

---

# Prevalence of positive skin prick test results in children with Down syndrome: a case-control study

Susan E. Mannan, MD; Ejaz Yousef, MD; and Jobayer Hossain, PhD

---

**Background:** Because many of the same otologic and nasal problems experienced by children with Down syndrome are also frequent in children with atopic disease, many children with Down syndrome are referred to an allergist for evaluation.

**Objective:** To determine the prevalence of positive skin prick test (SPT) reactions to common aeroallergens in children with Down syndrome.

**Methods:** Using a case-control design, we reviewed the medical records of children with Down syndrome who had undergone SPT. Each case was matched by sex and age with a control who had been evaluated by SPT at an initial visit.

**Results:** Thirty-nine cases and controls were identified. Eighteen percent of cases were found to have at least 1 positive SPT result compared with 54% of controls. This closely approximates the percentage of the general population with at least 1 positive SPT result (54.3%) as reported in the Third National Health and Nutrition Examination Survey.

**Conclusions:** Given the low prevalence of positive SPT results in children with Down syndrome, it is unlikely that allergic rhinitis will be identified as the cause of many of the chronic rhinitis symptoms that many of these children are referred to an allergy practice to have evaluated. It may be helpful to the parents and to the patients themselves to avoid involving another specialist and appointment because they frequently are involved with many specialists for medical care. A larger study would be helpful in confirming the prevalence of positive SPT results in children with Down syndrome.

*Ann Allergy Asthma Immunol.* 2009;102:205–209.

## INTRODUCTION

Down syndrome is a common chromosomal disorder, occurring in approximately 1 in 700 live births. It is characterized by a variety of well-described physical anomalies, including inner epicanthal folds, small ears, a small mouth with a protruding tongue, a short neck with redundant nuchal skin, and a single palmar crease. Along with these physical characteristics, the lives of these children are often complicated by congenital heart disease; gastrointestinal disorders, such as duodenal atresia; atlantoaxial instability; ocular disease; and thyroid disorders.<sup>1</sup> Because of the myriad problems that may arise, the care of children with Down syndrome is often shared between the primary care physician and a variety of specialist physicians.

Particularly frequent is referral to an otolaryngologist for evaluation of recurrent otitis media, obstructive sleep apnea (OSA), and chronic rhinosinusitis. Children with Down syndrome have a much higher incidence of chronic ear disease with resultant hearing loss and OSA than other children.<sup>2,3</sup> The prevalence of OSA is most likely due to an anatomical predisposition toward midfacial and mandibular hypoplasia, relatively large tonsils and adenoids, glossoptosis, increased secretions, and generalized hypotonia.<sup>3</sup> A study by Price et al<sup>4</sup>

examined the efficacy of adenoidectomy in children with Down syndrome, a procedure that commonly improves the symptoms of OSA. They reported that the nasal and middle ear symptoms improved in only 40% to 50% of patients with Down syndrome and that postoperative complications were more common.<sup>4</sup> The frequent and often difficult-to-treat episodes of otitis media are also likely to be related to anatomical variations, including abnormalities in the area of the nasopharynx where the eustachian tubes open, a more cylindrical and narrow eustachian tube, and hypotonia, which can cause decreased function of the muscles in the palate, which are responsible for opening and closing the eustachian tube.<sup>3</sup>

Because many of the same otologic and nasal problems are also frequent in children with atopic disease, many children with Down syndrome are referred to an allergist for evaluation. In fact, 1 review<sup>3</sup> of common otolaryngologic manifestations in Down syndrome recommends allergy testing in affected children with a family history of environmental allergies. However, there are currently no studies, to our knowledge, that explore the relationship of environmental allergen sensitization and chronic rhinorrhea in patients with Down syndrome. We sought to examine our own population of children with Down syndrome who have undergone allergy testing and to compare the prevalence with that of nonaffected children.

## METHODS

We retrospectively reviewed all children with Down syndrome seen by the allergy and immunology service at any

---

**Affiliations:** Division of Allergy and Immunology, Alfred I. duPont Hospital for Children, Wilmington, Delaware.

**Disclosures:** Authors have nothing to disclose.

Received for publication June 12, 2008; Accepted for publication November 17, 2008.

hospital in the Nemours system (including sites in Wilmington, Delaware; Atlantic City, New Jersey; Jacksonville and Orlando, Florida; and Philadelphia, Pennsylvania). Approval from the institutional review board of the Alfred I. duPont Hospital for Children (Wilmington) was obtained for the study. Data concerning all patients with Down syndrome undergoing allergen skin prick testing (SPT) were entered into a spreadsheet (Excel; Microsoft Corp, Redmond, Washington). The following variables were recorded: medical record number, age (in years) at evaluation, sex, race, reason for evaluation, and results of SPT. In all, 39 children with a diagnosis of Down syndrome who had undergone SPT to common aeroallergens were identified. A second retrospective review of randomly chosen age- and sex-matched control subjects was performed to compare the outcome of SPT.

At least 5 days before testing, all patients tested were required to have stopped using any antihistamines or other medications that may affect the results of SPT. The SPT was performed using Greer pricks to a panel of common aeroallergens, including grass mix, Bermuda grass, weed mix, ragweed mix, tree mix, house dust mites, cat dander, dog dander, cockroach, mold mix, *Aspergillus fumigatus*, *Alternaria*, *Horomodendrum*, and *Penicillium*. Negative (saline) and positive (10-mg/mL histamine base) controls were also included in all children. If the child was younger than 3 years at initial presentation, SPT was performed only to the indoor allergens. For these analyses of SPT data, we considered an allergen-specific skin test response to be positive if the difference between the wheal size of the allergen-specific test and the negative control was at least 3 mm.

Categorical variables are described using frequencies and percentages, and continuous variables are summarized using means, SDs, medians, and ranges. The Pearson  $\chi^2$  statistic

and the 2-sample *t* test for categorical and numerical variables, respectively, were used to examine the balance of distribution of study characteristics in the 2 groups (control and study). The prevalence of positive SPT results in the study and control groups was compared using the univariable logistic regression model and the  $\chi^2$  statistic. In addition, a multivariable logistic regression model was used to adjust simultaneously for the effects of the potential confounding variables on the association between the prevalence of positive SPT results and group (study and control). To enter into the multivariable model, a variable must have been significant at  $P < .2$ . All analyses were 2-tailed at the  $P < .05$  significance level. All the analyses were performed using a statistical package (SPSS version 14.0; SPSS Inc, Chicago, Illinois).

## RESULTS

There were 78 patients: 39 in the control group and 39 in the study group. The study was matched for sex and age. Table 1 provides the distribution of patients into the 2 groups with respect to study characteristics such as race, sex, age, and reason for referral. The distribution was more or less balanced for all these variables ( $P > .05$ ). Table 2 gives the distribution of SPT results with respect to the 2 groups and 4 other study characteristics. There was a significant difference of the distribution of SPT results between the 2 groups ( $P < .05$ ). The prevalence of positive SPT results is much lower in the study group (18%) than in the control group (54%). The distribution of SPT results is more or less equal with respect to sex and race. Although not significant, there is an observed difference in the ages of patients with positive vs negative SPT reactions ( $P = .19$ ). The age of patients with

Table 1. Characteristics of the Study and Control Groups

| Variable                     | Control group<br>(n = 39) | Study group<br>(n = 39) | Total<br>(N = 78) | P value <sup>a</sup> |
|------------------------------|---------------------------|-------------------------|-------------------|----------------------|
| Sex, No. (%)                 |                           |                         |                   | .91                  |
| Male                         | 20 (50)                   | 20 (50)                 | 40                |                      |
| Female                       | 19 (50)                   | 19 (50)                 | 38                |                      |
| Race, No. (%)                |                           |                         |                   | .38                  |
| African American             | 13 (54)                   | 11 (46)                 | 24                |                      |
| White                        | 21 (54)                   | 18 (46)                 | 39                |                      |
| Other                        | 5 (83)                    | 1 (17)                  | 6                 |                      |
| Missing data                 | 0                         | 9 (100)                 | 9                 |                      |
| Age, y                       |                           |                         |                   | .84                  |
| Mean (SD)                    | 4.37 (2.60)               | 4.49 (2.93)             | 4.37 (2.72)       |                      |
| Median                       | 4.00                      | 4.00                    | 4.00              |                      |
| Range                        | 0.75–14.00                | 0.92–17.00              | 0.75–17.00        |                      |
| Reason for referral, No. (%) |                           |                         |                   | .01                  |
| Chronic rhinitis             | 22 (54)                   | 19 (46)                 | 41                |                      |
| Recurrent/chronic sinusitis  | 1 (9)                     | 10 (91)                 | 11                |                      |
| Cough/wheezing               | 11 (73)                   | 4 (27)                  | 15                |                      |
| Other                        | 5 (46)                    | 6 (55)                  | 11                |                      |

<sup>a</sup> The *P* values are generated from either a  $\chi^2$  statistic or a 2-sample *t* test.

Table 2. Comparison of the Prevalence and Distribution of Skin Prick Test Results

| Variable                     | Skin prick test results |                      |                   | P value <sup>a</sup> |
|------------------------------|-------------------------|----------------------|-------------------|----------------------|
|                              | Negative<br>(n = 50)    | Positive<br>(n = 28) | Total<br>(N = 78) |                      |
| Group, No. (%)               |                         |                      |                   | .001                 |
| Control                      | 18 (46)                 | 21 (54)              | 39                |                      |
| Study                        | 32 (82)                 | 7 (18)               | 39                |                      |
| Sex, No. (%)                 |                         |                      |                   | .87                  |
| Male                         | 26 (65)                 | 14 (35)              | 40                |                      |
| Female                       | 24 (63)                 | 14 (37)              | 38                |                      |
| Race, No. (%)                |                         |                      |                   | .77                  |
| African American             | 14 (58)                 | 10 (42)              | 24                |                      |
| White                        | 25 (64)                 | 14 (36)              | 39                |                      |
| Other                        | 3 (50)                  | 3 (50)               | 6                 |                      |
| Missing data                 | 8 (89)                  | 1 (11)               | 9                 |                      |
| Age, y                       |                         |                      |                   | .19                  |
| Mean (SD)                    | 4.12 (2.73)             | 4.99 (2.76)          | 4.43 (2.75)       |                      |
| Median                       | 3.75                    | 5.00                 | 4.00              |                      |
| Range                        | 0.75–17.00              | 1.08–14.00           | 0.75–17.00        |                      |
| Reason for referral, No. (%) |                         |                      |                   | .17                  |
| Chronic rhinitis             | 22 (54)                 | 19 (46)              | 41                |                      |
| Recurrent/chronic sinusitis  | 9 (82)                  | 2 (18)               | 11                |                      |
| Cough/wheezing               | 12 (80)                 | 3 (20)               | 15                |                      |
| Other                        | 7 (64)                  | 4 (36)               | 11                |                      |

<sup>a</sup> The P values are generated from either a  $\chi^2$  statistic or a 2-sample *t* test.

positive SPT results (mean, 4.12 years; median, 3.75 years) was more than that in patients with negative SPT results (mean, 4.99 years; median, 5.00 years). There is an observed difference in the prevalence of positive SPT results between referral reasons, but it is not significant ( $P = .17$ ). Patients with chronic/recurrent sinusitis were likely to have the lowest prevalence (18%) of positive SPT results, followed by patients with cough/wheezing (20%). Patients with the chronic rhinitis were likely to have the highest prevalence (46%) of positive SPT reactions. Table 3 provides the crude association of the prevalence of positive SPT results with the 2 groups (study and control) and the other 4 study characteristics. There was a significantly lower (81%) prevalence of positive SPT results in the study group compared with the control group (prevalence odds ratio [POR], 0.19; 95% confidence interval [CI], 0.07–0.53). There was no other variable associated significantly with positive SPT results. Although not significant, there might have been an association of the prevalence of positive SPT results with age ( $P = .20$ ) and reason for referral. The prevalence of positive SPT reactions in patients with chronic/recurrent sinusitis was approximately 74% less than that in patients with chronic rhinitis (POR, 0.26;  $P = .11$ ). Patients with cough/wheeze were approximately 71% less likely to have positive SPT results compared with patients with chronic rhinitis (POR, 0.29;  $P = .08$ ). Table 4 compares the prevalence of the age- and referral-adjusted positive SPT results between the study and control groups using the multivariable logistic regression model. The significant difference in the prevalence of positive SPT results be-

Table 3. Univariable Logistic Regression Model of the Effect of Group and Other Factors on the Prevalence of Positive Skin Prick Test Results

| Variable                    | Prevalence<br>odds ratio<br>(95% CI) | P value |
|-----------------------------|--------------------------------------|---------|
| Group                       |                                      |         |
| Control                     | 1.0 (Reference)                      |         |
| Study                       | 0.19 (0.7–0.53)                      | .001    |
| Sex                         |                                      |         |
| Female                      | 1.0 (Reference)                      |         |
| Male                        | 0.92 (0.36–2.33)                     | .87     |
| Race                        |                                      |         |
| African American            | 1.0 (Reference)                      |         |
| White                       | 0.78 (0.28–2.22)                     | .65     |
| Other                       | 1.40 (0.23–8.42)                     | .71     |
| Reason for referral         |                                      |         |
| Chronic rhinitis            | 1.0 (Reference)                      |         |
| Recurrent/chronic sinusitis | 0.26 (0.05–1.34)                     | .11     |
| Cough/wheezing              | 0.29 (0.07–1.18)                     | .08     |
| Other                       | 0.66 (0.17–2.61)                     | .56     |
| Age                         | 0.89 (0.94–1.33)                     | .20     |

Abbreviation: CI, confidence interval.

tween the 2 groups, found in Table 3, prevails even after adjustment for age and reason for referral. The prevalence of age- and referral-adjusted positive SPT results in the study group was approximately 84% less compared with that in the control group (POR, 0.16; 95% CI, 0.05–0.51). There is a significant difference in the prevalence of pos-

Table 4. Unconditional Multivariable Logistic Regression Model of the Effect of Group and Other Factors on the Prevalence of Positive Skin Prick Test Results

| Variable                    | Prevalence odds ratio (95% CI) | P value |
|-----------------------------|--------------------------------|---------|
| Group                       |                                |         |
| Control                     | 1.0 (Reference)                |         |
| Study                       | 0.16 (0.05–0.51)               | .002    |
| Reason for referral         |                                |         |
| Chronic rhinitis            | 1.0 (Reference)                |         |
| Recurrent/chronic sinusitis | 0.35 (0.04–3.01)               | .34     |
| Cough/wheezing              | 0.21 (0.05–0.99)               | .048    |
| Other                       | 0.92 (0.19–4.36)               | .92     |
| Age                         | 1.15 (0.93–1.43)               | .19     |

Abbreviation: CI, confidence interval.

itive SPT results between patients with chronic rhinitis and those with cough/wheezing (POR, 0.21;  $P = .048$ ).

## DISCUSSION

These results demonstrate that children with Down syndrome are much less likely than “typical” children to have positive SPT reactions to common aeroallergens. The percentage of control subjects with positive SPT results closely approximates the prevalence in the US population as reported in the Third National Health and Nutrition Examination Survey.<sup>5</sup> This study looked at SPT to a panel of 9 common aeroallergens and 1 food (dust mite, cat, German cockroach, *Alternaria alternata*, short ragweed, white oak, perennial ryegrass and Bermuda grass, Russian thistle, and peanut) in patients aged 6 to 59 years. Fifty-four percent of this population had positive SPT responses to 1 or more allergens tested.<sup>5</sup> The present study is limited by the fact that the populations were from different geographic locations (Florida, Delaware, New Jersey, and Pennsylvania), which could affect their exposures and, thus, their sensitization to the antigens tested.

These results suggest that in children with Down syndrome, it is much less likely that their symptoms of chronic rhinitis, recurrent otitis media, and OSA are related to environmental exposures and more likely that they are the result of altered anatomy. Another potential contributing factor could be adenoid regrowth after surgical intervention, which is more common in children with Down syndrome than in other children.<sup>3</sup> In addition, gastroesophageal reflux disease is common in children with Down syndrome and is known to be linked to otolaryngologic disease in children.<sup>2</sup>

It is not clear, however, why children with Down syndrome have a lower incidence of allergic sensitization to common aeroallergens. Thirty of the 39 study patients reported a positive family history of atopy (as defined by  $\geq 1$  immediate family members with asthma, allergic rhinitis, or atopic der-

matitis) at their initial visit. This suggests that the genetic predisposition to atopic disease seen in other patients was present in this study group. Because this study was retrospective, we did not have access to the total IgE levels of most patients being evaluated. It would be interesting to compare the total IgE levels of patients with Down syndrome with those of typical patients. However, an elevated IgE level is not necessary for allergic sensitization. There have been studies evaluating the humoral immunity of patients with Down syndrome in the past. Cocchi et al<sup>6</sup> found no significant difference between children with Down syndrome and their control population in the levels of IgG and IgA. Levels of IgM were significantly lower in children with Down syndrome but were still within the reference range. The IgE levels were not investigated. Spina et al<sup>7</sup> reported reduced numbers of B cells in patients with Down syndrome. Their immunoglobulin expression findings were similar to those of Cocchi et al.<sup>6</sup> Mahmoud et al<sup>8</sup> evaluated 84 patients with dysmorphic disorders for immune defects. Eleven children with Down syndrome were included, and they were most commonly found to have decreased numbers of T cells and natural killer cells. Functional studies were not performed. Also, none of these patients had a significant history of recurrent infections.<sup>8</sup>

In summary, because environmental allergies are less likely to contribute to the nasal symptoms experienced by children with Down syndrome, these patients and their parents could possibly be spared an additional visit to a medical specialist. Although chronic rhinitis may have an impact on quality of life, it likely improves in these children as they get older and the anatomical abnormalities discussed previously enlarge and present less of a problem.<sup>3</sup> A larger study would be helpful in confirming these findings. However, because 18% of the study patients had sensitivities identified, it may be worthwhile to pursue an allergy workup if the patient has already had anatomy evaluated by an otorhinolaryngologist. In addition, because the Third National Health and Nutrition Examination Survey population was slightly older than the present study population, it may be helpful to revisit SPT in older patients with Down syndrome to determine whether sensitization takes place after several years of exposure.

## REFERENCES

1. American Academy of Pediatrics Committee on Genetics. Health supervision for children with Down syndrome. *Pediatrics* 2001;107:442–449.
2. Mitchell RB, Call E, Kelly J. Ear, nose and throat disorders in Down syndrome. *Laryngoscope*. 2003;113:259–263.
3. Shott SR. Down syndrome: common otolaryngologic manifestations. *Am J Med Genet C Semin Med Genet*. 2006;142C:131–140.
4. Price DL, Orvidas LJ, Weaver AL, Farmer SA. Efficacy of adenoidectomy in the treatment of nasal and middle ear symptoms in children with Down syndrome. *Int J Pediatr Otorhinolaryngol*. 2004;68:7–13.

- 
5. Arbes SJ, Gergen PJ, Elliott L, Zeldin DC. Prevalences of positive skin test responses to 10 common allergens in the US population: results from the Third National Health and Nutrition Examination Survey. *J Allergy Clin Immunol.* 2005;116:377–383.
  6. Cocchi G, Mastrocola M, Capelli M, Bastelli A, Vitali F, Corvaglia L. Immunological patterns in young children with Down syndrome: is there a temporal trend? *Acta Paediatr.* 2007;96:1479–1482.
  7. Spina CA, Smith D, Korn E, Fahey JL, Grossman HJ. Altered cellular immunity functions in patients with Down's syndrome. *Am J Dis Child.* 1981;135:251–255.
  8. Mahmoud SA, Lowery-Nordberg M, Chen H, Thurmon T, Ursin S,

Bahna SL. Immune defects in subjects with dysmorphic disorders. *Allergy Asthma Proc.* 2005;26:373–381.

*Requests for reprints should be addressed to:*  
Ejaz Yousef, MD  
Division of Allergy and Clinical Immunology  
Alfred I. duPont Hospital for Children  
1600 Rockland Rd  
Wilmington, DE 19803  
E-mail: eyousef@nemours.org

---