48; 10.4%). We suspect that a major part of the observed gender difference in PCT is due to the strong influence of the combination of maternal atopy with definite atopy and elevated cord-IgE among boys. This was further suggested by considering PCT of only those newborns having non-atopic mothers. Even if PCT tended to be lower in boys ($n = 31$; 274) than in girls ($n = 43$; 294), the difference was not significant ($P = 0.43$). Neither was there any gender-difference in PCT of newborns to atopic mothers ($P > 0.10$).

Table 3

Hematological parameters (arithmetic means $\pm$ 1 SD) in cord blood of various groups of infants

Group	Erythrocytes ($10^{12}/l$)	Hematocrit (%)	Hemoglobin (g/l)	MCV (fl)	MCH (pg)	MCHC (g/l)
Cord-IgE ≥ 1.20 IU/ml	4.5 (0.7)	45 (6.9)	153 (25)	102 (10)	34 (2.1)	334 (29)
Cord-IgE < 1.20 IU/ml	4.6 (0.5)	47 (5.0)	157 (17)	103 (6)	35 (1.7)	336 (17)
Atopic infants (A + B)	4.5 (0.5)	46 (6.4)	153 (23)	105 (9)	35 (1.2)	331 (31)
Non-atopic infants (C + D)	4.6 (0.5)	46 (4.8)	156 (18)	104 (5)	35 (1.6)	336 (16)
Definite atopic infants (A)	4.4 (1.0)	45 (7.6)	153 (30)	102 (10)	35 (1.5)	341 (44)
No infant atopy (D)	4.6 (0.6)	46 (5.4)	155 (18)	104 (6)	35 (1.6)	336 (16)
Atopic mothers	4.4 (0.5)	45 (5.4)	152 (19)	103 (5)	34 (1.5)	331 (13)
Non-atopic mothers	4.6 (0.5)	47 (5.0)	157 (18)	104 (6)	35 (1.6)	337 (20)
Boys	4.5 (0.6)	45 (5.8)	152 (19)	104 (6)	35 (1.6)	332 (14)
Girls	4.7 (0.5)	47 (4.5)	159 (18)	104 (6)	35 (1.6)	339 (22)

PCT, milk-associated problems and eczema

The PCT of infants who had experienced some kind of symptom to cow milk, e.g. vomiting, diarrhoea, eczema, aversion ($n = 15$; 272) were not different ($P = 0.81$) from those of infants without such symptoms ($n = 82$; 277), for either boys or girls.

Infants who developed definite atopic eczema had a tendency ($P = 0.10$) towards lower PCT ($n = 7$; 226) compared with infants with no such symptoms ($n = 78$; 278).

PCT and other parameters

The following parameters were found not to ($P > 0.10$) affect PCT in cord blood, even when each sex was considered separately. Smoking mothers compared with non-smoking; mothers receiving progesterone or β -mimetics during pregnancy compared with those not receiving these drugs; provoked (oxytocin) pregnancies compared with non-provoked; mothers receiving peridural anesthetic during labor compared with those without; mothers with pregnancy-associated diabetes compared with non-diabetics. Length, weight or gestational age of the newborn did not correlate with PCT (Spearman rank correlations; $n = 118$; $P \geq 0.20$).

Other hematological parameters in cord blood

To see whether the findings on PCT were not just non-specific and caused, e.g. by hemodilution during labor, other hematological parameters were also investigated. However, neither the erythrocyte count, hematocrit, hemoglobin concentration nor mean corpuscular volume (MCV), hemoglobin (MCH) and hemoglobin concentration (MCHC) were influenced ($P > 0.10$) by family history, infant atopy, gender or cord-IgE (Table 3).

DISCUSSION

It is well known that a number of factors and diseases influence PCT (6, 33, 42, 45). Keeping this in mind, as well as the relative difficulty in evaluating the atopic state of infants and their

parents by questionnaire, four major observations emerge from this study on PCT in cord blood. (i) There was significantly lower PCT in newborns with high cord-IgE compared with those with low cord-IgE, resulting in a weak but significant negative correlation between these two parameters; (ii) newborns to atopic mothers had lower PCT than those to non-atopic mothers; (iii) newborns who developed definite atopy later in infancy had lower PCT than those without any atopic symptoms, and (iv) the lowest PCT were observed when the mother was atopic and the infant developed definite atopy. In contrast, there was no such significant differences in any of the other hematological parameters investigated, suggesting that the results on PCT are not artefactual and caused, e.g., by hemodilution during parturition.

In agreement with the literature (29), we observed a mean PCT of 275 (range: 49 to 445). We attribute a major part of the observed gender-difference to a predominance of atopic boys having elevated cord-IgE and a positive maternal history (7, 22), as corroborated by statistics. Since the major findings were also statistically valid for boys alone, a possible influence of gender on our results seems excluded.

The data on PCT in cord blood reported here are in keeping with several older (37, 38, 40) and recent (4, 5, 27) reports suggesting that platelets directly or indirectly play a role in atopic diseases. Besides, a dysfunction in platelet aggregation was confined to asthmatics with a high total and specific serum IgE concentration (19), IgE-Fc $_{\epsilon}$ -receptor interactions rendered platelets cytotoxic (4, 5, 11), platelet mediators increased IgE-mediated histamine release from basophils (14) and platelet survival time *in vivo* was reduced in asthmatics (39).

Since our observations on PCT were made in cord blood, it may be assumed either that mediators produced during allergic reactions in the mother cross the placental barrier and affect fetal inflammatory cells; or that such cells, sensitized *in utero*, liberate mediators in response to allergens capable of crossing the placenta. While the first hypothesis is favored by our finding that maternal atopy influenced

PCT, the second is supported by the fact that the lowest PCT were found in those infants who had high IgE at birth and later developed definite atopy. Subclinical allergic reactions in both the mother and the fetus during late pregnancy might explain why the lowest PCT were observed when both the mother and the infant were atopic while maternal or infant atopy alone did not influence PCT. Moreover, it should be noted that most of our classified atopic infants to non-atopic mothers only developed probable disease ($n = 6$) and that the three infants who developed definite atopy had lower PCT (Fig. 3).

Although our findings might have several explanations, a speculative one is that a low PCT observed at birth in infants who later develop definite atopy reflects an on-going intrauterine sensitization. Parasitic (44), inhaled (12) and various ingested allergens (17, 24) have been implicated in possible intra-uterine sensitization and many food allergens have also been shown to cause thrombopenia in food-allergic individuals (3, 10, 18, 28, 32, 37). Moreover, Thiberge (40) showed that, for adult atopics with hay fever, asthma, conjunctivitis and skin allergy, the mean differences in PCT between acute allergic reactions and recovery were about 20,000 to 50,000/ μ l, with more striking individual differences. A similar mean decrease in PCT following antigen challenge has been reported in patients allergic to drugs and various ingested and inhaled antigens (10, 32, 38). These figures are similar to ours. We attribute the influence of maternal atopy on PCT to infant atopy and elevated cord-IgE. In cases of high PCT in the group of definite and probable atopic infants the explanation may lie in misclassification of some infants or that low PCT is transient in nature in the absence of stimulating allergen (19, 40), or because of corticosteroid medication (39). However, although cow milk has been implicated in a case of thrombopenia (3) and possible intra-uterine sensitization (26), we did not record any change in PCT of infants presenting with various symptoms to cow milk. The tendency towards lower PCT in infants manifesting eczema may indicate that sensitization to other allergens

may be involved.

We cannot entirely exclude that our results are due to drug intake other than progesterone and β -mimetics during pregnancy in atopic mothers, e.g. anti-histamines, theophylline and corticosteroids (19). However, it implies a state of drug-specific hypersensitivity with a highly specific aggregation pattern in most instances (10, 38). Besides, we found a significant difference in PCT between atopic and non-atopic infants having atopic mothers but not between atopic and non-atopic mothers having non-atopic children. In contrast, it is more likely that drugs, e.g. corticosteroids, could prevent thrombopenia by influencing platelet survival (39).

In conclusion, our data suggest a relation between a high cord serum IgE, subsequent infant atopy and low PCT in cord blood which could be an indication of an on-going sensitization *in utero*. If confirmed, a low PCT in cord blood might, besides its physiological implications, have some value, either alone or in addition to family history and cord IgE (7, 22, 26) in the prediction of atopy.

ACKNOWLEDGEMENTS

We wish to thank Prof. R. de Meyer and Dr. M. van Lierde, Les Cliniques Universitaires St Luc, Brussels, for permitting consultation of the medical records of their patients. An ICP-fellowship (CGMM) granted by the International Institute of Cellular and Molecular Pathology, University of Louvain, Brussels, and the grants from the National Association for Prevention of Asthma and Allergies, the Karolinska Institute, the Swedish Heart and Lung Foundation and the Consul Th Berghs Foundation are gratefully acknowledged.

REFERENCES

1. Ackroyd, J. F.: Allergic purpura, including purpura due to foods, drugs and infections. *Am. J. Med.* 14, 605-632, 1953.
2. Alexander, H. L. & Eyermann, C. H.: Allergic purpura. *J.A.M.A.* 92, 1029, 1929.
3. Caffrey, E. A., Sladen, G. E., Isaacs, P. E. T. & Clark, G. A.: Thrombocytopenia caused by cow's milk. *Lancet* ii, 316, 1981.
4. Capron, A., Ameisen, J. C., Joseph, M., Auriault, C., Tonnel, A. B. & Caen, J.: New functions for platelets and their pathological implications. *Int. Arch. Allergy Appl. Immunol.* 77, 107-114, 1985.
5. Capron, A., Joseph, M., Ameisen, J. C., Capron, M.,

- Pancré, V. & Auriault, C.: Platelets as effectors in immune and hypersensitivity reactions. *Int. Arch. Allergy Appl. Immunol.* 82, 307-312, 1987.
6. Cohn, J.: Thrombocytopenia in childhood: an evaluation of 433 patients. *Scand. J. Haematol.* 16, 226-240, 1976.
 7. Croner, S., Kjellman, N. I. M., Eriksson, B. & Roth, A.: IgE screening in 1701 newborn infants and the development of atopic disease during infancy. *Arch. Dis. Child.* 57, 364-368, 1982.
 8. Froese, A.: Receptors for IgE on mast cells and basophils. *Prog. Allergy* 34, 142-187, 1984.
 9. Harwell, W. B., Patterson, J. T., Lieberman, P. & Beachey, E.: Platelet aggregation in atopic and normal patients. *J. Allergy* 51, 274-284, 1973.
 10. Hoigné, R., Flückiger, J., Storck, H. & Koller, F.: Über die Bedeutung der Thrombocyten bei allergischen Vorgängen. 4. Mitteilung: Thrombocyten test "in vitro" in Fällen von medikamentöser Allergie. *Schweiz. Med. Wochenschr.* 84, 1168-1174, 1954.
 11. Joseph, M., Auriault, G., Capron, A., Vorng, H. & Viens, P.: A new function for platelets: IgE-dependent killing of schistosomes. *Nature* 303, 810-812, 1983.
 12. Kaufman, H. S.: Allergy in the newborn: skin test reactions confirmed by the Prausnitz-Küstner test at birth. *Clin. Allergy* 1, 363-367, 1971.
 13. Knauer, K. A., Lichtenstein, L. M., Franklin Adkinson, Jr., N. & Fish, J. E.: Platelet activation during antigen-induced airway reactions in asthmatic subjects. *N. Engl. J. Med.* 304, 1404-1407, 1981.
 14. Knauer, K. A., Kagey-Sobotka, A., Franklin Adkinson, Jr., N. & Lichtenstein, L. M.: Platelet augmentation of IgE dependent histamine release from human basophils and mast cells. *Int. Arch. Allergy Appl. Immunol.* 74, 29-35, 1984.
 15. Kopeloff, L. M. & Kopeloff, N.: Anaphylaxis in the rhesus monkey. I. Horse serum as an antigen. *J. Immunol.* 35, 83-99, 1939.
 16. Kopeloff, N. & Kopeloff, L. M.: Blood platelets in anaphylaxis. *J. Immunol.* 40, 471-481, 1941.
 17. Kuroume, T., Oguri, M., Matsumura, T., et al.: Milk sensitivity and soybean sensitivity in the production of eczematous manifestations in breastfed infants with particular reference to intra-uterine sensitization. *Ann. Allergy* 37, 41-46, 1976.
 18. Lavy, R.: Thrombocytopenic purpura due to *Lupinus termis* bean. *J. Allergy* 35, 386-389, 1964.
 19. Maccia, C. A., Gallagher, J. S., Ataman, G., Glueck, H. I., Brooks, S. M. & Bernstein, I. L.: Platelet thrombopathy in asthmatic patients with elevated immunoglobulin E. *J. Allergy Clin. Immunol.* 59, 101-108, 1977.
 20. Magnusson, C. G. M.: Maternal smoking influences cord serum IgE and IgD levels and increases the risk for subsequent infant allergy. *J. Allergy Clin. Immunol.* 78, 898-904, 1986.
 21. Magnusson, C. G. M. & Masson, P. L.: Immunoglobulin E assayed after pepsin digestion by an automated highly sensitive particle counting immunoassay. Application to human cord blood. *J. Allergy Clin. Immunol.* 75, 513-524, 1985.
 22. Magnusson, C. G. M.: Cord serum IgE in relation to family history and as predictor of atopic disease in early infancy. *Allergy* 43, 241-251, 1988.
 23. Malmgren, R., Grubbström, J., Olsson, P., Theorell, H., Tornling, G. & Unge, G.: Defective serotonin (5-HT) transport mechanism in platelets from patients with endogenous and allergic asthma. *Allergy* 37, 29-39, 1982.
 24. Matsumura, T., Kuroume, T., Oguri, M., et al.: Egg sensitivity and eczematous manifestations in breast-fed newborn with particular reference to intra-uterine sensitization. *Ann. Allergy* 35, 221-229, 1975.
 25. McDonald, J. R., Tan, E. M., Stevenson, D. D. & Vaughan, J. H.: Platelet aggregation in asthmatic and normal subjects. *J. Allergy* 54, 200-208, 1974.
 26. Michel, F. M., Bousquet, J., Greiller, P., Robinet-Levy, M. & Coulomb, L.: Comparison of cord blood immunoglobulin E concentrations and maternal atopy to the prediction of atopic disease in infancy. *J. Allergy Clin. Immunol.* 65, 422-430, 1980.
 27. Morley, J., Sanjar, S. & Page, C. P.: The platelet in asthma. *Lancet* ii, 1142-1144, 1984.
 28. Nilzén, Å.: The thrombocyte decrease in food allergy and the influence of ACTH theron. *Acta Dermatol. Venereol.* 33, 456-462, 1953.
 29. Oski, F. A. & Naiman, J. L.: Normal blood values in the newborn period. In: *Haematological problem in the newborn*, pp. 1-30. W. B. Saunders, Philadelphia, 1972.
 30. Osler, W.: The visceral lesions of purpura and allied conditions. *Br. Med. J.* 517-525, 1914.
 31. Page, C. P., Paul, W. & Morley, J.: Platelets and bronchospasm. *Int. Arch. Allergy Appl. Immunol.* 74, 347-350, 1984.
 32. Pohle, F. J. & Cohen, E. B.: Variations in blood platelets in allergic individuals following the ingestion of test food. *J. Lab. Clin. Med.* 32, 1395-1396, 1947.
 33. Shuper, A., Mimouni, F., Merlob, P., Zaizov, R. & Reisner, S. H.: Thrombocytopenia in small-for-gestational-age infants. *Acta Paediatr. Scand.* 72, 139-140, 1983.
 34. Solinger, A., Bernstein, I. L. & Glueck, H. I.: The effect of epinephrine on platelet aggregation in normal and atopic subjects. *J. Allergy* 51, 29-34, 1973.
 35. Solinger, A., Bernstein, I. L. & Glueck, H. I.: Platelet aggregation in asthmatic patients. *J. Allergy* 52, 318-319, 1973.
 36. Spiegelberg, H. L.: Structure and function of Fc receptors for IgE on lymphocytes, monocytes and macrophages. *Adv. Immunol.* 35, 61-88, 1984.
 37. Squier, T. L. & Madison, F. W.: Thrombocytopenia purpura due to food allergy. *J. Allergy* 8, 143-154, 1937.
 38. Storck, M., Biggliardi, P., Brenn, H. & Hoigné, R.: Über die Bedeutung der Thrombocyten bei allergischen Vorgängen. I. Mitteilung: Thrombocytenabfall in vivo nach Allergenexposition. *Schweiz. Med. Wochenschr.* 83, 692-697, 1953.
 39. Taytard, A., Guenard, M., Vuillemin, L., et al. Plate-

- let kinetics in stable atopic asthmatic patients. *Am. Rev. Respir. Dis.* 134, 983-985, 1986.
40. Thiberge, N. F.: The thrombocytes in allergy. A preliminary report. *New Orleans M. and S.* 91, 372-374, 1939.
41. Vargaftig, B. B., Lefort, J., Chignard, M. & Benveniste, J.: Platelet activating factor induces a platelet-dependent bronchoconstriction unrelated to the formation of prostaglandin derivatives. *Eur. J. Pharmacol.* 65, 185-192, 1980.
42. Walker, R. W. & Walker, W.: Idiopathic thrombocytopenia, initial illness and long term follow-up. *Arch. Dis. Child.* 59, 316-322, 1984.
43. Wasserman, S. I.: Mediators of immediate hypersensitivity. *J. Allergy Clin. Immunol.* 72, 101-115, 1983.
44. Weil, G. J., Hussain, R., Kumaraswami, V., Tripathy, S. P., Phillips, K. S. & Ottesen, E. A.: Prenatal allergic sensitization to helminth antigens in offspring of parasite-infested mothers. *J. Clin. Invest.* 71, 1124-1129, 1983.
45. Wilson, J. J., Neame, P. B. & Kelton, J. G.: Infection-induced thrombocytopenia. *Sem. Thomb. Hemostasis* 8, 217-233, 1982.

Address:

Dr. C. G. M. Magnusson

Department of Clinical Immunology

Karolinska Hospital

S-104 01 Stockholm

Sweden

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.