

Serum IgA, IgG, IgM and IgD in allergic (type I) and non-allergic respiratory diseases

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Summary

Serum immunoglobulin levels A, G, M, D have been studied in 902 patients suffering from allergic or non-allergic asthma, rhinitis and cough or various combinations of these disorders. In addition, a control group of asymptomatic persons was included. Serum IgA and IgD levels were significantly lower in both the allergic and non allergic groups of patients as compared to the control group, indicating that this decrease is a common feature for all patient groups studies. Serum IgA was significantly increased in amount in smokers. Serum IgA and IgG levels increased significantly with age. Females showed significantly higher serum IgM levels as compared to males. Atopic eczema did not seem to influence the serum level of immunoglobulin classes A, G, M or D.

Introduction

Serum immunoglobulin E differs significantly in amount between atopic (type I allergy) and non-atopic patients suffering from asthma and/or rhinitis. In addition there is significantly more IgE in asthmatic patients compared to those with rhinitis (Stevens & Vermeire, 1980b).

It was our intention to examine the amounts of immunoglobulins other than IgE, and we report the concentrations in serum IgA, IgG, IgM and IgD in a large group of patients with asthma, rhinitis, cough, or various combinations of these disorders. The influence of type I allergy, age, sex, smoking habits and atopic eczema on serum immunoglobulins are also reported.

Materials and methods

A group of 902 patients, suffering from asthma without rhinitis, rhinitis without asthma, both asthma and rhinitis, rhinitis and cough, and cough alone were studied

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Table 1. Amounts of immunoglobulins (mg/100 ml) in sera of the groups of allergic and non allergic patients and asymptomatic controls.

	IgA			IgG			IgM			IgD		
	<i>n</i>	$\bar{x}$	s.d.	<i>n</i>	$\bar{x}$	s.d.	<i>n</i>	$\bar{x}$	s.d.	<i>n</i>	$\bar{x}$	s.d.
Allergic												
Asthma	108	5.03	0.57	108	6.98	0.30	108	5.12	0.49	92	0.44	0.97
		153*			1078*			167*			1.55*	
Rhinitis	141	4.95	0.51	141	6.97	0.24	141	5.13	0.50	127	0.06	0.85
		142*			1063*			169*			1.06*	
Asthma and rhinitis	204	5.05	0.49	204	6.98	0.28	204	5.07	0.46	175	0.26	0.97
		155*			1079*			153*			1.29*	
Rhinitis and cough	27	4.89	0.53	27	6.90	0.30	27	4.95	0.41	26	0.14	0.76
		134*			922*			141*			1.15*	
All allergic	480	5.01	0.52	480	6.97	0.27	480	5.09	0.48	420	0.21	0.94
		150*			1069*			163*			1.24*	
Non-allergic												
Asthma	103	5.15	0.60	103	6.95	0.31	103	5.02	0.53	89	0.20	0.94
		172*			990*			151*			1.23*	
Rhinitis	109	5.04	0.60	109	7.02	0.28	109	5.08	0.48	84	0.15	0.85
		154*			1124*			160*			1.16*	
Asthma and rhinitis	73	5.07	0.57	73	6.99	0.27	73	5.10	0.54	61	0.36	1.01
		159*			1085*			165*			1.43*	
Rhinitis and cough	37	4.88	0.61	37	6.93	0.31	36	5.04	0.42	29	0.31	0.88
		131*			1023*			155*			1.36*	
Cough	69	5.00	0.58	70	6.95	0.33	69	5.04	0.48	54	0.32	0.94
		149*			1039*			154*			1.37*	
All non-allergic	391	5.05	0.59	392	6.97	0.30	391	5.06	0.50	317	0.25	0.93
		156*			1069*			157*			1.28*	
Controls	29	5.35	0.71	30	6.87	0.24	30	5.12	0.46	24	0.93	0.80
		212*			961*			170*			2.53*	

* Geometric mean

(Table 1). The patients were further subdivided into allergic (type I hypersensitivity) and non-allergic on the basis of history, skin testing with common inhalant allergens, RAST and nasal or bronchial provocation tests, as reported previously (Stevens & Vermeire, 1980a). When there was a discordance between the history, skin test results and the RAST, an allergen provocation was performed with the suspected allergen and patients were finally classified as allergic or non-allergic according to the result of the provocation test. In this way, allergic patients were differentiated from non-allergic (intrinsic or vasomotor asthma/rhinitis). Patients suffering from chronic bronchitis were excluded from this study. Thirty asymptomatic individuals served as a control group. For each individual the presence or absence of atopic eczema and the smoking habits were noted.

Serum immunoglobulin concentrations A, G, M and D were determined by the radial immunodiffusion technique.

Because of the great interindividual variability, values were logarithmically transformed (natural logarithm) in order to obtain a normal distribution. For IgD,

values smaller than 1 mg/100 ml, which could not be detected, were arbitrarily designated 0.5 mg/100 ml.

The patient groups were compared by analysis of variance (more than two groups) and the Student *t*-test (non-paired data). Differences were considered to be significant at the $P=0.05$ level. For IgA, abnormally low values were defined as less than mean minus 1.65 s.d. of the control group. The frequency of abnormally low IgA values were assessed by *chi*-square analysis.

Results

Table 1 shows the results of the immunoglobulin determinations in the different groups.

IgA

Analysis of variance revealed a significant difference between all groups (patients and controls) ($F, 9.891:2.45, P=0.009$). When all patient groups were considered without the control group, the difference was not significant ($F, 3.862:0.80, P=0.06$). When each patient group is compared to the control group, significantly lower values are found in all patient groups, except for non-allergic asthmatic subjects. There is no significant difference when the total group of allergic patients is compared with the total group of non-allergic patients ($P=0.29$).

Figures 1 and 2 are graphical presentations of the geometric means of serum IgA in different age groups in allergic and non-allergic patients. The allergic group of 51–60 years was too small to be included. Analysis of variance of these groups shows significant differences for allergic ($F, 4.466:16.38, P<0.0001$) and non-allergic ($F, 5.373:13.06, P<0.0001$) groups. There is a progressive increase of serum IgA with age in allergic patients. In non-allergic patients, highest values are found in the fourth decade. The frequency of abnormally low IgA values ($< \text{mean} - 1.65 \text{ s.d. of controls}$) (Table 2) is about equal in all groups.

Patients of the allergic and non-allergic group with rhinitis and cough have a higher frequency of abnormally low IgA value but comparison with the control group by a

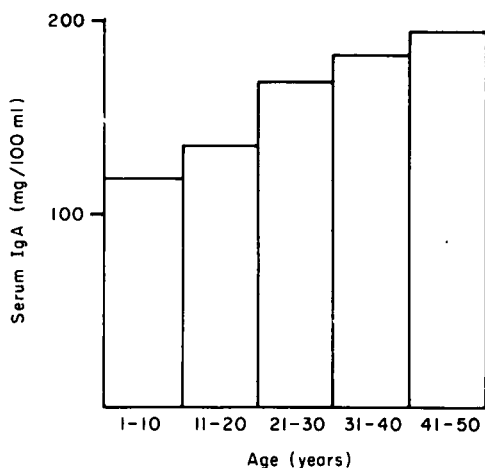


Fig. 1. Serum IgA (geometric mean) for allergic patients

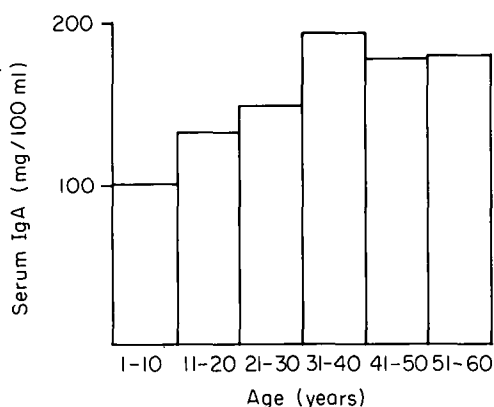


Fig. 2. Serum IgA (geometric mean) for non-allergic patients

Table 2. Frequency of abnormally low IgA values (< mean-1.65 s.d. of controls).

	Allergic	Non-allergic
Asthma	8/108 (7.4)	5/103 (4.9)
Rhinitis	11/141 (7.8)	6/109 (5.5)
Asthma and rhinitis	10/204 (4.9)	2/73 (2.7)
Rhinitis and cough	4/27 (14.8)	6/37 (16.2)
Cough	—	6/69 (8.7)
Controls	2/29 (6.9)	—

Table 3. Serum IgA in smokers and non-smokers (mean of logarithmically transformed data $\pm$ s.d.).

	Smokers	Non-smokers	P
Allergic	(103) 5.10 ± 0.49	(359) 4.98 ± 0.52	0.03
Non-allergic	(122) 5.18 ± 0.54	(259) 5.00 ± 0.61	0.007

Numbers in parentheses are the number in the sample
P, Student *t* probability

chi-square analysis gives no statistically significant differences (*chi*-square $P=0.37$ and 0.42 respectively). There is also no statistically significant difference in the frequency of abnormally low values of IgA when the total group of allergic patients and the total group of non-allergic patients are compared (*chi*-square $P=0.92$).

In allergic as well as in non-allergic groups smokers have significantly higher values than non-smokers (Table 3). Further subdivisions of patients according to sex and the presence or absence of atopic eczema yields no significant differences.

IgG

There are no significant differences for IgG between all groups (patients and controls)

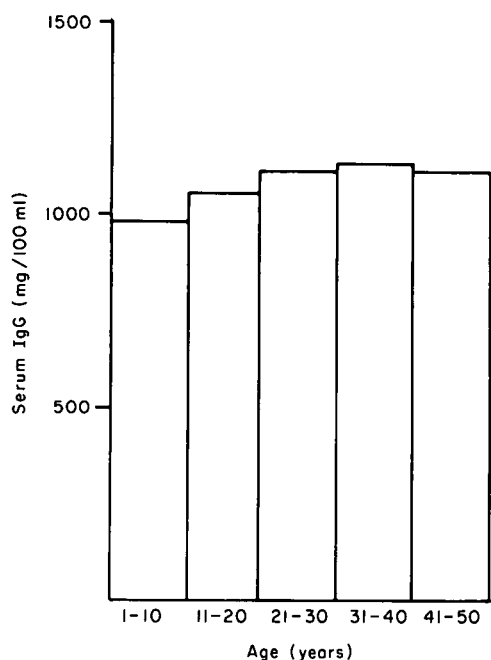


Fig. 3. Serum IgG (geometric mean) for allergic patients

(F , 9.892:1.41, $P=0.18$), nor between patient groups only (F , 8.863:1.06, $P=0.39$). The difference between all allergic and all non-allergic patients is not significant either.

Figure 3 presents geometric mean values of IgG for the different age groups of allergic patients. The findings of non-allergic patients were very similar. There are significant differences between age groups in allergic (F , 4.466:4.10, $P=0.003$) as well as in non-allergic groups (F , 5.374:3.25, $P=0.007$) owing to a slight increase of serum IgG with age. Smoking habits, sex and the presence or absence of atopic eczema do not affect serum IgG levels.

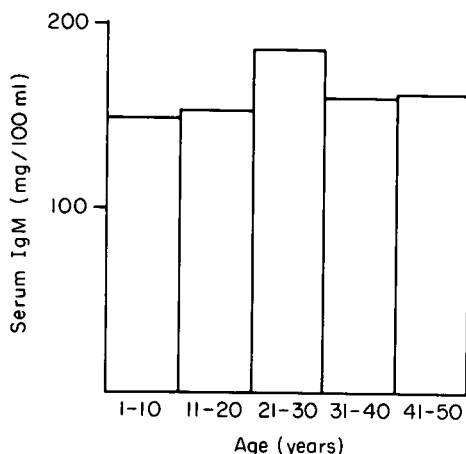


Fig. 4. Serum IgM (geometric mean) for allergic patients

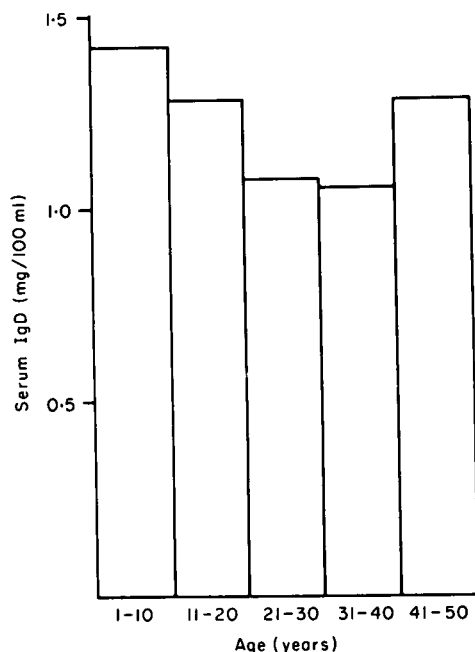
Table 4. Serum IgM according to sex (mean of logarithmically transformed data $\pm$ s.d.).

	Men	Women	<i>P</i>
Allergic	(259) 4.96 ± 0.45	(221) 5.25 ± 0.46	< 0.0001
Non-allergic	(194) 4.94 ± 0.48	(197) 5.18 ± 0.50	< 0.0001

Numbers in parentheses are the number in the sample
P, Student *t* probability

IgM

As for IgG, there are no significant differences between patient groups and controls and patient groups only (F , $9.891:0.77$, $P=0.64$ and F , $8.862:0.80$, $P=0.60$ respectively). Allergic and non-allergic patients are not significantly different either ($P=0.63$). Age distribution in allergic patients is presented in Fig. 4. Analysis of variance between age groups shows a significant difference for allergic patients (F , $4.466:4.21$, $P=0.003$). This difference is the result of higher IgM values in the third decade (Fig. 4). In non-allergic patients there are no significant differences (F , $5.373:0.66$, $P=0.65$). When patients are subdivided according to smoking habits and the presence or absence of atopic eczema, no significant differences are observed. Both allergic and non-allergic women have significantly higher IgM values than men (Table 4).

**Fig. 5.** Serum IgD (geometric mean) for allergic patients

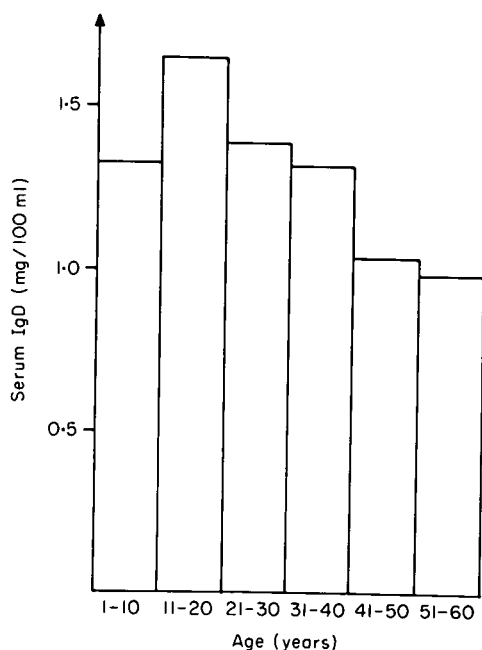


Fig. 6. Serum IgD (geometric mean) for non-allergic patients

IgD

Mean IgD values are significantly different between all patient groups and controls (F , 9.751:3.27, $P=0.0007$) (higher mean IgD in controls) (Table 1). Between patient groups, a slightly significant difference persists (F , 8.728:1.97812, $P=0.046$). There is no significant difference between allergic and non-allergic patients ($P=0.57$). Subdivision of patients according to the presence or absence of eczema and sex yields no significant difference either. Figures 5 and 6 represent the age distribution of serum IgD in allergic and non-allergic patients, with no significant difference, in allergic patients (F , 4.406:1.46, $P=0.21$), or in non-allergic patients (F , 5.302:2.30, $P=0.053$).

Discussion

Some studies indicate that serum immunoglobulins (except IgE) in adult asthmatic patients are not significantly different from a control population (Elgefors, Julin & Nilson, 1974; Kohler & Farr, 1967). However, in other studies, the results of the tests on allergic persons did not include a control group, but were compared to normal values published by WHO (Ferstl & Ferstl, 1973; Staud, 1978). In this study we examined serum immunoglobulins in patients suffering from asthma, rhinitis and cough. A further subdivision was made between allergic and non-allergic patients and an asymptomatic control group was included. Serum IgA, IgG, IgM and IgD did not differ significantly between allergic and non-allergic patients. Hence, the presence or absence of type I allergy did not affect these serum immunoglobulin levels.

Amounts of serum IgA and IgD were significantly less in patients when compared with controls, but amounts of IgG and IgM were not significantly different between these groups.

Decreased amounts of serum IgA have been reported by Saha *et al.* (1975) in sixty-nine asthmatic patients and was more evident in the atopic patients. Other sources report an increase in amounts of serum IgA (British Thoracic and Tuberculosis Committee, 1975) or normal amounts of IgA, independent of the atopic status. In some reports the frequency of below normal amounts of IgA in asthmatic patients was assessed but the definition of subnormal IgA concentration differed between authors (Kaufman & Hobbs, 1970; Ferstl & Ferstl, 1973; Perrin-Fayolle *et al.*, 1976; Lin *et al.*, 1977). Some studies were made on adults, in which decreased IgA was seen in 14.9% (Ferstl & Ferstl, 1973) and 2.7% (Perrin-Fayolle *et al.*, 1976), or made on children in which the frequency was 7% (Kaufmann & Hobbs, 1970) and 4.5% (Lin *et al.*, 1977). No decrease in the mean IgA concentration was found by Berger *et al.* (1978) when asthmatic children, subdivided according to age, were compared with normal children.

In our study, comparable frequencies of lowered IgA values were found between patients and controls. This means that the decrease of mean serum IgA in our patients is not due to an abnormal frequency of low IgA values. Soothill (1974) and Soothill *et al.* (1976) observed a correlation between low values of IgA in the first month of life and the subsequent development of allergic asthma. In our study a decrease of serum IgA is seen in all patient groups, even though greater in patients with rhinitis, although the differences between asthma and rhinitis were not significant. Although this study does not exclude the possible aetiological role of decreased serum IgA in the genesis of allergic respiratory disease, it seems that the decrease of serum IgA is rather a common characteristic of both asthma and rhinitis, allergic and non-allergic.

In spite of an overall decrease of serum IgA, there is still a progressive increase with age. We found significantly higher serum IgA values in smokers (allergic and non-allergic). This is in contradiction with the results of Gulsvik and Fagerhol (1979). These investigators found a decrease of IgA, IgG and IgM in smokers who smoked ten to nineteen cigarettes daily. In smokers who smoked more than twenty cigarettes daily there was a smaller decrease and in ex-smokers, higher IgA values were observed.

For IgG, different observations have been reported in the literature. Elgefors *et al.* (1974) noted a significant decrease of serum IgG in adult asthmatic patients under continuous prednisone therapy, which presumably accounts for this decrease (Posey *et al.*, 1978; Settupane, Pudupakkam & McGowan, 1978). In children suffering from asthma, Berger *et al.* (1978) found significantly decreased values for IgG in all age groups. Collins-Williams *et al.* (1967) found decreased values for IgG but also for IgA and IgM in children suffering from severe asthma. Others reported normal values (Chen & Chuang, 1976; Ferstl & Ferstl, 1973; Hsieh, 1976; Palma-Carlos & Palma-Carlos, 1971; Saha *et al.*, 1975; Staud, 1978) but increased values were also observed (Committee, 1975; Grove *et al.*, 1975). In our study no major abnormalities of serum IgG levels have been found.

As far as IgM is concerned, most authors found normal values for IgM in asthmatics (Chen & Chuang, 1976; Elgefors *et al.*, 1974; Ferstl & Ferstl, 1973; Grove *et al.*, 1975), although elevated IgM levels have been reported by others (Saha *et al.*, 1975; Berger *et al.*, 1978; Lin *et al.*, 1977). In our study we found normal IgM levels, which were, in contrast to other reports (Committee, 1975), not significantly influenced by age. On the contrary serum IgM levels differed significantly between males and females, as already reported by others (Committee, 1975; Lin *et al.*, 1977; McKay, Whittingham & Tait, 1977).

Normal (Grove *et al.*, 1975; Saha *et al.*, 1975) and elevated (Committee, 1975;

Kohler & Farr, 1967) IgD values have been reported in asthma. Berger *et al.* (1978) reported a high frequency of non detectable IgD values in asthmatic children. The meaning of our finding of decreased IgD in all patient groups is not clear.

Finally none of the serum immunoglobulins studied was influenced by atopic eczema in this study.

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