

SUPPLEMENTARY MATERIAL

Supplementary Table 1. Characteristics of individuals from the general adult population, stratified by IgE categories					
Factor	Serum total IgE				P-value
	Deficiency (<2.5 kU/L) (n=121)	Low (2.5-9.9 kU/L) (n=284)	Normal (10-100 kU/L) (n=765)	High (>100 kU/L) (n=346)	
Age (years)	59 (40-70)	52 (41-68)	52 (40-67)	50 (33-66)	0.001
Sex (female)	91 (75.2)	188 (66.2)	425 (55.6)	134 (38.7)	<0.001
Atopy (SPT-positivity)	4 (3.3)	9 (3.2)	141 (18.5)	178 (51.6)	<0.001
Nasal symptoms	29 (24.0)	65 (22.9)	205 (26.8)	127 (36.7)	<0.001
Bronchial symptoms	28 (23.1)	57 (20.1)	181 (23.7)	136 (39.3)	<0.001
Respiratory allergy	2 (1.7)	2 (0.7)	76 (9.9)	117 (33.9)	<0.001
Autoimmune thyroid disease	10 (8.3)	8 (2.8)	32 (4.2)	2 (0.6)	<0.001
Autoimmune disease	12 (9.9)	10 (3.5)	36 (4.7)	5 (1.4)	0.001
History of intestinal helminthiasis	2 (1.7)	4 (1.4)	8 (1.0)	4 (1.2)	0.603
Serum IgG (mg/dL)	981 (841-1180)	1070 (908-1240)	1090 (952-1250)	1080 (956-1260)	<0.001
Serum IgG deficiency	6 (5.0)	11 (3.9)	19 (2.5)	11 (3.2)	0.265
Serum IgA (mg/dL)	193 (146-243)	211 (154-266)	217 (165-288)	229 (170-301)	<0.001
Serum IgA deficiency	4 (3.3)	4 (1.4)	5 (0.7)	3 (0.9)	0.036
Serum IgM (mg/dL)	92 (65-130)	103 (71-137)	94 (64-136)	98 (70-138)	0.991
Serum IgM deficiency	9 (7.4)	19 (6.7)	47 (6.1)	22 (6.4)	0.667

Data are medians and interquartile ranges (within parentheses) or absolute numbers and percentages (within parentheses).

SPT, skin prick tests (unavailable for 2 individuals). The panel of SPT included house dust mites (*Dermatophagoides pteronyssinus* and *Lepidoglyphus destructor*), pollens (*Phleum pratense*, *Plantago lanceolata*, *Betula alba*, and *Parietaria judaica*), vegetable panallergens (profilin and peach lipid transfer protein [LTP]), moulds (*Alternaria alternata* and *Aspergillus* spp), and animal dander (dog and cat) (ALK-Abelló, Spain). The control SPT included 10 mg/ml histamine and saline solution. Wheals with a mean diameter greater than 3 mm after 15 minutes were deemed positive. The presence of at least one positive SPT was considered indicative of allergic sensitisation or atopy.

The history of bronchial symptoms, nasal symptoms and intestinal helminthiasis was assessed by questionnaire. A history of nasal symptoms indicative of rhinitis was defined as an affirmative response to the question: "Have you ever had a runny nose or nasal congestion when you didn't have a cold?". A history of bronchial symptoms indicative of asthma was defined as an affirmative answer to at least one of these three questions: "Have you ever had wheezing or ringing in your chest?", "Have you ever taken asthma inhalers?" or "Have you ever been diagnosed with asthma?". A history of intestinal helminthiasis was defined as a positive response to the question: "Have you ever had parasites in the intestine such as worms in the stool?". Individuals with atopy (SPT-positivity) and nasal and/or bronchial symptoms were considered to have respiratory allergy.

Autoimmune diseases were registered from the clinical records. Autoimmune thyroid disease consisted of hypothyroidism (including subclinical, i.e., elevated serum TSH with normal T4 concentrations) in 48 cases and hyperthyroidism (Graves' disease) in 4 cases. Additional autoimmune diseases included rheumatoid arthritis (3 cases), inflammatory bowel disease (2 cases), ankylosing spondylitis (1 case), pernicious anemia (1 case), cutaneous lupus (1 case), autoimmune hepatitis (1 case), and Sjögren syndrome (1 case).

Lower reference values defining immunoglobulin deficiency were as follows: IgG, 700 mg/dL; IgA, 70 mg/dL; and IgM, 40 mg/dL.

P-values in the table were obtained with a trend test (Jonkheere-Terpstra test for numerical variables and Chi-square test for categorical variables) in order to investigate the statistical significance of variation of the dependent variables (demographic, clinical, and immunological characteristics) in relation to the ordinal independent variable (IgE categories).

Individuals with IgE deficiency (<2.5 kU/L) showed older age (P=0.033), higher proportion of female sex (P<0.001), lower rate of atopy (P<0.001), lower rate of respiratory allergy (P<0.001), higher rate of autoimmune thyroid disease (p=0.002), lower levels of IgG (P<0.001), and lower levels of IgA (P<0.001) than individuals without IgE deficiency (i.e. the remaining IgE categories as a whole; Mann-Whitney test or Chi-square test, where appropriate).