

# Epidemiology of allergic reactions to hymenoptera stings in Irish school children

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The aim of this was to study generate the first epidemiological data regarding the prevalence of hymenoptera allergy among school children in Ireland. Questionnaires, including six sting-specific questions (1), were distributed to the parents of primary school children aged 6–8 and 11–13, divided equally between rural and urban backgrounds. From 110 schools, 4112 questionnaires were returned. A total of 1544 (37.5%) children had been stung in their lifetime. Among the total, 5.8% of children stung experienced a large local reaction, 3.4% had a mild (cutaneous) systemic reaction (MSR) and 0.8% experienced a moderate/severe systemic reaction (SSR); these figures respectively represent 2.2%, 1.3% and 0.2% of the total study group. On logistic regression analysis, older children and rural children were at a higher risk of being stung (OR 1.7; 95% CI 1.4–2.; OR 1.6; 95% CI 1.4–1.8 respectively). Rural dwellers and asthma sufferers were more likely to experience an SSR (OR 4.3; 95% CI 1.4–13.5 and OR 2.8; 95% CI 1.8–4.3, respectively). Hymenoptera stings are more common in rural than urban dwelling Irish children. Asthma imparted a greater risk of SSR in this study population. Severe reactions are unusual overall, occurring in < 1% of those stung, a lower prevalence than in Israeli teenagers but in keeping with other European reports relating to young children.

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Insect sting is second only to food allergy as the leading cause of anaphylaxis outside medical settings (in which drugs, latex and contrast media predominate) (1). Insect sting has been reported to cause severe allergic reactions in up to 2.8% of rural dwellers (2). Hymenoptera, which is one of the larger order of insects and includes honey bee and wasp, is one of the three leading causes of fatal anaphylaxis in the United States and United Kingdom (3–5). It is the only curable form of anaphylaxis, with success rates for injection immunotherapy (venom immunotherapy – VIT) being report as more than 98% in some studies (6, 7).

Questionnaires of several thousand girl and boy scouts aged 11–16 in the US carried out in the 1970s showed a low prevalence of systemic reactions to Hymenoptera stings of only

0.35–0.4%. However, the study population was scouts attending summer camps; this selection bias means that the results of the study could underestimate the true prevalence of insect sting allergies (8, 9). More recent epidemiological data on insect stings in older children, from Israel, showed that 56% of 13- to 14-yr-old children had experienced insect stings with 4.4% having had moderate to severe systemic reactions, that is not limited to the site of the sting (10). It appears, therefore, that insect stings in general, and multiple stings and severe allergic reactions in particular, are more common than that might have been previously thought. Some studies (11) found that anaphylactic reactions are more common in men than women (citing a 2:1 ratio).

The association between atopic conditions and insect sting allergy is unanswered. Italian

research on the correlation between insect sting allergy and atopic features found a significant and independent association between positive skin-prick test (SPT) to cow's milk and egg white and a positive SPT to Hymenoptera venom, but found no association with atopic diseases (12). In fact, most of the early studies found no association between insect sting allergies and atopic conditions (13). In a recent article, Graif et al. examined the association between atopic diseases and allergic reactions to insect stings in their Israeli population of school children and found that atopic conditions were associated with a higher rate and greater severity of allergic reactions to insect stings (14).

### Aim of this research

The aim of this study was to carry out the first epidemiological study on the prevalence of allergic reactions to insect stings in the Irish Paediatric population and to examine the association between atopic conditions and insect sting allergy.

### Materials and methods

In Cork city and county, 5560 questionnaires were distributed to primary schools. Cork city is the second largest city in Ireland with a population of 190,384, while the greater Cork area has a population of 380,000. The schools surveyed were chosen at random from a list of primary schools that was provided by the Department of Education. The schools selected were divided equally between urban and rural environments. The participants were parents of school children aged 6–8 attending first and second class, and 11–13 attending sixth class (the final year of the primary school cycle). Parents were asked to complete the questionnaire. The questionnaires were coded for school and school year but no individual child was identifiable. Sealable envelopes were provided for the return of completed questionnaires to the class teachers. The questionnaires were then collected 1 wk after distribution.

#### Questionnaire

Six questions regarding Hymenoptera stings and sting allergies were added to the International Study of Asthma and Allergies in Childhood standard core questionnaire. These six questions were based on those developed by Graif et al. (10).

The parents of the children were asked whether their child had ever been stung, if yes how many

times and whether or not they experienced a large location reaction, a mild systemic reaction or a severe systemic reaction. A large location reaction was defined as a swelling next to the sting site that was larger than 5 cm and lasted for more than 2 days. A mild systemic reaction was defined as a skin reaction such as rash or swelling in other body parts (except for sting site), within 1 h following the sting. A severe systemic reaction was defined as difficulties in breathing, an asthma attack, abdominal pain or loss of consciousness within 1 h following the sting. The final question related to hospital attendance as a result of the sting. If a parent answered 'yes' to the question 'has your child ever had asthma', then that child was considered to have asthma. If a parent answered 'yes' to the question 'has your child ever had hay fever', then that child was considered to have allergic rhinitis. If a parent answered 'yes' to the question 'has your child ever had eczema', then that child was considered to have eczema.

#### Statistics

Statistical analysis was completed using SPSS package 16.0 (SPSS Inc., Chicago, Illinois). A multiple logistic regression model was fitted to the data to evaluate various risk factors associated with being stung and developing an allergic reaction to a sting. A *p* value of <0.05 was considered significant.

### Results

#### Response rate

There was a 74% response rate. A total of 5560 questionnaires were distributed and 4112 fully completed questionnaires were returned.

#### History of stings

From 110 schools, 4112 questionnaires completed questionnaires were returned. Of the 4112 children in our study population, 1544 (37.5%) children had been stung in their lifetime, 1479 (94.6%) were stung between one and three times, 59 (3.8%) children were stung between four and 10 times and 5 (0.8%) children were stung more than 10 times.

The prevalence rates of stings by the characteristics of the study population are given in Table 1. Male subjects were significantly more likely to be stung than female subjects (*p* < 0.05). On logistic regression analysis, older children and children living in rural areas were at

Table 1. History of stings by characteristics of the study population

|                          | Ever stung    | 1–3 stings†  | 4–10 stings† | >10 stings %† |
|--------------------------|---------------|--------------|--------------|---------------|
| Total (n = 4112)         | 1544 (37.5%)  | 1478 (94.6%) | 59 (3.8%)    | 5 (0.8%)      |
| <i>Sex</i>               |               |              |              |               |
| Male (n = 2057)          | 807 (39.2%)*  | 770 (95.4%)  | 33 (4.1%)    | 4 (0.5%)      |
| Female (n = 2055)        | 737 (35.8%)   | 710 (96.3%)  | 26 (3.6%)    | 1 (0.1%)      |
| <i>Age group</i>         |               |              |              |               |
| 6–8 yrs (n = 3411)       | 1234 (36.2%)* | 1190 (96.5%) | 41 (3.3%)    | 3 (0.2%)      |
| 11–12 yrs (n = 701)      | 309 (44.0%)   | 289 (93.5%)  | 18 (5.8%)    | 2 (0.7%)      |
| <i>Area of residence</i> |               |              |              |               |
| Rural (n = 2276)         | 937 (41.2%)*  | 895 (95.5%)  | 40 (4.3%)    | 2 (0.2%)      |
| Urban (n = 1836)         | 607 (33.0%)   | 583 (95.8%)  | 19 (3.1%)    | 3 (0.5%)      |

\* $p < 0.0001$ .

†Percentage of children stung.

a higher risk of being stung, OR 1.7 (95% CI 1.4–2.0) for children in the older age group; OR of 1.6 (95% CI 1.4–1.8) for children living in rural areas.

#### Allergic reactions to stings

Of the 1544 children that had been stung in their lifetime, 93 of these children (5.8%) had a large local reaction (LLR), and 55 children (3.4%) had had a mild (cutaneous) systemic reaction (MSR). Thirteen of the children who had been stung (0.8%) experienced a moderate/severe systemic reaction (SSR).

These incidences of 93 LLRs, 55 MSRs and 13 SSRs represent 2.2%, 1.3% and 0.2% of the whole study population, respectively. Five of the 93 children with an LLR attended hospital (5%), as did three of the 55 children with an MSR (5%) and two of the 13 children who experienced an SSR (15%).

No significant difference in the rates of LLRs or SSRs was found between the two age groups of 6- to 8- and 11-to 13-yr-olds. However, the older age group of 11-to 13-yr-olds do experience significantly more MSRs than the younger age group ( $p = 0.04$ ). There was no significant difference between urban and rural dwellers in the rates of LLRs or MSRs. Rural dwellers,

however, were four times more likely to experience an SSR than urban dwellers ( $p = 0.013$ , OR 4.3 with a 95% CI of 1.4–13.5).

The prevalence rates of local and systemic reactions by the number of stings are shown in Table 2. Allergic reactions were not found to be more common in those who were stung more frequently.

#### Atopy and severity of allergic reaction

The relationship of a known history of atopy (based on parent's response to questions in ISAAC section of questionnaire) to the severity of allergic reactions in individuals was examined. There was no statistically significant association between children who experience LLRs to insect stings and children who suffer from atopic conditions. It was found, however, that there is a statistically significant association between experiencing an MSR to an insect sting and having eczema or allergic rhinitis ( $p < 0.05$  for both). If a child suffers from allergic rhinitis or eczema, they are twice as likely to suffer an MSR to an insect sting. Children with allergic rhinitis had an OR of 2.1 (95% CI 1.3–3.3), while eczema sufferers had an OR of 2.0 (95% CI 1.3–3.2). Children who had been given a diagnosis of asthma in the past were 2.8 times more likely to suffer a SSR than non-asthma sufferers (95% CI 1.8–4.3,  $p < 0.05$ ). Allergic rhinitis and eczema were not found to be associated with an SSR.

#### Hospital attendance reported by questionnaires

Twenty-two children representing 1.4% of children stung (0.5% of entire study population) were taken to hospital as a result of their sting. The number of stings the child experienced did not influence hospital attendance.

#### Discussion

To our knowledge, this is the first study on the prevalence of allergic reactions to insect stings in Ireland. It was found that 37.5% of the children

Table 2. Prevalence of allergic reactions and hospital attendance by number of stings

| No. of stings | Individuals  | LLR*      | MSR*      | SSR*      | Hospital attendance* |
|---------------|--------------|-----------|-----------|-----------|----------------------|
| Ever stung    | 1544 (37.5%) | 93 (5.8%) | 55 (3.4%) | 13 (0.8%) | 22 (1.37%)           |
| 1–3           | 1479 (95%)   | 83 (5.4%) | 47 (3.1%) | 13 (0.8%) | 20 (1.35%)           |
| 4–10          | 59 (3.8%)    | 10 (0.6%) | 4 (0.25%) | 0.0       | 2 (0.13%)            |
| >10           | 5 (0.8%)     | 0.0       | 1 (0.06%) | 0.0       | 0.0                  |

LLR, large local reaction; MSR, mild (cutaneous) systemic reaction; SSR, moderate/severe systemic reaction.

\*Percentage of children stung.

in our study had been stung one or more times by a member of the Hymenoptera species. This is a lower prevalence rate than the Israeli study where 56.3% of teenagers had been stung once or more (10). Several factors may contribute to this relatively lower prevalence rate in Ireland; firstly that the Israeli study involved an older age group than our study, and our results show that being in an older age group is a risk factor for stings. Secondly, Irish children may spend less time outdoors than Israeli children as a result of the more temperate climate and finally there are differences in flora and fauna between the two countries. Our results did find that rural children (who anecdotally spend more time outside) have an increased risk of being stung.

Boys were stung significantly more times than girls. Logistic regression revealed that both being in the older age group and living in a rural environment were independent risk factors for being stung. Presumably, these increased risks of being stung are results of increased time spent outdoors and thus increased exposure times. Boys are also known for more wild behaviour and could be willing to take more risks compared to girls. In a recent Spanish study of adults, it was found that males and participants living in rural habitats had an increased risk of being stung (15). In addition to their increased risk of being stung, rural dwellers were also four times more likely to develop an SSR to an insect sting than urban dwellers. A Greek study of adults also found that insect sting sensitization was more than twice as common in those living in rural areas than in those living in Athens (16).

Children that are 16 yrs of age and younger who have experienced cutaneous systemic reactions without other allergic manifestations (effectively MSRs) have approximately a 10% chance of having a systemic reaction if re-stung (17). Individuals who are sensitized to insect venom can react variably upon each re-exposure to the venom, although the risk of recurrent anaphylaxis is approximately only 60% (18), the risk of a repeated systemic reaction is generally lower in children (19). In our present study, 13 children (0.8% of the children stung) experienced a SSR, but only two attended A&E. These 13 children would benefit from VIT and so should have attended hospital. Venom immunotherapy in children results in a significantly lower risk of systemic reactions even 10–20 yrs after therapy is stopped, and this prolonged benefit is greater than that seen in adults (20). Research has also demonstrated the value of diagnostic sting challenges to detect children at risk of further systemic reactions (19), and so sting challenge

tests could also be used to help define the necessity of VIT in these children. According to our questionnaire results, only 1.4% of children stung presented to A&E. Graif et al. (10) reported that the emergency department was visited by 5.8% of Israeli children who were ever stung. However, in Israel, the first point of contact would often be the A&E department; but in Ireland, people would usually attend their general practitioner first; this could account for the variation in attendance to A&E between the two countries.

Food allergy is known to be associated with atopic disease (12). Early research by Settupane et al. into the relationship between atopy and anaphylactic reactions to Hymenoptera stings has shown that, although atopy does not predispose patients to Hymenoptera allergy, asthmatics who also have Hymenoptera allergy do have a significantly more severe reaction to stings than non-atopic patients (21). This present study supports the hypothesis that children with asthma have an increased risk of developing a severe reaction to an insect sting when stung (OR 2.8). Similarly, the Israeli study on the association between allergic reactions to insect stings and atopic conditions in children found that SSRs were more common in children with asthma (OR 3.64) (14). In our study, we found that, unlike asthmatics, children with allergic rhinitis and eczema did not have an increased risk of an SSR; however, these children do have an increased risk of an MSR. Settupane et al. (21) found that the type of sting reaction in people with allergic rhinitis without asthma resembled that of non-atopic people. The Israeli study, however, found that all three types of allergic reactions (LLR, MSR and SSR) were all more common in children with allergic rhinitis and eczema (14). In this present study, the parent of the child was the respondent, whereas in the Israeli research the child self-reported, this could account for some of the differences between the two studies.

Our study was limited by the fact that insect sting allergy is a relatively rare disease and, therefore, an effective study requires a very large sample size. Even with a large study population of 4112 children, only 13 children experienced a SSR. Although we do report associations found between individuals that experience allergic reactions to insect stings and various risk factors, the nature of our study design provides a very limited basis for causal inference. Finally, the association found between atopy and severe systemic reactions to hymenoptera stings could be explained by the fact that children with atopic

conditions do have higher levels of IgE antibodies, and insect sting allergy is an IgE-mediated disorder; however, no diagnostic tests were performed as part of this research.

This study does, however, fulfil its aim of establishing the prevalence of Hymenoptera sting allergy in Irish school children. It also identified individual risk factors for the development of systemic reactions to Hymenoptera stings and opens the door for further research in this field.

## Conclusions

Hymenoptera stings are common in Irish children but severe systemic reactions are unusual overall, occurring in <1% of those stung, a lower prevalence than in older Israeli children but in keeping with other European reports and North American paediatric reports. Male subjects, rural dwellers and older children were found to have an increased risk of being stung. Mild systemic reactions and severe systemic reactions occurred in 4.2% of children stung. SSRs to Hymenoptera stings are more common in rural than urban dwelling Irish children. Asthma was found to impart a greater risk of SSR in this study population.

The emergency department is the most common medical setting for diagnosis and management of anaphylaxis (22); therefore, the active targeting of accident and emergency physicians for allergy education is necessary to make advances in the acute management of anaphylaxis.

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