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Association of fatty acids in serum phospholipids with hay fever, specific and total immunoglobulin E

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The dietary intake of certain fatty acids might contribute to the development of allergic diseases such as hay fever and asthma. We investigated the association between the concentrations of fifteen fatty acids in serum phospholipids, as a marker of dietary intake and metabolism, and hay fever, allergic sensitisation and total IgE in adults. Data from a population-based cross-sectional study on respiratory health, including the measurement of fatty acids in the serum phospholipids of 740 adults between 20 and 64 years of age, were analysed. Positive associations were found between hay fever and arachidonic acid, and allergic sensitisation and oleic acid. No other fatty acids showed any association with hay fever or allergic sensitisation. Elevated levels of total IgE were not related to fatty acids. Concentrations of long-chain *n*-3 fatty acids, *trans* fatty acids or saturated fatty acids in serum phospholipids were not associated with allergic diseases in adults in this study. The present result on the association between hay fever and arachidonic acid is consistent with current hypotheses but warrants further research.

Allergic rhinitis: Sensitisation: Total IgE: Fatty acids: Phospholipids: European Community Respiratory Health Survey

The causes underlying the rising prevalence of allergic diseases such as asthma and hay fever in developed countries over the past three decades are still unknown. Because this increase in allergic diseases has coincided with large changes in environmental factors like air pollution or nutrition, these factors may be linked to its aetiology. In particular, the altered consumption of long-chain PUFAs was suggested to be linked with the rising prevalence of allergic diseases. Over the past few decades, the consumption of the *n*-6 fatty acid linoleic acid (18 : 2*n*-6) and of *trans* fatty acids rose, whereas the consumption of polyunsaturated *n*-3 fatty acids and saturated fatty acids fell, in Western countries (Sanders, 2000; Simopoulos, 2002).

Linoleic acid is a precursor of arachidonic acid, which can be converted to the pro-inflammatory eicosanoids leukotriene B_4 and prostaglandin E_2. Prostaglandin E_2 may shift the balance of T-helper cells from type 1 to type 2 and may thus lead to an enhanced production of immunoglobulin E (IgE) from B-cells (Seaton *et al.* 1994; Black, 1999). In contrast, eicosanoids derived from the *n*-3 fatty acid eicosapentaenoic acid (EPA) can down regulate the production of prostaglandin E_2 (Kankaanpää *et al.* 1999). It has been hypothesised that an increased consumption of linoleic acid in the diet results in an enhanced production of arachidonic acid-derived eicosanoids, while eicosanoids derived from EPA are produced in smaller quantities (Black & Sharpe, 1997).

Trans fatty acids in human nutrition are derived from the industrial process of the catalytic hydrogenation of vegetable oils for food manufacturing and appear in dairy fat because of ruminant activity (Larqué *et al.* 2001; Mozaffarian *et al.* 2004). In Germany, 79 % of *trans* fatty acids in 1995 were derived from natural animal sources (Hulshof *et al.* 1999), particularly butter (49·6 %) and cheese (14·0 %). A possible link between *trans* fatty acids and allergy is that they appear to impair the desaturation of linoleic acid and α-linolenic acid to their long-chain derivatives (Koletzko, 1992; Decsi & Koletzko, 1995).

The hypotheses on the influence of altered fatty acid consumption on allergic diseases are an increase in the ratio of *n*-6 : *n*-3 fatty acids, the contribution of single fatty acids and an altered fatty acid metabolism, for example a lack of Δ-6 fatty acid desaturase.

No substantial association between the ratio of ingested *n*-6 and *n*-3 fatty acids and hay fever or sensitisation was found in two recently published studies (Nagel *et al.* 2003; Trak-Fellermeier *et al.* 2004). In a previous paper using these data, we reported no association between the *n*-6 : *n*-3 ratio in serum phospholipids and hay fever or allergic sensitisation (Kompauer *et al.* 2004),

Abbreviation: EPA, eicosapentaenoic acid; IgE, immunoglobulin E.

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which is consistent with an Australian study on asthma and atopy (Woods *et al.* 2004). In this paper, we focus on the contribution of single fatty acids to hay fever, allergic sensitisation and the concentration of total IgE in serum, and use the concentration of fatty acids in serum phospholipids as a marker of intake and subsequent metabolism.

Methods

Study subjects

The present study is based on a sample from one of the two surveys conducted in Erfurt, East Germany as part of the European Community Respiratory Health Survey. This survey was conducted in adults aged 20–64 years in 1991–92. The study design and population sampling are described in detail elsewhere (Burney *et al.* 1994; Nowak *et al.* 1996). In brief, a total of 1282 participants answered the main questionnaire, and blood samples were drawn from 1258 participants for analysis of specific and total IgE. A serum sample was also stored at −80°C for later analyses. Additionally, a subset of the participants was asked to participate in a dietary survey, for which they filled in 3 d weighted records on their diet (Trak-Fellermeier *et al.* 2004). From this subset, unthawed serum samples were still available for 740 participants (313 women and 427 men). For the present study, these samples were used for the assessment of fatty acids in their serum phospholipids.

Questionnaire data and blood tests

Participants who answered 'Yes' to the question 'Do you have nasal allergies, including hay fever?' were categorised as participants who suffered from hay fever. Therefore subjects with both seasonal and perennial allergic rhinitis were included as 'hay fever' subjects as in other European Community Respiratory Health Survey papers.

Allergic sensitisation to common aeroallergens (house dust mite *Dermatophagoides pteronyssinus*, grass pollen, cat, *Cladosporium* and birch pollen as a local allergen in northern Europe) was assessed by specific serum IgE measurement, using the Pharmacia CAP System (Pharmacia Diagnostics, Uppsala, Sweden). Subjects with at least one specific IgE $\geq$ 0·7 kU/l was categorised as sensitised. We did not analyse asthma as an outcome variable, because only eighteen participants answered 'Yes' to the question 'Have you ever had asthma?'

The Ethics Committee of the Medical School, Erfurt, East Germany approved the study.

Analysis of fatty acids

Serum was kept frozen at −80°C until analysis in 2003 and was never thawed before measurement of fatty acids. Serum lipids were extracted with hexane–isopropanol (3:2 v/v). Phospholipids were isolated by TLC: phospholipids, triglycerides, cholesterol esters and nonesterified fatty acids were isolated by development of the plates in n-heptane-diisopropylether-glacial acetic acid (60:40:3, v/v/v) and fatty acid methyl esters were obtained by acid-catalysed trans-esterification in methanol. Methyl esters were extracted into hexane and frozen until analysis in a gas chromatograph: Hewlett Packard 5890 series II gas chromatograph (Hewlett Packard, Waldbronn, Germany) (Kolarovic & Fournier, 1986). In total, thirty-six fatty acids were measured, and the results were expressed as percentages of the total fatty acids in serum phospholipids.

Statistical analysis

From all thirty-six fatty acids analysed, we chose fifteen to assess the association with hay fever and allergic sensitisation, and eight to assess the association with total IgE in serum. We selected palmitic and stearic acids as a marker of saturated fatty acids in serum phospholipids. The monounsaturated fatty acids palmitoleic acid, oleic acid and *trans*-18 : 1 (*trans* 9, *trans* 11 combined) were chosen because they were associated with hay fever and allergic sensitisation in other studies (Weiland *et al.* 1999; Nagel *et al.* 2003; Trak-Fellermeier *et al.* 2004). Linoleic acid and its desaturation and elongation products were chosen because eicosanoids derived from the *n*-6 fatty acid arachidonic acid might promote allergic diseases, whereas eicosanoids derived from the *n*-3 fatty acid EPA might have a beneficial effect. All fatty acid values were normally distributed except for EPA, from which we extracted the square root to reach normal distribution.

Differences in the prevalence of allergic sensitisation or hay fever between women and men were assessed by the χ^2 test. The association between the concentration of certain fatty acids in serum phospholipids and allergic sensitisation or hay fever was assessed by using logistic regression models. Fatty acid values were divided into quartiles. Odds ratios were adjusted for sex, age group, BMI, education, smoking status and total energy intake. Additionally, we conducted a sex-stratified analysis for certain fatty acids as a sensitivity analysis.

Differences in total IgE in serum between the sexes were assessed using the Wilcoxon test. Because IgE values differed significantly between sexes, we applied only sex-stratified analyses. Values of total IgE were strongly skewed to the right and were therefore log-transformed to normalise the distribution. The association between total IgE and fatty acids was expressed as means ratios with 95 % CI. Means ratios were adjusted for age group, BMI, education, smoking status and total energy intake.

We did not adjust for a family history of atopy because this confounder showed no effect on the point estimates, and many participants were not aware of the atopic status of their parents, who were born long before 1950.

SAS version 8.2 (SAS Institute, Cary, NC, USA) was used for all calculations.

Results

Table 1 shows the basic characteristics of the study population included in this analysis. No statistically significant sex differences were observed in the prevalence of hay fever or allergic sensitisation assessed as at least one specific IgE $\geq$ 0·7 kU/l.

Total IgE in serum differed significantly between the sexes ($P<0{\cdot}0001$) with a geometric mean of 28·7 (95 % CI 24·5, 33·5) kU/l in women and 50·8 (95 % CI 44·4, 58·1) kU/l in men.

The largest proportion of fatty acids in the serum phospholipids were saturated (43·9 %), followed by *n*-6 polyunsaturated (34·5 %), monounsaturated (14·3 %) and *n*-3 polyunsaturated (6·2 %) fatty acids (Table 2).

Concerning the concentrations of single fatty acids, palmitic acid 16 : 0 formed the largest proportion, with 26·9 %, followed

Table 1. Characteristics of the study population

	Total (*n* 739)		Women (*n* 312)		Men (*n* 427)	
	Mean	SD	Mean	SD	Mean	SD
Hay fever* (%)	10·3		11·9		9·1	
Allergic sensitisation† (%)	22·9		22·8		23·0	
Age (years)	41·5	12·3	40·0	12·0	42·7	12·3
BMI	25·5	4·0	24·9	4·4	25·9	3·7
Energy intake (kcal/d)	2225	620	1837	436	2509	579
Smoking status (%)						
Never smokers	40·2		52·6		31·2	
Ex-smokers	27·7		19·5		33·7	
Current smokers	32·1		27·9		35·1	
Educational level (%)						
High	46·0		44·0		47·4	
Medium	32·4		34·1		31·2	
Low	21·6		21·9		21·4	

* Defined as answering 'Yes' to the question 'Do you have nasal allergies, including hay fever?'
† Defined as at least one specific IgE ≥ 0·7 kU/l.

by linoleic acid 18 : 2*n*-6 (20·2 %), arachidonic acid 20 : 4*n*-6 (9·6 %) and oleic acid 18 : 1*n*-9 (9·5 %) as shown in Table 2.

Table 3 shows adjusted odds ratios and corresponding 95 % CI for the association between the fifteen selected fatty acids in serum phospholipids and hay fever in the total population. Arachidonic acid showed the strongest association with hay fever. Odds ratios were 3·85 (95 % CI 1·67, 8·88) for the second, 2·54 (95 % CI 1·05, 6·11) for the third and 3·27 (95 % CI 1·39, 7·69) for the fourth quartile (Table 3). Similar associations were found for both sexes when the data were analysed in a sex-specific manner (unpublished results). We also observed a tendency for a positive association between docosahexaenoic acid and hay fever, but this was not significant.

Table 4 shows adjusted odds ratios and corresponding 95 % CI for the association between the fifteen selected fatty acids in serum phospholipids and allergic sensitisation in the total population. Oleic acid was positively associated with allergic sensitisation, but this was only significant in the third quartile with an odds ratio 2·03 (95 % CI 1·20, 3·43).

No consistent association was observed between the other measured fatty acids in serum phospholipids and allergic rhinitis or sensitisation (Tables 3 and 4).

Table 2. Fatty acid composition (%) in serum phospholipids of 739 adults

	Total (*n* 739)		Women (*n* 312)		Men (*n* 427)	
Fatty acid	Mean	SD	Mean	SD	Mean	SD
Saturated						
Palmitic acid (16 : 0)	26·86	1·72	27·33	1·64	26·52	1·70
Stearic acid (18 : 0)	13·42	1·36	13·05	1·48	13·70	1·20
Sum of saturated fatty acids*	43·88	1·63	43·82	1·04	43·93	1·95
Monounsaturated						
Palmitoleic acid (16 : 1*n*-7)	0·53	0·23	0·50	0·19	0·55	0·25
Oleic acid (18 : 1*n*-9)	9·48	1·27	9·32	1·06	9·60	1·40
trans-18 : 1	0·36	0·15	0·36	0·14	0·35	0·16
Sum of monounsaturated fatty acids†	14·29	1·49	14·01	1·18	14·49	1·65
n-6 Series polyunsaturated						
Linoleic acid (18 : 2*n*-6)	20·23	2·69	20·51	2·62	20·03	2·73
γ-Linolenic acid (18 : 3*n*-6)	0·10	0·04	0·09	0·04	0·11	0·04
Dihomo-γ-linolenic acid (20 : 3*n*-6)	2·87	0·59	2·93	2·86	2·82	2·76
Arachidonic acid (20 : 4*n*-6)	9·61	1·50	9·44	1·43	9·73	1·55
Adrenic acid (22 : 4*n*-6)	0·34	0·07	0·32	0·06	0·35	0·07
n-6-Docosapentaenoic acid (22 : 5*n*-6)	0·24	0·14	0·26	0·12	0·22	0·20
Sum of *n*-6 fatty acids‡	34·47	2·35	34·66	2·06	34·33	2·54
n-3 Series polyunsaturated						
α-Linolenic acid (18 : 3*n*-3)	0·18	0·06	0·19	0·06	0·18	0·06
Eicosapentaenoic acid (20 : 5*n*-3)	1·09	0·59	1·03	0·59	1·13	0·59
n-3-Docosapentaenoic acid (22 : 5*n*-3)	0·96	0·21	0·84	0·21	1·04	0·17
Docosahexaenoic acid (22 : 6*n*-3)	3·85	0·93	4·05	0·91	3·71	0·93
Sum of *n*-3 fatty acids§	6·22	1·43	6·25	1·43	6·19	1·44

* Sum of saturated fatty acids 14 : 0 + 16 : 0 + 18 : 0 + 20 : 0 + 22 : 0 + 24 : 0.
† Sum of monounsaturated fatty acids 16 : 1*n*-7 + 18 : 1*n*-7 + 18 : 1*n*-9 + 20 : 1*n*-9 + 22 : 1*n*-9 + 24 : 1*n*-9.
‡ Sum of *n*-6 fatty acids (18 : 2*n*-6 + 18 : 3*n*-6 + 20 : 2*n*-6 + 20 : 3*n*-6 + 20 : 4*n*-6 + 22 : 2*n*-6 + 22 : 4*n*-6 + 22 : 5*n*-6) divided by total fatty acids.
§ Sum of *n*-3 fatty acids (18 : 3*n*-3 + 18 : 4*n*-3 + 20 : 3*n*-3 + 20 : 5*n*-3 + 22 : 5*n*-3 + 22 : 6*n*-3) divided by total fatty acids.

Table 3. Adjusted odds ratios and corresponding 95 % CI for the association between selected fatty acids in serum phospholipids (%) and hay fever* (*n* 737)

	Adjusted odds ratio (95 % CI)†		
	2nd quartile‡	3rd quartile‡	4th quartile‡
Fatty acid			
Saturated			
Palmitic acid (16 : 0)	0·84 (0·43–1·63)	0·63 (0·31–1·28)	0·60 (0·29–1·25)
Stearic acid (18 : 0)	1·23 (0·61–2·48)	0·96 (0·44–2·08)	1·48 (0·72–3·04)
Monounsaturated			
Palmitoleic acid (16 : 1*n*-7)	0·80 (0·41–1·55)	0·75 (0·38–1·48)	0·78 (0·38–1·59)
Oleic acid (18 : 1*n*-9)	1·62 (0·85–3·10)	0·95 (0·47–1·91)	0·73 (0·33–1·60)
trans-18 : 1	0·89 (0·43–1·84)	1·56 (0·81–3·01)	0·77 (0·36–1·63)
n-6 Series polyunsaturated			
Linoleic acid (18 : 2*n*-6)	0·64 (0·29–1·37)	0·91 (0·44–1·87)	1·33 (0·66–2·67)
γ-Linolenic acid (18 : 3*n*-6)	1·24 (0·63–2·45)	0·94 (0·45–1·97)	1·41 (0·67–2·98)
Dihomo-γ-linolenic acid (20 : 3*n*-6)	0·92 (0·45–1·86)	1·19 (0·60–2·34)	1·25 (0·61–2·55)
Arachidonic acid (20 : 4*n*-6)	3·85 (1·67–8·88)	2·54 (1·05–6·11)	3·27 (1·39–7·69)
Docosatetraenoic acid (22 : 4*n*-6)	1·01 (0·51–2·00)	1·00 (0·50–2·00)	1·04 (0·51–2·11)
n-6-Docosapentaenoic acid (22 : 5*n*-6)	1·57 (0·79–3·11)	1·09 (0·53–2·26)	0·99 (0·47–2·09)
n-3 Series polyunsaturated			
α-Linolenic acid (18 : 3*n*-3)	0·86 (0·44–1·69)	1·07 (0·56–2·05)	0·60 (0·29–1·25)
Eicosapentaenoic acid (20 : 5*n*-3)	0·89 (0·43–1·84)	1·22 (0·61–2·43)	1·33 (0·65–2·71)
n-3-Docosapentaenoic acid (22 : 5*n*-3)	0·96 (0·46–1·99)	1·17 (0·54–2·54)	1·25 (0·57–2·72)
Docosahexaenoic acid (22 : 6*n*-3)	2·07 (1·00–4·29)	1·30 (0·60–2·82)	1·92 (0·90–4·10)

* Defined as answering 'Yes' to the question 'Do you have nasal allergies, including hay fever?'
† Adjusted for age group (20–29, 30–39, 40–49, 50–59, ≥60 years), sex, education (low, middle, high), smoking status (never, ex, current), BMI (continuous) and total energy intake (kcal/d, continuous).
‡ The first quartile was set as the reference category.

Neither oleic acid (18 : 1*n*-9) nor linoleic acid (18 : 2*n*-6), dihomo-γ-linolenic acid (20 : 3*n*-6), arachidonic acid (20 : 4*n*-6), docosatetraenoic acid (22 : 4*n*-6), α-linolenic acid (18 : 3*n*-3), EPA (20 : 5*n*-3) or *trans*-18 : 1 showed any relationship with the concentration of total IgE in serum (unpublished results).

Discussion

n-6 *Fatty acids*

We found a positive association between arachidonic acid in serum phospholipids and hay fever, but these results were not reflected in the association between arachidonic acid and allergic

Table 4. Adjusted odds ratios and corresponding 95 % CI for the association between selected fatty acids in serum phospholipids (%) and allergic sensitisation* (*n* 737)

	Adjusted odds ratios (95 % CI)†		
	2nd quartile‡	3rd quartile‡	4th quartile‡
Fatty acid			
Saturated			
Palmitic acid (16 : 0)	0·64 (0·38–1·08)	1·11 (0·68–1·79)	0·75 (0·44–1·27)
Stearic acid (18 : 0)	0·92 (0·55–1·52)	0·96 (0·57–1·60)	0·76 (0·44–1·31)
Monounsaturated			
Palmitoleic acid (16 : 1*n*-7)	1·21 (0·73–2·01)	1·25 (0·75–2·08)	1·29 (0·76–2·18)
Oleic acid (18 : 1*n*-9)	1·65 (0·97–2·83)	2·03 (1·20–3·43)	1·70 (0·98–2·92)
trans-18 : 1	0·98 (0·60–1·61)	1·11 (0·68–1·80)	0·67 (0·40–1·13)
n-6 Series polyunsaturated			
Linoleic acid (18 : 2*n*-6)	1·05 (0·63–1·75)	1·29 (0·78–2·15)	0·99 (0·58–1·69)
γ-Linolenic acid (18 : 3*n*-6)	1·03 (0·62–1·72)	1·65 (0·99–2·74)	1·27 (0·73–2·19)
Dihomo-γ-linolenic acid (20 : 3*n*-6)	1·31 (0·80–2·12)	0·81 (0·48–1·36)	1·02 (0·61–1·72)
Arachidonic acid (20 : 4*n*-6)	0·99 (0·59–1·66)	1·19 (0·71–1·97)	1·14 (0·68–1·89)
Docosatetraenoic acid (22 : 4*n*-6)	0·85 (0·51–1·40)	0·99 (0·61–1·62)	0·87 (0·52–1·45)
n-6-Docosapentaenoic acid (22 : 5*n*-6)	1·36 (0·83–2·23)	0·92 (0·55–1·56)	1·10 (0·65–1·86)
n-3 Series polyunsaturated			
α-Linolenic acid (18 : 3*n*-3)	0·90 (0·54–1·48)	1·10 (0·68–1·79)	1·01 (0·61–1·68)
Eicosapentaenoic acid (20 : 5*n*-3)	1·13 (0·68–1·88)	1·29 (0·78–2·15)	1·51 (0·90–2·55)
n-3-Docosapentaenoic acid (22 : 5*n*-3)	0·96 (0·57–1·63)	1·07 (0·61–1·87)	1·21 (0·68–2·12)
Docosahexaenoic acid (22 : 6*n*-3)	1·42 (0·86–2·33)	1·04 (0·62–1·76)	1·50 (0·89–2·52)

* Defined as at least one specific IgE ≥ 0·7 kU/l.
† Adjusted for age group (20–29, 30–39, 40–49, 50–59, ≥60 years), sex, education (low, middle, high), smoking status (never, ex, current), BMI (continuous) and total energy intake (kcal/d, continuous).
‡ The first quartile was set as the reference category.

sensitisation. Hay fever was self-reported, and individuals might be sensitised against allergens other than the five we had measured, which might have caused misclassification, but to us this seems unlikely. Although sensitisation reflects the susceptibility of an individual to develop allergic diseases, hay fever is the clinical outcome of the disease. Arachidonic acid might be an important factor in the clinical manifestation of allergic diseases such as hay fever.

Woods *et al.* (2004) did not observe any association between atopy, as assessed by a skin-prick test or several outcome variables for asthma, and arachidonic acid content in serum phospholipids in adults. Interestingly, they observed a positive association between asthma and dihomo-γ-linolenic, the direct precursor of arachidonic acid, but no association with atopy. The authors applied linear regression models, whereas we applied logistic regression models because the association between hay fever and arachidonic acid was not linear in our study.

Two studies conducted on children did not find significantly elevated arachidonic acid levels in serum or plasma phospholipids, respectively, in atopic and healthy children (Leichsenring *et al.* 1995; Yu & Björkstén, 1998). Leichsenring *et al.* (1995) even found a significantly lower proportion of arachidonic acid in the plasma cholesterol esters of children with atopic bronchial asthma. However, only 45 (Yu & Björkstén, 1998) and 27 (Leichsenring *et al.* 1995) participants were included in the two studies. Analysing the dietary data of this study, Trak-Fellermeier *et al.* (2004) did not find an association between arachidonic acid intake and hay fever in adults. In a European Prospective Investigation into Cancer and Nutrition (EPIC) substudy conducted in Germany, Nagel *et al.* (2003) observed a falling tendency towards an adult onset of the clinical symptoms of hay fever from the first to the fourth quartile of arachidonic acid intake. Thus, published results on the association between hay fever and arachidonic acid in serum phospholipids, as well as arachidonic acid intake, are not consistent.

In the present study, the arachidonic acid concentration in serum phospholipids was 9·6 %, which was nearly half that of linoleic acid, at 20·2 %. While less than 300 mg arachidonic acid per day is consumed in the human diet, a typical Western diet provides 10–15 g of linoleic acid per day (Calder & Miles, 2000). In general, the composition of fatty acids in serum phospholipids shows a pattern different from that of other fat moieties in the blood (triacylglycerols, cholesterol esters). Due to the metabolic handling, serum phospholipids have recently been established, and are widely used, as biomarkers of fatty acid intake. However, it does not reflect fatty acid proportions as found in a typical Western diet.

One might speculate that the low-point estimate in the first quartile might be an indicator of metabolic protection. Individuals with the lowest concentrations of arachidonic acid in their serum phospholipids might have metabolic features that inhibit the synthesis or enrichment of arachidonic acid in the serum phospholipids. Another possible explanation is that arachidonic acid is a marker of inflammation, although this seems unlikely to us, because only 10 % of the population are affected by hay fever, but the risk of this disease is high in the second to fourth quartile, which applies 75 % of the population. Nevertheless, our findings might be due to chance.

These results, showing a positive association between hay fever and arachidonic acid in serum phospholipids, are in accordance with the underlying hypothesis, because a higher availability of arachidonic acid might promote the production of inflammatory mediators that play an important role in allergic diseases. Therefore, the relationship between arachidonic acid concentration in the serum lipids and allergic diseases deserves further investigation.

In the present study, we did not find an association between the linoleic acid concentration of serum phospholipids and allergic diseases in adults, which is in accordance with the results of Woods *et al.* (2004). Studies on the association between the dietary intake of linoleic acid and adult-onset hay fever (Nagel *et al.* 2003) or atopic diseases in adults (Trak-Fellermeier *et al.* 2004) also did not find a significant relationship.

Neither the precursors of arachidonic acid, γ-linolenic acid and dihomo-γ-linolenic acid, nor the elongation and desaturation products adrenic acid and *n*-6 docosapentaenoic acid, showed any association with hay fever, sensitisation or total IgE in serum in the present study.

n-*3 Fatty acids*

In our study EPA and *n*-3 docosapentaenoic acid showed no association with hay fever or allergic sensitisation, which is consistent with the results of Woods *et al.* (2004) on atopy. Nagel *et al.* (2003) did not find an association between the overall intake of *n*-3 PUFA and adult-onset hay fever, but these authors reported a negative association between EPA intake and hay fever. It is hypothesised that a high intake of *n*-3 fatty acids, especially EPA, leads to a partial replacement of arachidonic acid in the cell membranes by EPA. This results in a suppressed production of arachidonic acid-derived pro-inflammatory eicosanoids such as 4-series leukotrienes (Calder, 2003). Wakai *et al.* (2001) found a positive association between the dietary intake of *n*-6 PUFA, but no association between the dietary intake of *n*-3 PUFA, and symptoms of seasonal allergic rhinoconjunctivitis in women.

Because fatty fish and fish oils are rich in EPA and docosahexaenoic acid, numerous epidemiological and clinical studies have been conducted on the association between fish intake or fish oil supplementation and asthma. Clinical trials on fish-oil supplementation for patients with asthma showed little evidence for a beneficial effect of marine fatty acids on asthma (Woods *et al.* 2003). Epidemiological studies on the association between asthma and fish consumption show inconsistent results, and studies on the association between hay fever and fish consumption are rare. A study conducted on teenagers in Taiwan failed to find an association between fish intake and allergic rhinitis (Huang *et al.* 2001). On the other hand, a Norwegian study reported a negative association between the introduction of fish into the diet before the age of 12 months and allergic rhinitis at the age of 4 years (Nafstad *et al.* 2003). Because sensitisation to allergens occurs early in life (Jones *et al.* 1996), fish might have to be included in the maternal diet or be eaten at a very early age to induce effects, a situation that is not common in most other Western countries.

Another reason for the lack of association between EPA or docosahexaenoic acid could be that the dietary intake of fish and fish products was very low in the present study population. Fifty-four per cent of the study population did not report any fish intake in their dietary records. For the participants who ate fish, the mean intake was 40 g/d and the median intake 32 g/d, and only 6 % reported an intake of more than 100 g fish and fish products a day. Therefore, the intake and consequently concentration of EPA and docosahexaenoic acid in phospholipids might be too low for any effect to be seen.

We observed no association between α-linolenic acid concentration in serum phospholipids and hay fever or allergic sensitisation, which is consistent with the results of Woods *et al.* (2004) and data on the dietary intake of α-linolenic acid (Nagel *et al.* 2003; Trak-Fellermeier *et al.* 2004).

Monounsaturated fatty acids

Two recently published studies reported a positive association between the dietary intake of oleic acid and adult-onset hay fever in adults (Nagel *et al.* 2003) and allergic sensitisation and hay fever in females (Trak-Fellermeier *et al.* 2004). This is consistent with the results of Heinrich *et al.* (2001), who observed a positive association between the energy-adjusted intake of monounsaturated fatty acids and the prevalence of allergic sensitisation in Europe, and our findings on the association between allergic sensitisation and oleic acid concentration in serum phospholipids.

Conversely, Woods *et al.* (2004) did not see any association between allergic sensitisation, as assessed by a skin-prick test, and oleic acid concentration in serum phospholipids. Nagel *et al.* (2003) speculated that a high intake of oleic acid is concomitant with a high intake of *trans*-fatty acids, because they appear in the same foods.

In an ecological study, Weiland *et al.* (1999) observed a positive association between the dietary intake of *trans* fatty acids and the prevalence of asthma, allergic rhinoconjunctivitis and atopic eczema in children aged 13–14 years in fourteen European countries. In the present study on adults, we have not found any association between the intake of monounsaturated *trans*-18 : 1 and hay fever or allergic sensitisation. However, we could not separate both isomers of *trans*-18 : 1, elaidic acid (9*trans*-18 : 1), which is the predominant *trans* isomer in partially hydrogenated vegetable oil, and vaccenic acid (11*trans*-18 : 1), which is predominant in ruminant fat.

In Germany, *trans* fatty acid intake is low compared with that of other Western countries, and 79 % of *trans* fatty acids in 1995/96 were derived from milk and ruminant fat, which is the highest proportion in Western Europe (Hulshof *et al.* 1999). In the Norwegian diet only 28 % (Hulshof *et al.* 1999), and in the American diet only 5 %, of *trans* fatty acids are derived from animal fat, the remaining 95 % coming from partially hydrogenated vegetable oils (Semma, 2002). In their ecological study, Weiland *et al.* (1999) observed a stronger positive association between asthma, allergic rhinoconjunctivitis and atopic eczema in children and *trans* fatty acid intake when they restricted their analysis to foods that contained predominantly partially hydrogenated oils. Several studies on coronary heart disease have also found a positive association with the dietary intake of *trans* fatty acids from partially hydrogenated vegetable oils, but not with *trans* fatty acids occurring in milk and ruminant fat (Meijer *et al.* 2001).

One might speculate that only elaidic acid has an influence on atopic diseases, although there is no clear biological explanation for different effects of elaidic and vaccenic acid (Meijer *et al.* 2001). Elaidic acid is contained in fast food and baked products such as cake and biscuits, so the intake of this *trans* fatty acid might also be an indicator of a certain lifestyle.

Fatty acids and total immunoglobulin E

To assess the association between fatty acids and total IgE in serum, the eight fatty acids oleic acid (18 : 1*n*-9), linoleic acid (18 : 2*n*-6), dihomo-γ-linolenic acid (20 : 3*n*-6), arachidonic acid (20 : 4*n*-6), docosatetraenoic acid (22 : 4*n*-6), α-linolenic acid (18 : 3*n*-3), EPA (20 : 5*n*-3) and *trans*-18 : 1 were considered. None showed any influence on the concentration of total IgE in serum. This is consistent with the interim results of an Australian study on *n*-3 fatty acid supplementation in infants. Mihrshahi *et al.* (2003) found no difference in the level of total IgE in serum between infants who received *n*-3 fatty acid supplementation in the first 18 months of life and those who did not. Yu & Björkstén (1998) reported lower concentrations of EPA in the serum phospholipids of children with a total IgE above the median and higher concentrations of 20 : 2*n*-6. However, the biological function of this minor fatty acid is unknown (Yu & Björkstén, 1999). To our knowledge, no other studies have yet been published on the association between fatty acids and total IgE.

We measured fatty acid concentrations in serum phospholipids as a biomarker of recent fatty acid intake (Ma *et al.* 1995; Arab, 2003) and of metabolism, because fatty acid concentrations in the serum phospholipids better reflect fatty acid availability in the body. It has been nicely shown in intervention studies administering *n*-3 PUFA that its content increased in plasma phospholipids in a time- and dose-dependent manner and was followed by an enrichment in the white and red blood cells (von Schacky *et al.* 1985; Gibney & Hunter, 1993; Kew *et al.* 2004). Although less distinct, this is also observable after high dosages of *n*-6 polyunsaturated and monounsaturated fatty acids.

We do not know the extent to which ingested fatty acids get metabolised in the body. There are some factors that influence the measured fatty acid biomarker level, for example genetic polymorphisms of elongase and desaturase enzymes, and nutritional status (Arab, 2003).

It might be possible that the long-term storage of serum samples has led to the oxidation of the long-chain PUFA. To the present authors, however, it seems unlikely that predominantly *n*-3 or *n*-6 PUFA were damaged. Zeleniuch-Jacquotte *et al.* (2000) reported that the storage of serum samples for up to 12 years at −80°C protected the fatty acids in phospholipids against oxidation very well.

We used self-reported hay fever as an outcome variable, but this was not confirmed by a physician. Because allergic sensitisation, measured by the analysis of specific IgE in serum, showed similar associations with most fatty acids in serum phospholipids, we do not think that the self-reported diagnosis caused a strong bias.

The results of the present study should be interpreted with caution because of the cross-sectional nature of our study design, which does not establish a relationship between cause and effect. Furthermore, the power of our study is questionable and could be criticised. We conducted a secondary analysis with a relatively high number of participants, but by categorising the fatty acid values into quartiles, information is lost. Owing to the inconsistent results on the association between fatty acids and allergic diseases in studies conducted so far, we think this topic warrants further investigation.

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