

## METHODS

### Population

Patients were recruited in chest clinics in 5 cities through a standardized protocol, as were population-based control subjects. Inclusion criteria were place of birth, area of residence, age, familial structure, and a positive answer to 4 standardized questions based on international questionnaires: Have you ever had attacks of breathlessness at rest with wheezing? Have you ever had asthma attacks? Was this diagnosis confirmed by a physician? Have you ever had an asthma attack in the last 12 months? Of the population of 764 patients and control subjects from the EGEA, 53 asthmatic control subjects (16 women, 22 men, 4 girls, and 11 boys) and 6 subjects missing information on asthma were excluded.

### Allergy markers, lung function, and asthma severity

Total IgE levels were measured by means of RIA (Phadebas PRIST technique; Pharmacia Diagnostics, AB, France). Specific IgE levels to a mixture of several inhalant allergens (pollens, house dust mites, molds, and animal epithelia) were assessed by using the Phadiatop (Pharmacia Diagnostics, AB). The exact composition of the aeroallergens present in the Phadiatop has not been reported by the manufacturer, but information on its constituents is available, and *Aspergillus* and *Blatta* species were not included in Phadiatop. SPT allergens studied were cat, *Dermatophagoides pteronyssinus*, *Cladosporium herbarum*, *Alternaria tenuis*, timothy grass, olive, birch, *Parietaria judaica*, ragweed, *Aspergillus* species, and *Blatta germanica*. The prevalence of positive results is expressed by using a cutoff of mean wheal diameter of 3 mm or greater than that elicited by the negative control.

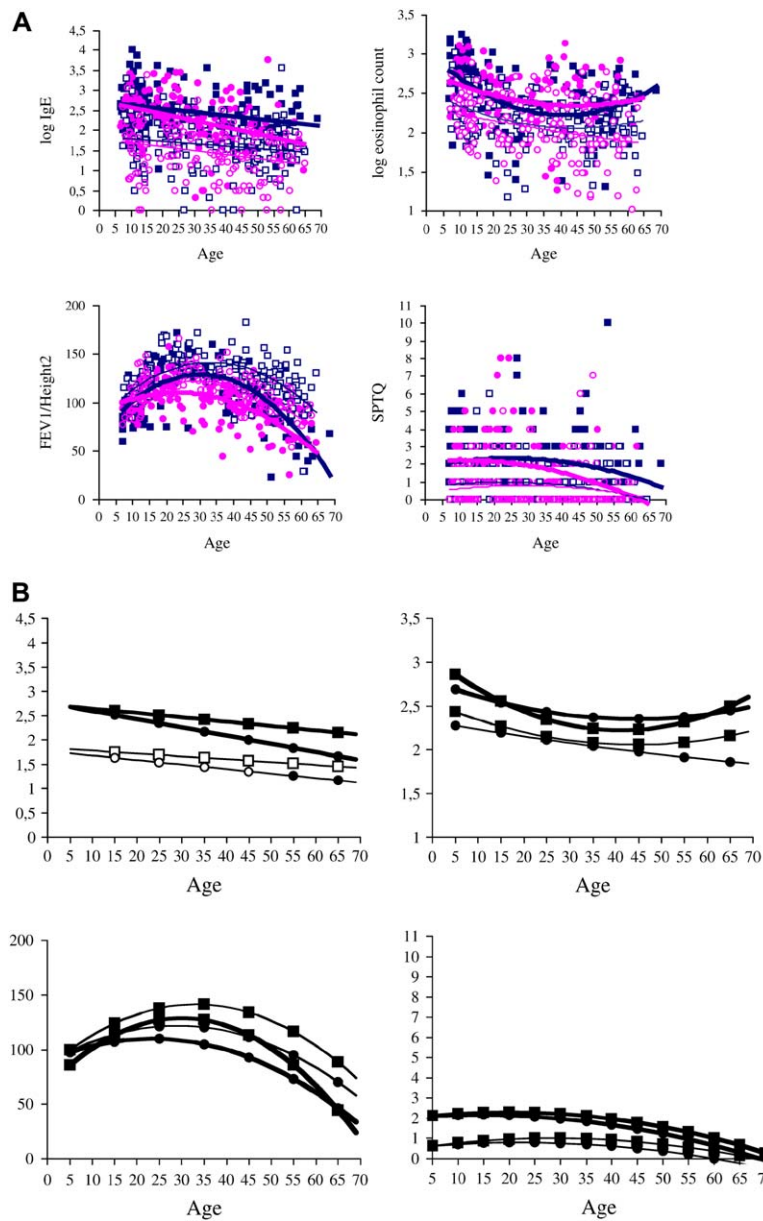
Spirometry was conducted according to the European Community Respiratory Health Survey protocol, with slight modifications.<sup>E1</sup> A Biomedin spirometer (Biomedin Srl, Padua, Italy) was used in all centers, except in Lyon, where a Pneumotach Jaeger spirometer (Jaeger) was used. The maximum FEV<sub>1</sub> of 3 maneuvers was used. Predicted values for FEV<sub>1</sub> were derived from age, sex, and height

on the basis of the 1983 European references<sup>E2</sup> for subjects aged 18 years or more and based on those from Polgar and Weng<sup>E3</sup> for those younger than 18 years.

A score (1-4) was calculated in 2 steps to assess asthma severity, as previously described.<sup>E4</sup> In step 1 the sum of the following clinical items regarding the last 12 months was computed: frequency of attacks (<1 attack per month [0], <1 attack per week [1], <1 attack per day [2], and  $\geq 1$  attack per day [3]); symptoms between asthma attacks (none [0], wheezing [1], wheezing and dyspnea [2], and activities limited by dyspnea [3]); and hospitalization for asthma (no [0], yes [1]). Subjects were classified in 4 classes (0, 1, 2, and  $\geq 3$ ). Then in step 2 the 4-category variable built in step 1 was combined with treatment level (none, treatment without inhaled steroids, and treatment with inhaled steroids). This combination is derived from the last Global Initiative for Asthma guidelines,<sup>E5</sup> here modified because information on inhaled steroid dose was unavailable.

## REFERENCES

- E1. United Medical and dental Schools of Guy's and St Thomas's Hospitals, Department of Public Health Medicine. Protocol for the European Community Respiratory Health Survey. London: United Medical and dental Schools of Guy's and St Thomas's Hospitals, Department of Public Health Medicine; 1993.
- E2. Quanjer PH, Tammeling GJ. Summary of recommendations. In: Quanjer PH, editor. Standardized lung function testing. Bull Eur Physiopathol Respir 1983;19:7-10.
- E3. Polgar G, Weng TR. The functional development of the respiratory system from the period of gestation to adulthood. Am Rev Respir Dis 1979; 120:625-95. [Q8]
- E4. Le Moual N, Siroux V, Pin I, Kauffmann F, Kennedy S. on behalf of the Epidemiological Study on the genetics and Environment of Asthma (EGEA). Asthma severity and exposure to occupational asthmagens. Am J Respir Crit Care Med 2005;172:440-5.
- E5. National Heart, Lung and Blood Institute. Global strategy for asthma management and prevention. Bethesda (MD): National Institutes of Health; 2002. NIH publication no. 02-95-3659.



**FIG E1. A**, Associations of total IgE levels, eosinophil counts, and FEV<sub>1</sub>/H<sup>2</sup> by age and sex in patients and control subjects over the lifespan. The best fit was obtained considering age for IgE levels and age<sup>2</sup> for eosinophil counts and FEV<sub>1</sub>/H<sup>2</sup>. Male and female control subjects are represented by *open squares* and *circles/thin curves* and male and female patients by *solid squares* and *circles/thick curves*. **B**, Associations of total IgE levels, eosinophil counts, and FEV<sub>1</sub>/H<sup>2</sup> by age and sex in patients and control subjects over the lifespan (tendency curves only). The best fit was obtained considering age for IgE levels and age<sup>2</sup> for eosinophil counts and FEV<sub>1</sub>/H<sup>2</sup>. Male and female subjects are represented by *open squares* and *circles/thin curves* and male and female patients by *solid squares* and *circles/thick curves*.

[Q9] **TABLE E1.** IgE level (in international units per milliliter) according to SPT responses

	Children				Adults			
	Patients		Control subjects		Patients		Control subjects	
	Unadjusted	Adjusted*	Unadjusted	Adjusted*	Unadjusted	Adjusted†	Unadjusted	Adjusted†
SPT positivity, any allergen								
No	235	228	31	30	96	137	22	22
Yes	425§	398	86¶	86	248	260¶	73	68
SPT positivity, indoor allergen								
No	348	386	36	37	100	127	25	25
Yes	413	324	118¶	120¶	288	308	82	80
SPT positivity, outdoor allergen								
No	380	358	32	32	146	189	25	25
Yes	433	397	189	218	282¶	261	100	93

Indoor allergens include cat, *Dermatophagoides pteronyssinus*, and *Blatta germanica*. Outdoor allergens include timothy grass, olive, birch, and ragweed. IgE levels are expressed as geometric means.

Comparison of SPT negativity and SPT positivity: ‡ $P \leq .05$ ; § $P \leq .10$ ; || $P \leq 0.001$ ; ¶ $P \leq .01$ .

\*Adjusted on age and sex.

†Adjusted on age, sex, smoking, and country living.

**TABLE E2.** Relationships between asthma severity and IgE levels, eosinophil counts, and SPTQ scores

Asthma severity score*	Children				Adults			
	N	IgE (IU/mL)	SPTQ score	Eosinophil counts (nb/mm <sup>3</sup> )	n	IgE (IU/mL)	SPTQ score	Eosinophils (nb/mm <sup>3</sup> )
1	25	319.5	2.12	437.2	11	207.0	1.82	210.2
2	36	433.0	2.11	401.0	47	194.2	2.15	231.2
3	19	415.9	2.11	509.5	32	167.3	1.53	239.2
4	30	404.9	1.93	445.4	66	236.7	1.91	226.9
<i>P</i> value		.78	.93	.66		.73	.56	.98

IgE levels and eosinophil counts are expressed as geometric means.