

Short communication

High prevalence of IgE antibodies among blood donors in Sweden and Norway

Background: Reactions after a blood transfusion could be allergic because of passive transfer of immunoglobulin E (IgE) antibodies from allergic donors.

Aims of the study: To compare spectrum and prevalence of IgE antibodies in blood donors from Sweden and Norway.

Methods: Using the ImmunoCAP method, serum samples from 1002 blood donors from Sweden and 500 from Norway were analysed for IgE antibodies to common inhalant and food allergens and allergens common in a hospital environment, such as penicilloyl G and latex.

Results: As many as 23.6–27.3% of the donors had IgE antibodies to at least one of the 14 allergens tested. Of these 6.8–16.7% had extremely high concentrations, i.e. $> 35 \text{ kU}_A/\text{l}$ corresponding to 100 times the cut-off for a positive allergy test. Most donors were sensitized to pollens, dander and mite but several had very high levels of IgE antibodies to penicilloyl G, latex and peanut. The pattern of sensitizing allergens differed between Sweden and Norway.

Conclusions: High serum levels of IgE antibodies to various allergens are common among blood donors and the degree of sensitization and spectrum of involved allergen varies between geographical regions. Present routines to identify IgE sensitized, potential risk, donors are not satisfactory; the sensitivity of selection procedures is about 25%.

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The blood transfusion speciality has, for decades, been aware of the risk of transferring an allergic reaction by transfusion (1) and tried, through questionnaires, to identify and eliminate potentially hazardous, allergic blood donors. However, this selection has not been very successful. In a previous study, the prevalence of immunoglobulin E (IgE)-sensitization to common inhalant and food allergens, among donors claiming not to be allergic, was 12.3% (2). Several of these sensitized donors had high concentrations of IgE antibodies and thus the potential to passively sensitize the blood recipient (3).

The aim of this study was to compare the prevalence of IgE antibodies to common inhalant and food allergens among blood donors in Sweden and Norway and to investigate if there had been any change in Sweden over the last 12 years. In addition, the presence of IgE antibodies to penicilloyl G, suxamethonium and latex was evaluated.

Material and methods

Blood donors

At the Karolinska University Hospital (Karolinska), Solna, Sweden, approximately 10 000 blood donors are registered. From 1002 consecutive donors blood was collected and serum stored at -20°C pending analyses. The donors were asked to fill in the same question on allergy as they did when volunteering: 'Do you suffer from a severe allergy or have you experienced a severe reaction to drugs or foods?' The study in Sweden was approved by the Ethics Committee of the Karolinska Institute and all participating donors gave his/her consent to participate in the study.

At Haukeland University Hospital, Bergen, Norway samples were collected from 500 blood donors using donor selection criteria comparable with the ones at Karolinska. The donors were asked to fill in a questionnaire with two questions related to allergy: 'Are you allergic?' and 'What kind of allergy?' The participants gave their informed consent and blood sampling was approved by the Regional Committee for Medical Research Ethics, Western Norway.

IgE assays

Each serum sample was tested for IgE antibodies to a mix of common inhalant allergens, Phadiatop [*Dermatophagoides pteronyssinus* (d1), *D. farinae* (d2), birch (t3), timothy (g6), mugwort (w6), cat (e1), dog (e2), horse (e3) and *Cladosporium* (m2)], a mix of common food allergens, fx5 [cow's milk (f2), egg white (f1), cod fish (f4), soya bean (f14), peanut (f13), wheat flour (f4)], and a special allergen mix with hospital environment relevant allergens [penicilloyl G (c1), suxamethonium (Rc202), latex (k82)] and hazel nut (f17). Analyses were performed by ImmunoCAPTM (Pharmacia Diagnostics AB, Uppsala, Sweden) following the instruction of the manufacturer. A serum with a positive Phadiatop (>0.35 kU_A/l) was tested for IgE antibodies to timothy (g6), birch (t3), cat (e1) and all Norwegian and the first 500 Swedish sera also to *D. pteronyssinus* (d1). A positive test to any of the other two mixes was followed by testing to all allergens included.

Statistical methods

The chi-square test was used for statistical analysis of differences in distribution between populations.

Results

IgE antibodies to allergen mixes

In total 34.0% of Swedish and 29.6% of Norwegian donors were sensitized to at least one allergen included in

the panels. As many as 26.0% of the donors in Sweden and 25.2% in Norway were IgE sensitized to common inhalant allergens (Table 1). High concentrations, >3.5 kU_A/l, which corresponds to 10 times the cut-off value, were found in 14.6% and 10.6%, respectively. In addition, 3.9% and 3.0%, respectively, were positive to common food allergens and 4.1% and 1.4% to the special allergen mix (Table 1).

IgE antibodies to individual allergens

Sera with a positive Phadiatop were tested against four important allergens in this mix. Positive tests to timothy, birch and cat were equally common in Sweden and Norway (Table 2). However, a significantly ($P < 0.01$) higher percentage in Norway were positive to mite, 11.6% vs 6.6% (Table 2). Interestingly, a significantly ($P < 0.001$) higher proportion of Phadiatop-positive donors in Norway, 12.7% and 1.9%, respectively, was negative to all four individual allergens.

Of the Phadiatop-positive donors 30–50% had high levels of IgE antibodies to individual inhalant allergens (Table 2). Extremely high concentrations, i.e. >35 kU_A/l, were found in 3–10% of the samples and one donor had an extraordinarily high value to cat, 249 kU_A/l.

Table 1. Number of samples positive to Phadiatop, food (fx5) and special allergen mixtures grouped according to IgE antibody concentration range

IgE antibody, range (kU _A /l)	Phadiatop		Food mixture		Special allergen mixture	
	SE	NO	SE	NO	SE	NO
0.35–1.0	43 (16.5)	37 (29.4)	25 (64.1)	15 (100)	29 (70.7)	4 (57.1)
1.1–3.5	72 (27.6)	36 (28.6)	11 (28.2)	0	10 (24.4)	2 (28.6)
3.6–10.0	71 (27.2)	25 (19.8)	0	0	2 (4.9)	0
10.1–35.0	57 (21.8)	25 (19.8)	1 (2.6)	0	0	1 (14.3)
35.1–100	16 (6.1)	3 (2.4)	2 (5.1)	0	0	0
>100	2 (0.8)	0	0	0	0	0
Total	261 (26.0)	126 (25.2)	39 (3.9)	15 (3.0)	41 (4.1)	7 (1.4)

The percentage of positive tests relative to the number of positive tests for the whole group is given in brackets. The total number of positive tests is also given, in brackets in percentage of number of samples screened; 1002 in Sweden (SE) and 500 in Norway (NO).

Table 2. Serum samples from donors positive to Phadiatop, 261 in Sweden and 126 in Norway, were re-tested against the four most important individual allergens of the mix

IgE antibody, range (kU _A /l)	Timothy		Birch		Cat		Mite	
	SE	NO	SE	NO	SE	NO	SE	NO
0.35–1.0	37 (23.4)	7 (11.9)	24 (17.3)	17 (26.6)	29 (31.5)	9 (33.3)	14 (42.4)	20 (34.5)
1.1–3.5	28 (17.7)	21 (35.6)	31 (22.3)	10 (15.6)	32 (34.8)	9 (33.3)	9 (27.3)	18 (31.0)
3.6–10.0	31 (19.6)	16 (27.1)	32 (23.1)	24 (37.5)	19 (20.7)	4 (14.8)	5 (15.2)	13 (22.4)
10.1–35.0	48 (30.4)	11 (18.6)	38 (27.3)	8 (12.5)	9 (9.8)	5 (18.5)	4 (12.1)	6 (10.3)
35.1–100	12 (7.6)	4 (6.8)	9 (6.5)	5 (7.8)	2 (2.2)	0	1 (3.0)	1 (1.7)
>100	2 (1.3)	0	5 (3.6)	0	1 (1.1)	0	0	0
Total	158 (60.5)	59 (46.8)	139 (53.3)	64 (50.8)	92 (35.2)	27 (21.4)	33 (6.6)	58 (11.6)

The distribution of positive tests thus found to timothy (g6), birch (t3), cat (e1) and mite (d1) are given. Please note that a serum may be positive to several allergens. The numbers of positive tests at each IgE antibody level interval are given in absolute numbers and, in brackets, in percentage of number of positive to that allergen. Total numbers are given, in brackets in percentage of Phadiatop-positive (see Table 1).

As many as 111 food-positive tests were found among the Swedish donors compared with significantly ($P < 0.001$) fewer, 11, among the Norwegian (Tables 3 and 4). However, only 3.9% and 3.0%, respectively, were sensitized (Table 1) and the IgE antibody levels were usually low, i.e. $< 1.0 \text{ kU}_A/\text{l}$. However, 26.1% of the Swedish sera had high levels to peanut (Table 3), four of them are very high ($> 10 \text{ kU}_A/\text{l}$).

Significantly ($P < 0.001$) more of the Swedish, 4.1%, than Norwegian, 1.4%, donors were sensitized to the special allergen mix (Table 1). Two Norwegian sera were low to moderately positive to suxamethonium, but no one among the Swedish samples (Table 4), while latex-positive sera were significantly ($P < 0.001$) more common in Sweden, 2.6%, than in Norway 0.2%. Two donors in Sweden and two in Norway had IgE antibodies to penicilloyl G and one of the Norwegian samples had a very high level ($17 \text{ kU}_A/\text{l}$).

Of the donors in Sweden 27.3% had IgE antibodies to at least one allergen compared with 23.6% in Norway. High levels, $> 3.5 \text{ kU}_A/\text{l}$, were found in 15.3% in Sweden but significantly ($P < 0.005$) less often, 11.4%, in Norway. Extremely high, $> 35 \text{ kU}_A/\text{l}$, concentrations were found in 2.4% and 1.6%, respectively.

Allergic disease

The question about allergy in the routine questionnaire was answered with a 'Yes' or a 'Yes ?' by 10.4% of Swedish and 22.7% of Norwegian donors and they were classified as allergic. Allergy was combined with a positive Phadiatop test in 23.4% and with a negative test in 5.8% sera in Sweden and in 60.3% and 9.9%, respectively, in Norway. Of the allegedly asymptomatic donors 23.6% of the Swedish and 13.0% of the Norwegian were sensitized.

Discussion

Because an IgE sensitization can be transferred by blood transfusion (3) blood donors should not have IgE antibodies to allergens that the recipient could be exposed to. However, present routines based on questionnaires leave a high proportion sensitized donors undetected. In 1990, the prevalence in Sweden was found to be 23.1% (2) and among those stating that they were not allergic, 12.3%. In the present study, 27.3% in Sweden and 23.6% in Norway had IgE antibodies to at least one allergen. In

Table 3. All serum samples from donors positive to the food mix, 39 in Sweden and 15 in Norway, were re-tested to the individual allergens of the mix: peanut (f13), soya bean (f14), egg white (f1), cow's milk (f2), cod fish (f4) and wheat flour (f4)

IgE antibody, range (kU_A/l)	Peanut		Soya bean		Egg white		Cow's milk		Cod fish		Wheat flour	
	SE	NO	SE	NO	SE	NO	SE	NO	SE	NO	SE	NO
0.35–1.0	11 (47.8)	2 (66.7)	14 (70)	0	5 (100)	3 (100)	6 (85.7)	0	0	0	10 (50)	1 (50)
1.1–3.5	6 (26.1)	1 (33.3)	6 (30)	0	0	0	1 (14.3)	0	1 (100)	0	9 (45)	1 (50)
3.6–10.0	2 (8.7)	0	0	0	0	0	0	0	0	0	1 (5)	0
10.1–35.0	3 (13.0)	0	0	0	0	0	0	0	0	0	0	0
35.1–100	1 (4.3)	0	0	0	0	0	0	0	0	0	0	0
>100	0	0	0	0	0	0	0	0	0	0	0	0
Total	23 (58.9)	3 (17.6)	20 (51.3)	0	5 (12.8)	3 (17.6)	7 (17.9)	0	1 (2.6)	0	20 (51.3)	2 (11.8)

Please note that a serum may be positive to several allergens. The numbers of positive tests at each IgE antibody level interval are given in absolute numbers and, in brackets, in percentage of number of positive to that allergen. Total numbers are given, in brackets in percentage of food mix positive (see Table 1).

Table 4. All serum samples from donors positive to the special allergen mix, 41 in Sweden and seven in Norway, were re-tested against all individual allergens in the mix: penicilloyl G (c1), suxamethonium (Rc202), latex (k82) and hazel nut (f17)

IgE antibody, range (kU_A/l)	Penicilloyl G		Suxamethonium		Latex		Hazel nut	
	SE	NO	SE	NO	SE	NO	SE	NO
0.35–1.0	2 (100)	1 (50)	0	1 (50)	15 (57.7)	0	20 (57.1)	2 (66.7)
1.1–3.5	0	0	0	1 (50)	9 (34.6)	1 (100)	12 (34.3)	1 (33.3)
3.6–10.0	0	0	0	0	1 (3.9)	0	3 (8.6)	0
10.1–35.0	0	1 (50)	0	0	1 (3.9)	0	0	0
35.1–100	0	0	0	0	0	0	0	0
>100	0	0	0	0	0	0	0	0
Total	2 (4.9)	2 (28.6)	0	2 (28.6)	26 (63.4)	1 (14.3)	35 (49.3)	3 (4.3)

Please note that a serum may be positive to several allergens. The numbers of positive tests at each IgE antibody level interval are given in absolute numbers and, in brackets, in percentage of number of positive to that allergen. Total numbers are given, in brackets in percentage of special allergen mix positive (see Table 1).

addition, 12.7% of the Phadiatop-positive Norwegian donors were negative to the four tested individual allergens indicating other specificities.

When comparing sensitization to the individual allergens with corresponding data from 1990 essentially the same percentage of samples with moderately to high levels, $> 3.5 \text{ kU}_A/\text{l}$, of IgE antibodies was found.

In this study, the donors were screened for IgE antibodies (4) to inhalant allergens (Phadiatop), common food allergens ($\times 5$) and special allergens expected to be present in the hospital environment. The allergens most often causing sensitization differed in Sweden and Norway. Although 14–16% in Sweden and 12–13% in Norway were sensitized to pollens there was a significant difference for house dust mite; 6.6% in Sweden compared with 11.6% Norway supporting geographical differences in allergen exposure.

The IgE antibodies to foods were less common in Norway, 2.2%, compared with Sweden, 11.1%, although, in most cases the concentrations were low-to-moderate. One exception was peanut sensitization, which in Sweden has become quite common, 2.3%, but more importantly as many as 26.1% of the peanut-positive donors had high levels of IgE antibodies; four of them actually had very high levels (20–50 kU_A/l).

The IgE sensitization to drugs was not common, but even the single, Norwegian donor with the very high level of IgE antibodies to penicilloyl G, 17 kU_A/l , is most alarming. It is interesting that no donor in Sweden was IgE sensitized to suxamethonium while in Norway, two had low-to-moderate IgE antibody levels. Severe anaphylaxis to neuromuscular blocking agents, e.g. suxamethonium, has been reported during general anaesthesia (5) and such reactions are more common in Norway than in Sweden (6).

Transfusion of blood with moderate-to-high amounts of IgE antibodies leads to IgE-sensitized basophils and mast cells that will stay sensitized for weeks (3). Upon allergen exposure an IgE-mediated allergic reaction ranking from mild skin urticaria to severe anaphylaxis can develop. Typical risk allergens in the hospital

environment are, e.g. drugs-like penicillin and suxamethonium, latex and basic foods-like hen's egg and cow's milk. At home cat dander, house dust mites, snacks-like peanuts and hazel nuts and outdoor allergens-like pollens, will represent a risk.

If the donor IgE antibody threshold for blood transfusion was to be set at 3.5 kU_A/l , it would have the consequence that 15% of Swedish and 11% of Norwegian donors should not give blood for transfusion. This low threshold could be restricted to allergens within the hospital environment while for allergens at home a more liberal threshold, e.g. 10 kU_A/l , might be acceptable. With that threshold less donors, but significantly more Swedish (9.8%), than Norwegian (6.4%), would have been excluded (Table 1).

In conclusion, this study confirms that high levels of IgE antibodies are common among blood donors but that the degree and specificity of sensitization may vary between geographical regions. It also supports previous reports that the routines of transfusion service aimed at identifying allergic donors with potentially harmful levels of IgE antibodies have a low sensitivity. To avoid potentially dangerous passive IgE sensitizations it is recommended that each donor is tested, using a reliable immunoassay, for specificity and concentration of IgE antibodies to risk allergens. It should be noted that questionnaires, even professionally taken case histories (7) and skin tests (8) cannot be used to reliably detect IgE-sensitized donors.

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References

1. Ramirez MA. Horse asthma following blood transfusion. *JAMA* 1919;**73**:984.
2. Stern A, van Hage-Hamsten M, Sondell K, Johansson SGO. Is allergy screening of blood donors necessary? *Vox Sang* 1995;**69**:114–119.
3. Johansson SGO, Nopp A, van Hage M, Olofsson N, Lundahl J, Wehlin L et al. Passive IgE-sensitization by blood transfusion. *Allergy* 2005;**60**:1192–1199.
4. Wide L, Bennich H, Johansson SGO. Diagnosis of allergy by an in-vitro test for allergen antibodies. *Lancet* 1967;**2**:1105–1107.
5. Mertes P-M, Laxenaire MC. Adverse reactions to neuromuscular blocking agents. *Curr Allergy Asthma Rep* 2004;**4**:7–16.
6. Florvaag E, Johansson SGO, Öman H, Venemalm L, Degerbeck F, Dybendal T et al. Prevalence of IgE antibodies to morphine. Relation to the high and low incidences of NMBA anaphylaxis in Norway and Sweden, respectively. *Acta Anaesthesiol Scand* 2005;**49**:437–444.
7. Brock Williams P, Ahlstedt S, Barnes JH, Söderström L, Portnoy J. Are our impressions of allergy test performances correct? *Ann Allergy Asthma Immunol* 2003;**91**:26–33.
8. Wood RA, Phipatanakul W, Hamilton R, Eggelston PA. A comparison of skin prick tests, intradermal skin tests, and RASTs in the diagnosis of cat allergy. *J Allergy Clin Immunol* 1999;**103**:773–779.