Correlations Between Allergic and Infectious Diseases – Results of the Latest German National Health Survey (NHS98) and the German Health Interview and Examination Survey for Children and Adolescents (KiGGS)

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Abstract: In the literature, according to the hygiene hypothesis, infections should be expected to correlate with fewer allergies. However, several studies clearly show that infections – especially infections of the upper respiratory tract – and surrogate parameters such as the use of antibiotics or paracetamol correlate with a higher rate of allergies. This article reviews the literature (50 articles are analyzed) on possible connections between infections and allergies and offers some possible explanations. Original data from population-based health interviews and examination surveys of adults, children and adolescents are added. These data show a clear correlation between most infections and an enhanced allergy rate. Nevertheless, although the correlastions obtained seem intriguing, it has to be kept in mind, that no clear direction of the correlations can be stated since the database does not allow for such interpretation. So, the data do not necessarily add to the picture of the hygiene hypothesis, as the infections could have followed the allergies. The probability of suffering from an allergy rises with the number of infections (or vice versa) a person has had (e.g. the risk for adults of developing asthma is enhanced to 1.3 CI-95% 1.2-1.4 with enhanced numbers of former infections with pertussis, chickenpox, scarlet fever, dysentery or typhoid/paratyphoid). This applies especially to pertussis (e.g. 15.8% CI-95% 13.6-18.3% of children with hayfever had pertussis versus 7.6% CI-95% 6.9-8.3% of the healthy children) and chickenpox infections (e.g. 84.7% CI-95% 82.7-86.6% of children with hayfever had chickenpox versus 66.8% CI-95% 65.8-67.8% of the healthy children), both of which are preventable by vaccination.

INTRODUCTION

CORRELATIONS BETWEEN INFECTIONS AND ALLERGIES/ASTHMA

Although no longer undisputed, the hygiene hypothesis forms a basis for possible explanations of the increase in allergic diseases, including allergic bronchial asthma, in countries with western standards of living. The following literature review presents hypotheses for possible correlations between infections and allergic diseases. Although infections should be expected – according to the hygiene hypothesis – to correlate with fewer allergies, many studies show the contrary. Some infections seem to reduce allergies, while others seem to enhance allergic diseases or elsewise allergies and infections seem to be linked by deficiencies of the immune system.

There is a considerable amount of data showing that children who grow up with older siblings, in rural areas or with domestic animals, or go to a nursery or crèche, are less likely to develop allergies in later life than children where this is not the case [e.g. 1]. These parameters are interpreted as surrogate parameters for early childhood infections. The hypothesis is linked with findings on immunological development in early childhood. T-cells can differentiate into two different cell types, with T(H2) cells associated with allergic diseases and T(H1) cells with anti-infective defences. This seems to suggest that if there is a lack of stimulation towards T(H1) differentiation as a result of fewer infections in early childhood, the T(H2) response could predominate and thus promote the development of allergic diseases.

It has since been recognized that these interrelations seem not always that simple. By no means all infections in early childhood seem to lead generally, or when added together, to a reduction in allergic diseases. Many possible modifications to the initial hypothesis have since been suggested.

In the case of bronchial asthma it seems that certain infections – e.g. of the respiratory tract [2-8] and the ear [9] – actually increase the risk rather than reducing it. But here, too, there are qualifications. For example, it is suspected that it is not the infections themselves, but the use of antibiotics and paracetamol that might be connected with an increase in asthma cases [6, 7, 10]. And it is uncertain whether the antibiotics themselves are the cause of the increase or whether the need to consult a doctor to obtain antibiotics leads to an earlier diagnosis of allergic diseases [11]. Furthermore, it seems more likely that acute respiratory infections increase the risk, whereas prolonged, intermittent infectious diseases/infections reduce it [12].

In other studies, the impact of past infections on the subsequent development of allergic diseases seems to vary according to the kind of infection. It is thought that infections involving intracellular pathogens in particular, such as tuberculosis, measles and hepatitis, generate a strong T(H1) response and can thus have a protective effect [13]. Infections of the intestinal, respiratory and urinary tracts are believed to

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be particularly related to food allergies [14], parasitic infections of the intestines to allergic skin diseases [15]. Even neonatal sepsis seems to reduce the rate of later allergic diseases in predisposed children [16].

However, the connection between infections and allergies could also be very different. The quoted work [17] points out that both the T(H1) and the T(H2) response might be disturbed in allergy sufferers, and this then results in allergies and infections. Fitting into this picture, the quoted study [18] shows that sensitized test persons show not only an increased T(H2) response, but also an increased T(H1) response (to diphtheria and tetanus toxins).

We hope to be able to add another piece of the puzzle to the described picture, although our database does not allow for giving proof of the direction of correlations between infections and allergies. But as our data were collected from nationwide and, to the greatest possible extent, representative investigations and surveys among adults, children and adolescents and we are able to confirm clear positive correlations between infections and allergies, may they be directed from infections to allergies or may they show that allergies are followed by an increase of infectious diseases, we are convinced that these data will be helpful in generating hypothesis for former longitudinal studies.

Conclusion: All in all, the results of the enormous number of studies in the field of possible correlations between infectious and allergic diseases are contradictory, as illustrated by the above-mentioned studies. This situation has led one author [19] to conclude that not specific infectious diseases encourage or discourage the development of allergies, but that everything depends on the infection pattern and on the time in a person's life when the respective infection occurs.

CORRELATIONS BETWEEN SPECIFIC INFECTIOUS DISEASES AND ALLERGIES/ASTHMA

In our studies, people were queried on whether they had had pertussis, measles, mumps, rubella, chickenpox or scarlet fever in the past. We also asked about diphtheria, tuberculosis and typhoid or paratyphoid among the adults, and mononucleosis, herpes and salmonellae infections and hepatitis among the children. There are also reports in literature on possible correlations between vaccinations for various diseases including some of the above-mentioned infections (e.g. against diphtheria, tuberculosis and measles/mumps/rubella) on the one hand, and allergic diseases on the other. These reports are also considered in the following. Analyses on vaccination patterns in our study will have to follow later.

In the literature, the risk of asthma is supposed to decrease after an infection with rubella, but not with pertussis [20]. The weak impact of mononucleosis infections on allergic sensitization [21] has not been sufficient to explain existing differences in sensitization rates between western and eastern Germany. Atopias are supposed to be rarer after food-borne or orofaecal infections, but not after infections such as measles, mumps, rubella or chickenpox [22]. Early measles infections are also supposed to have a protective effect against wheezing [23]. Another study [24] discovers that scarlet fever provides protection from the risk of allergic sensitization in general, and chickenpox from sensitization to grasses. The overall risk of allergic sensitization grew with the number of childhood diseases a person had had. Chickenpox infections are reputed to lead to an improvement in existing neurodermatitis.

The considerable amount of existing literature on possible correlations between tuberculosis and sensitization or atopic diseases seems in general to suggest that a past tuberculosis infection will tend to protect a person against allergies. The same applies to asthma [25]. Results of the ISAAC (International Study of Asthma and Allergies in Childhood) study showed that asthma and allergies were rarer among 13-to-14-year-olds in countries where tuberculosis was more common. Although the results have been confirmed overall by an extended study, the trend towards a reduction in asthma seemed to be more pronounced among individuals who had had tuberculosis at a young age; it seemed to diminish later [26]. More recent results suggest that it would be worthwhile to examine the sex distribution of the two age groups, because that study found that childhood tuberculosis infections only protected women against asthma and allergies, but not men [27].

There are also indications of negative correlations between atopic diseases and herpes infections and hepatitis A in combination with other infections [28-30]. There are hardly any correlations in the case of vaccinations, and where they do exist they are usually only weak positive correlations with asthma or allergies. We would like to explicitly emphasize here, however, that the blessings of the vaccinations that are administered today would still far outweigh any slight risk of a certain increase in sensitizations and atopic diseases.

In addition to many studies that have found no increased risk of atopies after vaccinations [31-39], there are some works which suggest that a certain risk might be possible. A greater risk of allergy-induced respiratory-tract symptoms was observed after DTP (diphtheria, tetanus and polio) and tetanus-only vaccinations among children [40]; a greater risk of asthma (23.1%) and allergies (30%) was also observed after DTP and polio-only vaccinations; but although the unvaccinated comparison group shows an impressive 0% risk, the group size of n = 23 is very small [41]. Another author has been engaged in research relating to the above-mentioned desire to determine patterns, describing that the DPT vaccination only represents an asthma risk if it is not preceded by a BCG (tuberculosis) vaccination [42]. Another pattern is described finding no increase in the risk of asthma or atopy from individual vaccinations against measles, mumps, rubella, DTP, hepatitis B and polio among young adults, but a weak correlation between full immunization and asthma.

Protection against asthma and allergies is discussed particularly in relation to BCG and pertussis vaccinations. In the case of the pertussis vaccination it seems plausible that avoiding pertussis might represent a protection against asthma [43, 44]; however, atopic diseases in general are also supposed to be rarer after a pertussis vaccination (depending partly on the vaccine used) [44, 45]. A BCG vaccination seems able to reduce the risk of later allergic diseases [46, 47], although there is still disagreement over whether the

frequency of atopies, allergic rhinitis and asthma in later life is affected by the age when a person has the BCG vaccination. This was not the case in a study that compared vaccination at the ages of 1 and 7 [48]. Individual authors have also tried to identify patterns in this research field. In a study of 12-to-16-year-olds, although no association was found between a BCG vaccination in childhood and asthma and allergies in general, the frequency of asthma in patients with pre-existing allergic rhinitis was 37% lower after a BCG vaccination than among those who had not had such a vaccination [49]. It was observed that when a person with pre-existing asthma was given a BCG vaccination, this also led to a clinical improvement in lung function, and that a booster vaccination a year later could increase this effect [50]. Other authors have also found a clinical improvement in existing asthma after a BCG vaccination [51]. This led to an attempt to make therapeutic use of the observed benefit. Several authors have tried to use heat-deactivated mycobacteria or their active components to improve bronchial asthma [52, 53].

Most of the a.m. studies deal with children or very young adults and do not have a data base that is representative of the population. Rather, their data were collected in a small number of national centres. For this reason, we would like to complement the existing data situation by adding an overview of possible correlations between the above-mentioned factors in the adult German population of 1998 and current data on children and adolescents aged between 0 and 17 years, even though we are aware that the informative value of the studies is limited by the survey methodology.

Conclusion: Although the picture offered by the available data on possible correlations between past infections on the one hand, and bronchial asthma and allergic diseases or sensitization on the other, is still not homogenous, it clearly indicates that certain patterns of infections, including their sequence and timing in (early) childhood, could certainly be closely related to the risk of allergic diseases.

DATA MATERIAL AND METHODS

Publications are available on the methods used in the two health surveys – NHS98 and KiGGS – including response and weighting [54, 55]. Complete data sets on 6,973 participants between the ages of 18 and 79 from the NHS98 data pool, and 17,641 participants aged between 0 and 17 from the KiGGS survey were used for this study.

To identify allergic disorders, we used the test persons' replies to questions asked in a computer-assisted medical interview (CAPI) on whether they had been diagnosed with the corresponding diseases. The data on past infections were taken from the respective self-completed forms (or, depending on the children's age, from forms filled in by the parents in the case of KiGGS).

Versions 12.0 and 14.0 of the "Statistical Package for the Social Sciences" (SPSS) for Windows were used to evaluate the available data sets. Correlations between allergies and bronchial asthma on the one hand and the individual infections queried on the other were studied using cross-tabulation; all variables were included in the regression models. The KiGGS data were evaluated using complex-samples procedures.

Because of the necessary weightings by age, sex and residence in western or eastern Germany, the absolute figures for NHS98 deviate slightly from the number of data sets; this also applies for KiGGS as a result of the use of the complex samples.

Conclusion: Data from two national health studies in adults, children and adolescents as far as possible representative for the German population are presented.

RESULTS

NHS98

The prevalence of the allergic diseases studied here and bronchial asthma, as well as their distribution over important socio-demographic impacting factors, has already been described in detail elsewhere [56].

431 (6.2%) of the test persons had had diphtheria, 1,590 (23.0%) pertussis, 4,354 (63.0%) measles, 3,258 (47.2%) mumps, 2,218 (32.2%) rubella, 3,656 (52.9%) chickenpox, 1,005 (14.6%) scarlet fever, 157 (2.3%) tuberculosis, 88 (1.3%) dysentery and 90 (1.3%) typhoid/paratyphoid. It can be seen that the sample sizes are large enough to search for correlations with existing allergic diseases, with the exception of dysentery and typhoid/paratyphoid where the absolute numbers in the table cells are very small. This will be noted in the following analysis where appropriate.

In the analysis using cross-tabulation (see Table **1** respectively), bronchial asthma predominantly shows a positive correlation with past infections; i.e. the more common the infection, the more common the bronchial asthma and vice versa. This correlation is significant for pertussis, chickenpox, scarlet fever and typhoid/paratyphoid. With rubella there is a negative correlation that is numerically distinct, but not quite numerically significant.

An analysis of correlations between all the infections in the model (multiple logistic regression) and bronchial asthma – after adjusting for age, sex, residence in eastern or western German, rural or urban residence and social strata – only shows a significant positive correlation for chickenpox (OR 1.7 CI-95% 1.1-2.5), but a significant negative correlation for diphtheria (OR 0.5 CI-95% 0.3-0.9) and rubella (0.7 CI-95% CI 0.5-1.0).

A small but significant risk (OR 1.1 CI-95% 1.0-1.2) already results if the number of diseases a person has had (omitting diphtheria and rubella) is related to bronchial asthma in the logistic regression. If only the infections that show a positive correlation are counted (pertussis, chickenpox, scarlet fever, dysentery, typhoid/paratyphoid), irrespective whether this correlation is significant or not, there is a more marked risk of 1.3 CI-95% 1.2-1.4.

In the case of hay fever, too, the bivariate evaluation predominantly shows a positive correlation with past infections. This correlation is significant in the case of pertussis, rubella, chickenpox and scarlet fever.

The multivariate regression model (the adjustment factors are always as described above under bronchial asthma) shows a significant positive correlation between hay fever and pertussis (OR 1.3 CI-95% 1.1-1.7) and chickenpox (OR 1.6 CI-95% 1.2-2.1).

Table 1. Correlations Between Infectious and Allergic Diseases (NHS98) *

Numbers in %		Asthma		Hay Fever		Contact Eczema		Neurodermatitis		Food Allergy		Urticaria	
		Yes	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**
Diphteria	Yes	8.3	6.1	5.9	6.3	4.7	6.5	5.0	6.3	4.3	6.4	6.4	6.2
Pertussis	Yes	**30.2**	**22.6**	**27.4**	**22.2**	**29.0**	**22.0**	26.0	22.9	**33.2**	**22.4**	34.6	22.0
Measles	Yes	61.5	63.1	66.0	62.4	**66.1**	**62.5**	60.3	63.1	**67.5**	**62.7**	71.7	62.2
Mumps	Yes	47.2	47.2	49.7	46.7	**53.1**	**46.1**	45.4	47.2	**52.9**	**46.8**	51.4	46.8
Rubella	Yes	28.5	32.4	**35.8**	**31.5**	**37.2**	**31.3**	**39.5**	**31.9**	**38.1**	**31.8**	40.1	31.5
Chickenpox	Yes	**63.0**	**52.5**	**66.4**	**50.4**	**65.1**	**50.8**	**65.7**	**52.5**	**67.9**	**52.0**	62.3	52.1
Scarlet fever	Yes	**17.5**	**14.4**	**16.5**	**14.2**	16.0	14.4	19.5	14.4	15.1	14.6	20.4	14.1
Tuberculosis	Yes	3.0	2.2	3.2	2.1	2.9	2.2	2.9	2.2	2.0	2.3	2.7	2.2
Dysentery	Yes	1.5	1.3	1.0	1.3	0.8	1.3	2.1	1.2	1.3	1.3	1.8	1.2
Thyphus Paratyphoid	Yes	**2.8**	**1.2**	0.8	1.4	1.1	1.3	0.8	1.3	1.5	1.3	1.6	1.3

* The percentage figures relate to the test persons who have the above-mentioned allergic diseases (e.g. asthma – diphtheria: 8.3% of the test persons with asthma once had diphtheria, compared to only 6.1% of the test persons who do not suffer from asthma). Figures in bold type show significant differences.

The total number of all past diseases the person has had already shows a significant positive correlation with hay fever (OR 1.1 CI-95% 1.1-1.2). If only the infections that show a positive correlation are included (pertussis, measles, chickenpox, tuberculosis, dysentery), the risk is more marked at 1.2 CI-95% 1.1-1.3.

Allergic contact dermatitis also shows predominantly positive correlations with individual past infections. This correlation is significant for pertussis, measles, mumps, rubella and chickenpox respectively.

The multivariate regression model only confirms a significant positive correlation between allergic contact dermatitis and pertussis (OR 1.4 CI-95% 1.1-1.7).

The total number of all past diseases the person has had shows a significant positive correlation with allergic contact dermatitis (OR 1.1 CI-95% 1.0-1.1). If only the infections with a positive correlation are included (pertussis, measles, mumps, rubella, chickenpox, tuberculosis), the risk is hardly higher and also rounded to 1.1 CI-95% 1.0-1.1.

The picture as regards neurodermatitis is more varied than with the allergic diseases considered up to now; many past infections seem to be unrelated to the disease. Significant positive correlations exist only with rubella and chickenpox. There is a significant negative correlation with diphtheria, although the sample size is small: only 12 test persons in the group of patients with neurodermatitis have had diphtheria.

The correlations between neurodermatitis and scarlet fever (OR 1.6 CI-95% 1.0 to 2.5) and tuberculosis (OR 2.8 CI-95% 1.0-7.8), which, when observed individually, are only numerically positive, become significant in the multivariate regression model. However, here, too, the informative value is severely restricted because of the small number of 7 test persons in the group of neurodermatitis patients who have had tuberculosis.

In line with this varied picture, there is no correlation between neurodermatitis and the number of past infections.

Food allergies reveal the familiar picture of predominantly positive correlations with individual past infections. This correlation is significant for pertussis, measles, mumps, rubella and chickenpox.

The multivariate regression model only confirms a significant positive correlation between food allergies and pertussis (OR 1.6 CI-95% 1.2-2.2); measles shows a negative correlation with food allergies (OR 0.7 CI-95 0.5-1.0%) in the model.

The total number of all past diseases shows a significant positive correlation with food allergies (OR 1.1 CI-95% 1.0-1.2). If only the infections with a positive correlation are counted (pertussis, mumps, chickenpox, scarlet fever, dysentery, typhoid/paratyphoid), the risk turns out higher at 1.2 CI-95% 1.1-1.3.

Urticaria has exclusively positive correlations with all past infections. They are significant in the case of pertussis, measles, mumps, rubella, chickenpox and scarlet fever.

The multivariate regression model confirms a significant positive correlation between urticaria and both pertussis (OR 2.1 CI-95% 1.6-2.8) and scarlet fever (OR 1.5 CI-95% 1.1-2.0).

Accordingly, the number of all past diseases shows a significant positive correlation with urticaria (OR 1.1 CI-95% 1.1-1.2).

Conclusion: Overall, a clear correlation between infections and allergic diseases in adults is existing. Most clear is this relationship between allergies and pertussis and chickenpox. The risk for developing allergies increases slightly

Table 2. Correlations Between Infectious and Allergic Diseases (KiGGS) *

Numbers as %		Asthma		Hay Fever		Neurodermatitis		Contact Ekzema	
		Yes	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**
Pertussis	Yes	**14.9**	**8.1**	**15.8**	**7.6**	**11.4**	**8.0**	**15.6**	**7.3**
Measles	Yes	**10.3**	**6.9**	**10.4**	**6.7**	7.6	7.0	**10.3**	**6.4**
Mumps	Yes	4.3	3.8	**5.6**	**3.6**	3.4	3.9	**5.2**	**7.3**
Rubella	Yes	**12.3**	**7.9**	**11.1**	**7.7**	9.3	7.9	**12.9**	**7.3**
Chickenpox	Yes	**80.7**	**68.2**	**84.7**	**66.8**	**75.8**	**67.8**	**82.5**	**66.9**
Scarlet fever	Yes	**31.3**	**21.9**	**31.2**	**21.3**	**29.7**	**21.3**	**30.1**	**21.2**
Mononuleosis	Yes	3.7	2.2	**5.4**	**1.9**	**3.4**	**2.1**	**4.1**	**2.0**
Herpes	Yes	**30.0**	**20.7**	**28.5**	**20.3**	**25.2**	**20.6**	**31.7**	**19.6**
Salmonellae	Yes	5.3	3.9	**5.9**	**3.7**	**5.2**	**3.8**	**4.7**	**3.9**
Hepatitis	Yes	1.3	0.9	1.2	0.9	**1.6**	**0.9**	**1.0**	**0.9**

* The percentage figures relate to the test persons who have the above-mentioned allergic diseases (e.g. asthma – pertussis: 14.9% of test persons with asthma once had pertussis, compared to 8.1% of test persons who do not suffer from asthma). Figures in bold type show significant differences.

but significantly with the number of former infections or vice versa.

KiGGS

The prevalence of bronchial asthma and the allergic diseases studied here, and their distribution over important socio-demographic impacting factors, has already been described in detail [57]. As far as infections are concerned, the picture is as follows:

1,046 (8.4%) of the test persons had had pertussis, 972 (7.1%) measles, 634 (3.9%) mumps, 1,302 (8.1%) rubella, 11,392 (68.6%) chickenpox, 3,216 (22.4%) scarlet fever, 349 (2.3%) mononucleosis, 3,277 (21.2%) herpes, 675 (4.0%) salmonellae, and 142 (0.9%) hepatitis. It can be seen that the sample sizes are large enough to search for correlations with existing allergic diseases, with the exception of hepatitis where absolute numbers in the table cells could become very small. This is noted where appropriate in the following analysis.

The analysis using cross-tabulation (see Table **2**) shows a predominantly positive correlation between bronchial asthma and past infections, i.e. the more frequent the infection, the more frequent the bronchial asthma and vice versa. This correlation is significant for pertussis, measles, rubella, chickenpox, scarlet fever and herpes.

An analysis of correlations between all the infections in the model (multiple logistic regression) and bronchial asthma – after adjusting for age, sex, residence in eastern or western German, rural or urban residence and social strata – also shows a significant positive correlation with pertussis (OR 1.5 CI-95% 1.1-1.9) and herpes (OR 1.4 CI-95% 1.1-1.8); in the case of scarlet fever the correlation is not quite significant.

The model shows a small but significant risk (OR 1.1 CI-95% 1.0-1.2) of bronchial asthma as the number of past infections increases.

The univariate analysis shows a significant positive correlation between hay fever and all queried past infections except hepatitis. However, this statement needs to be qualified by recalling the small overall sample size of children and adolescents who have ever had hepatitis. Table **3** shows in exemplary form the extent of the differences and the complex correlation possibilities between hay fever and the infections.

After the above-mentioned adjustments have been made, the multivariate regression model also shows a significant positive correlation between hay fever and chickenpox (OR 1.3 CI-95% 1.1-1.6), scarlet fever (OR 1.2 CI-95% 1.0-1.4), mononucleosis (OR 1.9 CI-95% 1.3-2.8) and herpes (OR 1.3 CI-95% 1.1-1.5). In this model, the explanation probability for hay fever is a respectable 17.7% according to Nagelkerke's R^2.

The model shows a small, but significant risk of hay fever (OR 1.1 CI-95% 1.1-1.2) as the number of past infections increases.

Neurodermatitis also shows predominantly positive correlations with the queried past infections. These are significant in the case of pertussis, chickenpox, scarlet fever, mononucleosis, herpes, salmonellae and hepatitis.

After the above-mentioned adjustments have been made, the multivariate regression model also shows a significant positive correlation between neurodermatitis and scarlet fever (OR 1.3 CI-95% 1.1-1.6); the correlation is not quite significant in the case of pertussis.

The model shows a small but significant risk of neurodermatitis (OR 1.2 CI-95% 1.1-1.3) as the number of past infections increases.

The univariate analysis, in turn, shows exclusively significant positive correlations between allergic contact dermatitis and all queried past infections.

Table 3. Correlations Between Hay Fever and the Queried Infections *

Numbers as %		Hay Fever N=1713		%	Hay Fever Yes
Pertussis	Yes	Yes	No	Yes	19.8
		15.8	7.6	No	9.5
Measles	Yes	Yes	No	Yes	15.4
		10.4	6.7	No	10.1
Mumps	Yes	Yes	No	Yes	15.3
		5.6	3.6	No	10.3
Rubella	Yes	Yes	No	Yes	14.4
		11.1	7.7	No	9.9
Chickenpox	Yes	Yes	No	Yes	13.2
		84.7	66.8	No	4.6
Scarlet fever	Yes	Yes	No	Yes	14.7
		31.2	21.3	No	9.0
Mononuleosis	Yes	Yes	No	Yes	25.0
		5.4	1.9	No	10.1
Herpes	Yes	Yes	No	Yes	14.2
		28.5	20.3	No	9.4
Hepatitis	Yes	Yes	No	Yes	15.7
		5.9	3.7	No	10.2

Example: 15.8% of the hay-fever patients once had pertussis, compared to only 7.6% of healthy individuals. 19.8% of patients who once had pertussis suffer from hay fever, compared to only 9.5% of those who never had pertussis.

After the above-mentioned adjustments have been made, the multivariate regression model also shows a significant positive correlation between contact dermatitis and pertussis (OR 1.5 CI-95% 1.1-1.9), rubella (OR 1.4 CI-95% 1.1-1, 9), mononucleosis (OR 1.6 CI-95% 1.0-2.3) and herpes (OR 1.3 CI-95% 1.1-1.5); in the case of chickenpox the correlation is not quite significant.

The model shows a small but significant risk of contact dermatitis (OR 1.2 CI-95% 1.1-1.3) as the number of past infections increases.

Conclusion: In children, the correlation between infectious and allergic diseases is more pronounced. All allergies show significant correlations with pertussis, chickenpox and Herpes. As in adults, the risk for developing allergies increases slightly but significantly with the number of former infections (or vice versa).

DISCUSSION

NHS98

This survey was a cross-sectional study that could not record the time of past infections; as a result, the direction of a possible correlation with the queried allergic diseases must remain uncertain. Furthermore, it is impossible to exclude a systematic bias caused, for example, by chronically ill people (in this case allergies sufferers) having a better retrospective memory of past diseases. Even so, the data sets presented here are the only possibility for seeking correlations at a largely population-representative level to complement research activity and form hypotheses. We are convinced that both possible directions of the shown clear positive correlation between allergies and infections are noteworthy for the treatment of allergies. In the case of allergies following infections – most of them preventable by vaccination – prevention of special infections could lead to less allergic diseases. In the case of allergies leading to more infections, it could be beneficial to amend our vaccination programmes especially for allergic children.

The queried infections had been common among the NHS98 test persons, with over 50% of the interviewees having had them. A memory bias cannot be ruled out, especially with reference to children's diseases, which for most adults meant looking back quite a few years, but also with reference to other infections.

All the allergic diseases studied, with the exception of neurodermatitis, showed general, positive correlations both with infections and with the total number of past infections. Relatively speaking, the results for bronchial asthma and neurodermatitis, which are only partially allergic diseases, seem the most contradictory. In the case of neurodermatitis, an additional factor is that the survey of older adults does not necessarily show clear correlations between a pre-existing neurodermatitis condition and the queried infections, which might have developed later. Past infections with diphtheria and rubella seem to have a negative correlation with bronchial asthma; the only aspect the two infections have in common is that they both primarily affect the upper respiratory tract. Diphtheria also seems to have a negative correlation with neurodermatitis – although the small sample size must be taken into account here.

Two infections stand out which have a significant positive correlation with 5 of the 6 queried allergic diseases: pertussis and chickenpox.

KiGGS

The correlations are more distinct in this study, probably because the time interval between the development of the allergies and the infections is shorter, and/or because the parents interviewed here can remember their children's past infections more clearly.

The proportion of children who have had specific infections has fallen compared to the adults surveyed (pertussis: 8.4% / 23.0%; measles: 7.1% / 63.0%; mumps: 3.9% / 47.2%; and rubella: 8.1% / 32.2%) – probably thanks to the vaccination programmes. It should be borne in mind here, however, that the children were incorporated in the study from birth, so that further infections may occur in the study population. Precisely for this reason, the increases in chickenpox (from 52.9% in adults to 68.6% in children) and scarlet fever (from 14.6% to 22.4%) is striking.

The positive correlations between infectious and allergic diseases are especially marked in children. There is a correlation between pertussis, chickenpox and scarlet fever on the one hand, and all the queried allergies on the other. "Chickenpox parties" appear particularly questionable in view of these results, be it because allergic diseases are more likely as a result of past infections, be it because – as postulated in the quotes from literature at the beginning – allergies are in fact a sign of a generally defective immune system, which makes infections more likely.

Future longitudinal studies should explore the direction of this correlation.

CONCLUSIONS

In both adults and children, pertussis and chickenpox show strong positive correlations with various allergic diseases. Both diseases are preventable by vaccination. Irrespective of the direction of this correlation improved vaccination programmes could help to either prevent allergies or to help children with allergies to suffer less from preventable infections. The direction of this positive correlation between allergies and infections should be studied in longitudinal studies.

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