

The effect of infectious burden on the prevalence of atopy and respiratory allergies in Iceland, Estonia, and Sweden

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Background: Epidemiologic reports on the effect of microbe exposure on the development of atopy and allergic asthma are inconsistent.

Objectives: The study investigates the association between serologic markers of infections and occurrence of atopy, allergic asthma, and rhinitis among adults in Iceland, Sweden, and Estonia.

Methods: Individuals (n = 1249; mean age, 42 years) from Iceland, Sweden, and Estonia underwent a structured interview and blood sampling. Specific IgE was measured against 4 allergens, and IgG antibodies were measured against *Helicobacter pylori*, *Toxoplasmosis gondii*, hepatitis A virus, herpes simplex virus 1, *Chlamydia pneumoniae*, EBV, and cytomegalovirus.

Results: Nonatopic subjects more often had positive serology for *Helicobacter pylori*, herpes simplex virus 1, *Chlamydia pneumoniae*, and cytomegalovirus. Having a low number (≤ 3) of IgG antibodies against the various infectious agents was an independent risk factor for atopy (odds ratio [OR], 1.43; 95% CI, 1.06-1.93), allergic asthma (OR, 1.82; 95% CI, 1.12-2.98), and allergic rhinitis (OR, 1.69; 95% CI, 1.21-2.37). The proportion of atopy that can be explained by a lower number (≤ 3) of infections was 6.7% in Iceland, 9.2% in Estonia, and 16.4% in Sweden, and 6.7%, 48.2%, and 33.4% for allergic asthma, respectively.

Conclusion: Our data are consistent with cumulative protective effect of infections against atopy and respiratory allergies irrespective of route of infection.

Clinical implications: The study indicates what microbes or combination of microbes play a role in the complex interplay between hygiene and allergy and may contribute toward the understanding of the allergy epidemic. (J Allergy Clin Immunol 2007;119:1-10.)

Key words: Atopy, allergic asthma, allergic rhinitis, hygiene hypothesis, infection, epidemiology, *Helicobacter pylori*/immunology, hepatitis A/immunology, *Chlamydia pneumoniae*/immunology, herpes simplex/immunology

The prevalence of atopy rose steadily in the second half of the 20th century, and the highest rates are seen in countries with a Western lifestyle and urbanization.¹ These changes have been well demonstrated in East and West Germany^{2,3} as well as in Finland and Russia.⁴ The reasons for this epidemic are unknown, but many epidemiologic data suggest that reduced microbial exposure of children caused by a Westernized lifestyle is partly responsible for this phenomenon, an explanation that has been named the hygiene hypothesis. There is also accumulating evidence suggesting that not only subclinical or overt infections but also environmental exposure to nonviable microbial products⁵⁻⁷ might pertain to the hygiene hypothesis. There may be several interacting immunologic mechanisms accounting for the observations that the hygiene hypothesis encompasses. The most commonly quoted mechanism is the lack of skewing of the T_H2/T_H1 balance away from allergy-promoting T_H2 cells toward T_H1 cells, which usually takes place with increasing age and exposure to microbes. This may be the result of the reduced production of IL-12 and IFNs by innate immune pathways that are stimulated by bacterial products through their Toll-like receptors.⁸ An alternative view is that the lower microbial burden does not act by inducing a lower production of T_H1-polarizing cytokines but by decreasing the activity of T-regulatory cells.⁹

Further understanding of immunologic mechanisms is necessary for interpretation of epidemiologic data and is a prerequisite for development of preventive measures.

Single infections with foodborne and orofecally transmitted infections like *Helicobacter pylori*,¹⁰⁻¹³ *Toxoplasmosis gondii*, and hepatitis A virus (HAV)¹⁴⁻¹⁹

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Abbreviations used

BMI:	Body mass index
ECRHS:	European Community Respiratory Health Survey
HAV:	Hepatitis A virus
HSV-1:	Herpes simplex virus 1
OR:	Odds ratio
PAR:	Population attributable risk
RR:	Risk ratio
TIM:	T-cell immunoglobulin and mucin domain-containing molecule

have all been associated with less subsequent atopy and respiratory allergies, but results have not been consistent.²⁰⁻²⁵ In some studies, airborne infections like lower respiratory tract illnesses,²⁶ tuberculosis,²⁷ and measles²⁸ appear to exert a protective effect on atopy. However, studies on BCG vaccination, rubella, mumps, and varicella²⁹; BCG vaccination and atypical mycobacteria³⁰; and repeated infections early in life³¹ have shown no effect on atopy.

In view of the complexity of the association between hygiene and allergy and the multiple associated immunologic mechanisms, it is unlikely that studies of single microbes in diverse populations will contribute much to unravel the hygiene hypothesis. A more promising epidemiologic model is to study accumulated effects of multiple infections with different modes of action on the immune system. This is also a more natural model because single microbes very rarely travel alone; they can be regarded as a proxy for hygiene, overcrowding, and poverty; and multiple microbes are a better proxy than single ones. Studies using this approach in populations from Italy,¹⁴ the United States,¹⁷ Denmark,¹⁸ and Finland-Russia²⁵ have supported the main assumptions of the hygiene hypothesis but with different contributions from the various microbes.

The aim of the current study was to clarify the role of microbial exposure in the allergy epidemic, both for single microbes and combinations and for accumulated effects. The seroprevalence of 7 microbes was assessed and regarded as a surrogate marker of the load of orofecal-foodborne and contact-airborne infections and as an indicator of the factors modulating the immune responses.

METHODS

Study sites and population

The European Community Respiratory Health Survey (ECRHS)-I³² has been a project to study geographical differences in the prevalence and incidence of asthma and atopy and their risk factors in young adults. Individuals age 20 to 44 years were randomly selected during the period 1990 to 1994 from the population of 22 nations at 48 study sites. Interviews were performed and blood samples collected (www.ecrsh.org).

Our study population is composed of all subjects living in Reykjavik, Uppsala, and Tartu who participated in ECRHS I and were invited for a repeated study in 1999 to 2001 (ECRHS II).³³ Out of a total of 2033 participants in the ECRHS I from Reykjavik,

Uppsala, and Tartu, 1620 (76.6%) participated in ECRHS II. The median length of follow-up was 8.4 years. Blood samples for determination of microbe seroprevalence were collected from 1249 subjects, 595 men and 654 women, of whom 499 were from Reykjavik, 475 from Uppsala, and 275 from Tartu. The appropriate Ethics Committees' approvals were obtained in all countries.

Serologic methods

IgG antibodies against microbial agents were measured by using commercially available immunoassays. *H pylori* status was determined by the presence of anti-*H pylori* IgG antibodies using Captia *H pylori* IgG ELISA from Trinity Biotech, Bray, Ireland. The presence of *T gondii* IgG antibodies was determined by an ELISA method with reagents obtained from Novatec Immundiagnostica GmbH, Dietzenbach, Germany. The presence of HAV IgG antibodies was measured by competitive electrochemi-luminescence immunoassay with an Elecsys 2010 automated instrument (Roche, Switzerland). ELISA methods were also used to determine the presence of IgG antibodies against EBV (viral capsid antigen), herpes simplex virus 1 (HSV-1), and of IgG antibodies against cytomegalovirus and *Chlamydia pneumoniae* with reagents from Immuno Biological Laboratories, Hamburg, Germany. Serum samples that gave indefinite results in antibody measurements were always classified as seronegative.

Definition of infectious load

A cumulative index of exposure (IgG seropositivity) for all 7 microorganisms was calculated. A low infectious burden was arbitrarily defined as having positive IgG antibodies to ≤ 3 microorganisms. For the 3 orofecal-foodborne microbes (HAV, *H pylori*, and *T gondii*), a low infectious load was defined as not having any positive IgG antibodies (<1), while having ≤ 2 was used as the cutoff value for the contact/airborne infections (HSV-1, EBV, *C pneumoniae*, and cytomegalovirus).

Questionnaire

The subjects underwent a structured interview that included detailed information on smoking history, occupation, and early life exposure. From the questionnaire, the subjects were divided into 3 smoking history categories: never-smokers, ex-smokers, and current smokers. The following early life exposure variables were included in the analysis: mother's age when the participant was born, hospitalizations before the age of 5 years for lung disease, age when attending day care, bedroom sharing with other children before the age of 5 years, pets during childhood, and rural versus urban living when under the age of 5 years. A more detailed description of the early life variables can be found in this article's Table E1 in this article's Online Repository at www.jacionline.org.

Socioeconomic status was defined from information on the subject's occupation provided during ECRHS I according to the United Kingdom social classification.³⁴ Using this classification, the subjects were divided into (1) professionals and semiprofessionals, (2) skilled nonmanual workers, (3) skilled manual workers, (4) unskilled manual workers, and (5) undefined. Current pet keeping was assessed with the questions, "Do you keep a cat?" and "Do you keep a dog?"

Body mass index

Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters.

Allergy testing and definitions of allergy and asthma

Total and specific serum IgE was determined by using the Pharmacia CAP System (Pharmacia Diagnostics, Uppsala, Sweden).

TABLE I. Characteristics of nonatopic and atopic subjects (means $\pm$ SDs and percentages) and the prevalence of positive serology for orofecal-foodborne and contact-airborne infections

	Nonatopic (n = 922)	Atopic (n = 327)	P value	All
Age (y)	42.4 $\pm$ 7.2	40.9 $\pm$ 7.3	.002	42.1 $\pm$ 7.2
Women	54.8	43.8	.001	52.0
Smoking history			.008	
Ex-smokers	31.3	25.7		29.9
Current smokers	28.1	23.9		26.2
BMI (kg/m ²)	25.7 $\pm$ 4.3	25.5 $\pm$ 4.5	.69	25.6 $\pm$ 4.3
Orofecal/foodborne infections				
<i>H pylori</i>	36.6	24.8	<.001	33.5
HAV	13.6	15.8	.32	14.1
<i>T gondii</i>	26.2	22.6	.21	25.2
No orofecal-foodborne infections	45.6	54.1	<.008	47.8
Contact/airborne infections				
HSV-1	76.7	67.4	.001	74.3
EBV	90.9	88.1	.15	90.1
<i>C pneumoniae</i>	68.0	58.8	.002	65.6
Cytomegalovirus	81.0	74.6	.01	79.3
Two or fewer	21.1	31.4	<.001	23.8
contact/airborne infections				
≤ 3 All infections	34.8	51.7	<.001	39.2

In all centers, specific IgE was measured against *Dermaphagoides pteronyssinus*, timothy grass, cat, and *Cladosporium herbarum*.

Detection of specific IgE (>0.35 kU/L) was used as the definition of sensitization. Atopy was defined as being sensitized to any of these allergens. Ever-asthma was defined as ever having physician-diagnosed asthma, whereas current asthma was defined as having ever-asthma and having had asthma-related symptoms or attacks of asthma in the preceding 12 months.³⁵ Allergic asthma was defined as being atopic and having ever-asthma or current asthma. Allergic rhinitis was defined as being atopic and answering yes to the question, “Do you have any nasal allergies, including hay fever?” The degree of sensitization was defined by using a continuous variable—sum of specific IgE—that was defined as the sum of the specific IgE titers for the investigated allergens.³⁶ A titer below the detection level (<0.35 kU/L) was arbitrarily given the value 0.17 kU/L.³⁷

Bronchial responsiveness

Methacholine challenge was performed by using a dosimeter (Mefar, Brescia, Italy). The level of bronchial responsiveness was expressed by using a dose response slope.³⁸

Statistics

Adjusted odds ratios (ORs) were calculated by logistic regression. The final model included only socioeconomic and childhood exposure values that were significantly associated with atopy. The adjusted ORs and 95% CI were first analyzed on pooled data from all 3 centers, adjusting for center, and then calculated separately at each center. Potential heterogeneity between centers was examined by using standard methods for random-effects meta-analysis.³⁹ The association between continuous variables (bronchial responsiveness, total IgE, and sum of specific IgE) and infectious burden was made with multiple linear regression including the same confounders described. In these analyses, total IgE and sum of specific IgE were log-transformed. The proportion of atopy, allergic asthma, and rhinitis in the population that could be explained by a low number of infections was calculated as the population attributable risk (PAR). The adjusted risk ratios (RRs) were calculated by generalized linear

modeling. PAR was calculated using the formula (PAR) = proportion of cases exposed multiplied by (RR-1/RR).³⁹

RESULTS

There were 1249 subjects included in the study, 595 men and 654 women, of whom 499 were from Reykjavik, 475 from Uppsala, and 275 from Tartu. Mean age was 42.1 ± 7.2 years (Table I). Nonatopic subjects were significantly older and more often smokers than atopic subjects, and they more often had positive serology for *H pylori*, HSV 1, *C pneumoniae*, and cytomegalovirus. Nonatopic subjects were also more likely to have a low infectious load of both foodborne and airborne/contact-related microbes (Table I).

Atopic subjects had a lower mean number of infections than nonatopics (3.5 ± 1.4 vs 3.9 ± 1.3 ; $P < .001$). The atopic/nonatopic ratio was >1 in subjects having 0 to 3 infections but <1 in subjects with 47 infections (Fig 1).

Having a low number of IgG antibodies against the various infectious agents (≤ 3) was an independent risk factor for atopy, rhinitis, ever-asthma, and current allergic asthma after adjusting for age, sex, center, smoking history, BMI, pet keeping in childhood, childhood hospitalizations, and mother's age (Fig 2). A low infectious burden was also independently related to the degree of sensitization but not to total IgE (Table II). There was a negative association between sum of specific IgE and the number of IgG antibodies (β coefficient, -0.049 [$-0.07, -0.03$]; $P < .0001$), whereas no significant association was found between the number of IgG antibodies and total IgE (Table II). No significant association was found between infectious burden and bronchial responsiveness. There was no significant difference between

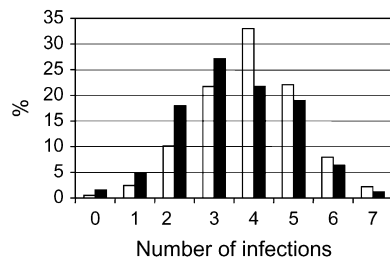


FIG 1. Proportion of subjects having positive serology for 0 to 7 infectious agents. The atopics are shown in *black* and the non-atopics in *white*.

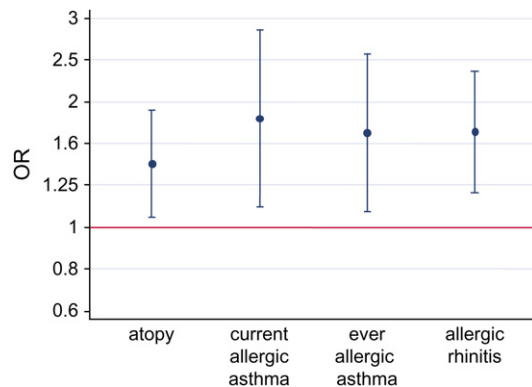


FIG 2. Odds ratios and 95% CIs for atopy, current allergic asthma, ever-allergic asthma and allergic rhinitis in subjects with low number of IgG antibodies against the various infectious agents (≤ 3). The ORs are adjusted for age, sex, center, smoking history, BMI, pet keeping in childhood, childhood hospitalizations, and mother's age.

the centers for the association between a low infectious burden and atopy (Fig 3), and the same was true for the association between low infectious load, allergic asthma, and allergic rhinitis (P for heterogeneity = .21 and .47, respectively).

The association between allergy and orofecal-food-borne versus contact-airborne infections is presented in Table III. The adjusted ORs were generally in the same magnitude for the 2 types of transmissions.

Uppsala had the highest proportion of atopics and subjects with a low number of IgG antibodies against infections. The proportion of atopy, allergic asthma, and allergic rhinitis in the population that could be explained by a low number of infections is presented in Table IV.

Subjects that participated in the current study were slightly older, had a higher BMI, and had a higher prevalence of current asthma and rhinitis than subjects who only participated in ECRHS I (see this article's Table E2 in the Online Repository at www.jacionline.org).

DISCUSSION

Our study showed that accumulated microbial burden was inversely related to the prevalence of atopy and

TABLE II. Geometric mean (95% CI) for the sum of specific IgE (*D pteronyssinus*, timothy grass, cat, and *C herbarum*) and total IgE in subjects with ≤ 3 and > 3 IgG antibodies against all infections*

	≤ 3 IgG	> 3 IgG	Adjusted P value
Sum of specific IgE	1.45 (1.29-1.62)	0.99 (0.93-1.06)	.017
Total IgE	33.0 (29.1-37.4)	31.9 (28.9-35.2)	.61

*The P value is adjusted for age, sex, center, smoking history, BMI, pet keeping in childhood, childhood hospitalizations, and mother's age.

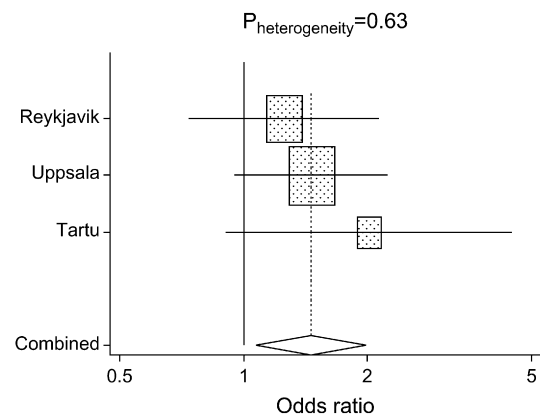


FIG 3. Odds ratios and CIs for the association between low number of IgG antibodies against the various infectious agents (≤ 3) and atopy in the 3 centers. The combined random effects estimate is shown by the *dashed line*. The OR is adjusted for age, sex, center, smoking history, BMI, pet keeping in childhood, childhood hospitalizations, and mother's age.

respiratory allergies in all 3 populations studied. Cumulative effect is indicated by the fact that the atopic/nonatopic prevalence ratio was > 1 in subjects with a relatively low microbe load (0-3 microbes), whereas the ratio was < 1 in subjects with a high load (4-7 microbes). The high infectious burden protected against atopy, allergic rhinitis, and allergic asthma. Subdivision into orofecal-foodborne infections (*H pylori*, HAV, and *T gondii*) and contact-airborne infections (HSV-1, EBV, *C pneumoniae*, and cytomegalovirus) showed no significant difference between the 2 groups. The microbes HSV-1, EBV, *C pneumoniae*, and cytomegalovirus are associated with close contact and can be characterized as contact-airborne and markers of overcrowding.^{40,41} All findings were unaffected after adjusting for early life exposure and demographic and social characteristics, and there was no significant difference between the centers regarding the associations between infections and atopy.

There are 4 main new findings in this study.

1. The protective effect of infectious burden is not confined to so-called "orofecal infections."
2. Hepatitis A virus does not provide a protective effect.

TABLE III. Odds ratios for atopy, allergic asthma, and rhinitis in subjects with IgG antibodies against no foodborne and 0 to 2 airborne microbes*

	Foodborne <1	Airborne ≤2
Atopy	1.21 (0.90-1.63)	1.21 (0.88-1.66)
Allergic asthma	1.40 (0.87-2.26)	1.16 (0.71-1.88)
Allergic rhinitis	1.31 (0.94-1.83)	1.18 (0.83-1.67)

*Adjusted for age, sex, center, smoking history, BMI, pet keeping in childhood, childhood hospitalizations, and mother's age.

3. The break point for accumulated protective effect was >3 microbes, which has not been well defined in previous studies.
4. The negative association between infections and IgE sensitization was also found when specific IgE was expressed as a continuous variable, whereas no association was found between IgG antibodies and total IgE.

There are 4 previous studies that focus on infectious burden, atopy, and respiratory allergies using material and methodology similar to those of the present one. The studies are from Italy,¹⁶ the United States,¹⁷ Denmark,¹⁸ and Finland-Russia.²⁵ In our study, atopy was defined as a positive response (specific IgE > 0.35kU/L) to any of 4 allergens tested. The same criteria were used in the Danish study,¹⁸ but 6 allergens were tested. A skin prick test with 10 to 11 allergens was used in the Italian,¹⁶ US,¹⁷ and Finnish-Russian²⁵ studies. These methods should give comparable measures of atopy. All the studies were based on adult populations and had a cross-sectional design. Measurements of IgG antibodies were used to estimate the microbial load and questioners or interviews used to assess allergies and respiratory symptoms. The Italian,¹⁶ Danish,¹⁸ and US¹⁷ studies tested developed populations, whereas the Finnish-Russian²⁵ and the current study covered populations with a wider spectrum of socioeconomic development.

The main findings of our study are that a cumulative effect of infections is protective against atopy and respiratory allergies. In contrast with the Italian study,¹⁶ we found that infection with the contact-airborne microbes HSV-1, EBV, *C pneumoniae*, and cytomegalovirus had a protective effect on atopy similar to that of the orofecal-foodborne microbes. The Italian study¹⁶ showed that accumulated effect from airborne microbes, measles, mumps, rubella, chickenpox, cytomegalovirus, and HSV-1 increased the risk of atopy. The characteristics of these microbes can be described as highly infectious-airborne in the Italian study¹⁶ and close contact—overcrowding—related in our study. It is of interest that HSV-1 was significantly associated with protection against atopy in the US study,¹⁷ as also found in our study.

The Italian,¹⁶ US,¹⁷ and Danish¹⁸ studies showed dose-related protection of atopy and respiratory allergy with orofecal-foodborne microbial load, unlike the findings of the current study. Compared to the 3 studies,¹⁶⁻¹⁸ the

TABLE IV. Prevalence and PAR for having IgG antibodies against (≤3) microbial agents in Reykjavik, Uppsala, and Tartu

	Reykjavik	Uppsala	Tartu
Prevalence			
Infections (≤3)	32.1	60.7	15.9
Atopy	16.9	37.2	22.8
PAR			
Atopy	6.7	16.4	9.2
Allergic asthma	6.7	33.4	48.2
Allergic rhinitis	26.5	19.0	18.6

prevalence of HAV infection was low in our study (14 %), and more than half of the positive subjects came from Estonia. This may have decreased the power of our study to detect a significant relationship between orofecal-foodborne microbial load and atopy. HAV infection contributed to the protective effect on atopy from orofecal-foodborne infections in the Italian,¹⁶ Danish,¹⁸ and US¹⁷ studies. The Finnish-Russian²⁵ study did show a protective effect on atopy from orofecal-foodborne infections on the basis of *H pylori* infection, but HAV infection had the opposite trend, a result that was also seen in the current study. The studies that have shown a protective effect associated with HAV infection have been predominantly from developed populations,^{16,17-19} whereas others not showing a protective effect have been mostly from underdeveloped populations.^{20-24,42} Orofecal-foodborne infections are regarded as an accumulated proxy for microbial exposure associated with unhygienic social or household conditions. The HAV, however, may be not only a surrogate marker of poor hygiene but also a direct immune modulator. The receptor for the HAV is T-cell immunoglobulin and mucin domain-containing molecule (TIM)-1. This receptor and its ligand, TIM-4, belong to a family of proteins that are involved in the regulation of CD4 T-cell differentiation, airway inflammation, and airway hyperresponsiveness.^{43,44} It is an enigma why HAV infection has such an inconsistent effect on atopy in different populations. One possible explanation may relate to different times of infection in populations with different degrees of Westernization, resulting in variable modulation of the immune system. Further confounding factors are the multiple mechanisms through which HAV infection can affect the phenotypes of allergic disease. HAV infection is also of short duration, and the microbe is permanently eliminated, whereas most of the other microbes produce a lifelong infection.

The current study indicated that *H pylori* has a protective effect against atopy, as does the Finnish-Russian study,²⁵ in which *H pylori* infection accounted for a substantial part of the difference in atopy prevalence between Finland and Russia.

The current study showed that the low microbe load contributed to the atopy and respiratory allergy prevalence to different degrees in the 3 countries. The proportion of atopy in the populations that can be explained by a lower

number (≤ 3) of infections was 6.7% in Iceland, 9.2% in Estonia, and 16.7% in Sweden, whereas the corresponding figures for allergic asthma were 6.7%, 48.3%, and 33.4%, respectively (Table III).

Our study site was the Nordic Baltic Region, and the populations today span the spectrum from highly developed (Sweden, Iceland) to moderately developed (Estonia).⁴⁵ More importantly, during the childhood period of the study populations, around 1970, the populations spanned the spectrum from developed (Sweden and Iceland) to relatively underdeveloped (Estonia).⁴⁵ Previous studies have shown differences in the intestinal microflora between children in Sweden and Estonia,⁴⁶ which can be regarded as an indicator of different degrees of Westernization of the 2 countries. The current study confirms and expands results from previous studies and shows the protective effect of infections on atopy in 3 populations with different degrees of Westernization. The division of infections into orofecal-foodborne versus contact-airborne may be too simplistic to contribute to understanding of the complex interplay between infections and the immune system.

The mechanism of protection may possibly be explained by multiple and chronic ligation of Toll-like receptors with microbial components. Toll-like receptors are expressed predominantly on cells of the immune system such as dendritic cells, macrophages, neutrophils, and monocytes. The multiple and chronic ligation may also explain the accumulated effect of microbes shown in our study. *H pylori* is a Gram-negative bacteria; *T gondii* and *C pneumoniae* are intracellular parasites; and HAV, HSV-1, EBV, and cytomegalovirus are viruses, and most of these microbes ligate different Toll-like receptors.⁴⁷ The break point for accumulated protective effect may be >3 ligations, as shown in Fig 1.

The main weakness in this study is that it is not possible to draw firm conclusions on the cause-effect association between infections and atopy because this is a cross-sectional epidemiologic study. Also, we cannot totally rule out selection bias because we did find that subjects with allergic symptoms were slightly more likely to participate than those without asthma and rhinitis. Nevertheless, our data are consistent with a cumulative protective effect of infections against atopy and respiratory allergies in Iceland, Estonia, and Sweden irrespective of route of infection.

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TABLE E1. Wording of early life variables

[Q18]. Mother's age	Were you hospitalized before the age of 5 years for lung disease?
Hospitalization	Did you have a serious respiratory infection before the age of 5 years?
Day care	At what age did you first attend a school, play school, day care, or nursery?
Bedroom sharing	How many <i>other</i> children regularly slept in your bedroom before you were 5 years old?
Dog	Was there a dog in your home? (First year, 1-4, 5-15 y)
Cat	Was there a cat in your home? (First year, 1-4, 5-15 y)
Urban or rural	What term best describes the place you lived most of the time when you were under the age of 5 years? (Rural: farm/l village in rural area; urban: small town, suburb of a city, inner city) [Q19].

TABLE E2. Characteristics of participants and nonparticipants based on data collected in the European Community Respiratory Health Survey I (1990-1994)

	Participant (n = 1249)	Nonparticipant (n = 784)	P value
Age (y)	33.7 ± 7.2	32.1 ± 7.0	<.0001
Women, mean age (y)	52.1	54.1	.34
Smoking history			.12
Exsmokers	21.8	19.6	
Current smokers	32.4	36.8	
BMI	24.0 ± 3.9	23.2 ± 3.7	.0001
Ever-asthma	12.8	9.6	.03
Nasal allergy	31.3	23.6	<.0001