Purpose of the Study. For outpatient treatment of anaphylaxis, inhaled epinephrine from a metered-dose inhaler is sometimes recommended as a simple and easily administered alternative to injectable epinephrine. This study evaluated the practicality of inhaled epinephrine in a pediatric population at risk for anaphylaxis by evaluating the rate and extent of epinephrine absorption after inhalation.

Study Population. A total of 19 children ages 6 to 14 years with a history of allergy and anaphylaxis.

Methods. This was a prospective, randomized, placebo-controlled parallel group study with observer blinding. Based on the child’s weight, 10, 15, or 20 inhalations of epinephrine or placebo were administered. Plasma levels of epinephrine were monitored before and at intervals from 5 to 180 minutes postdosing, along with blood glucose, heart rate, blood pressure, and adverse effects.

Results. The 11 children in the epinephrine group were able to inhale 11 ± 2 inhalations (range: 3–30 puffs), which represented 74% ± 7% of the precalculated dose. The 8 children in the placebo group were able to inhale 12 ± 2 (range: 8–20) puffs, or 89% ± 3% of the precalculated dose. Peak plasma epinephrine concentrations were 1822 ± 413 for the epinephrine group and 1316 ± 247 for the placebo group. There were no differences between the groups in epinephrine levels, heart rate, or blood pressure.

Conclusion. Even with expert coaching, children were unable to achieve adequate plasma epinephrine concentrations with inhaled epinephrine.

Reviewer’s Comments. This is a well-conducted study with an important message that inhaled epinephrine should not be used as an alternative to injectable epinephrine.

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ANAPHYLAXIS IN THE UNITED STATES: AN INVESTIGATION INTO ITS EPIDEMIOLOGY

Neugut AI, Ghatak AT, Miller RL. Arch Intern Med. 2001;161:15–21

Purpose. Anaphylaxis is a severe, life-threatening allergic reaction that affects both children and adults in the United States. However, data regarding the incidence and prevalence of anaphylaxis and the number of deaths caused by it are limited. The purpose of this study was to provide a better understanding of the magnitude of the problem of anaphylaxis in the United States.

Study Population and Methods. A thorough review of the current medical literature was conducted to obtain prevalence estimates on each of the 4 major subtypes of anaphylaxis (food, drugs, latex, and insect stings). They calculated an overall estimate of the risk of anaphylaxis by calculated an overall estimate of the risk of anaphylaxis by evaluating the rate and extent of epinephrine absorption after inhalation.

Results. Known rates or cases of anaphylaxis were 0.0004% for food, 0.7% to 10% for penicillin, 0.22% to 1% for radiocontrast media, and 0.5% to 5% after insect stings. There were 220 cases after latex exposure. Considering the 1999 US population of 272 million, the population at risk for anaphylaxis from food is 1099, from penicillin is 1.9 million to 27.2 million, from radiocontrast media is 22 000 to 100 000, from latex is 220, and from insect stings is 1.36 million to 13.6 million. These calculations yield a total of 3.29 million to 40.9 million individuals at risk of anaphylaxis.

Conclusions. The occurrence of anaphylaxis in the United States is not as rare as is generally believed. On the basis of our figures, the problem of anaphylaxis may, in fact, affect 1.21% to 15.04% of the US population.

Reviewer’s Comments. It’s a little hard to know what to make of studies like this. Most of us don’t have much problem identifying anaphylaxis attributable to antibiotics, radiocontrast media, insect stings, and latex. The idioPATHIC cases are the ones that make us all crazy.

Allen Adinoff, MD
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INSECT STING ALLERGY WITH NEGATIVE VENOM SKIN TEST RESPONSES


Purpose of the Study. To increase awareness about the patient with a negative skin test response and insect sting allergy and to determine the frequency and significance of negative skin test responses in patients with a history of systemic reactions to insect stings.

Study Population. Subjects were recruited for insect sting challenge study using advertisements. Subjects with a history consistent with a systemic immunoglobulin E (IgE)-mediated allergy to insects were evaluated.

Methods. Venom skin testing, serologic IgE venom testing, and insect sting challenges were conducted. Intradermal skin testing to venom extracts (ALK-Abello Labs, Copenhagen, Denmark) was conducted in a range from 0.001 μg/mL to 1.0 μg/mL. Venom-specific serum IgE was detected using radioallergosorbent testing (RAST) (on-site assay using precommercial venom preparations). Sting challenge was performed using standards reported by this group with stings classified as mild, moderate, or severe based on defined criteria.

Results. After 4 years of recruitment, 307 subjects were enrolled. Skin testing was positive in 208 (68%) of patients. Skin testing was negative in 99 (32%) of whom 56 (57%) also had a negative RAST and 43 (43%) had a positive RAST. Of those with negative skin testing and positive RAST, 36 had a low-level RAST (1–3 ng/mL) and 7 had a high-level RAST (4–243 ng/mL). Sting challenge was conducted in 51 of the 99 patients with negative skin tests. Systemic reactions occurred in 11 of these 51 patients: 9 had low-level RAST and 2 had no specific IgE. Positive sting challenge was mild in 7 patients and moderate in 4, with no patient demonstrating a severe reaction. All systemic reactions occurred with yellow jacket stings, the focus of this group’s research. The systemic reaction rate to sting challenge in skin test negative patients (22%) was not different from the systemic reaction rate (21%) in skin test positive patients. The reaction rate was higher in patients with negative skin tests and positive RAST results (24%) than in those with negative RAST results (14%). Additionally, there was no significant difference in the severity of the reported past systemic reactions by patients with positive or negative skin tests, with both groups reporting 25% mild, 55% moderate, and 20% severe reactions.

Conclusions. The authors conclude that negative venom test results do not exclude the possibility of a systemic reaction. Authors also note their low recruitment of patients with negative skin tests and RAST for sting challenge make it possible that the overall frequency of reaction is as low as 11%; however, this does not diminish the potential risk of reaction in patients with a convincing history and negative testing. These results likely reflect limited diagnostic sensitivity of current testing methods. Authors recommend that patients with a convincing his-
of systemic reaction and negative skin testing to insects should be evaluated by means of RAST analysis and repeated in testing after 3 to 6 months. If all results are negative, the authors suggest that patients be counseled to the limitations of testing and the possibility of systemic reaction, as well as appropriate avoidance and treatment recommendations.

**Reviewer’s Comments.** This study provides a practical assessment of an important aspect of insect sting allergy. Current practice guidelines state that patients with negative skin tests are not candidates for immunotherapy, but they provide no guidance for the management of these patients. The authors of this study have thus provided insight into the clinical risks for these patients and have provided practical diagnostic and management suggestions to more fully evaluate and care for these patients. In addition, this study highlights the need for improved diagnostically testing for insect sting allergy.

**Stacie M. Jones, MD**
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**TREATMENT OF 193 EPISODES OF LARYNGEAL EDEMA WITH C1 INHIBITOR CONCENTRATE IN PATIENTS WITH HEREDITARY ANGIOEDEMA**

**Bork K, Barnstedt SE. Arch Intern Med. 2001;161:714–718**

**Purpose.** Hereditary angioedema (HAE) is an autosomal dominant disease (Mendelian Inheritance in Man 106100) caused by an inherited deficiency of C1 inhibitor (C1-INH) function. The clinical symptoms include skin swelling, abdominal pain, and life-threatening episodes of upper airway obstruction. The authors evaluated the efficacy of C1-INH concentrate for treating sudden airway compromise.

**Patient Population and Methods.** A series of 95 patients with HAE and a functional deficiency of C1-INH belonging to 59 families underwent screening for laryngeal edema. Double-blind treatment of randomized patients was not justifiable because of the life-threatening nature of this condition. Efficacy was evaluated by determining the interval from injection of C1-INH concentrate to the beginning of resolution of symptoms. The mean duration of episodes of laryngeal edema was compared in treated and untreated patients. Clinical information was obtained from emergency department physicians, the hospitals involved, reports of the general practitioners, and patients and their relatives.

**Results.** Forty-two patients had 517 episodes of laryngeal edema. Eighteen patients received 500- or 1000-U injections of C1-INH concentrate in 193 episodes. The C1-INH concentrate was effective in all laryngeal edemas. The interval from injection to interruption in progress of symptoms ranged from 10 minutes to 4 hours (mean standard deviation: 19.9 minutes). The mean standard deviation duration of laryngeal edema was 15.3 ± 9.3 hours in patients who received C1-INH concentrate and 100.8 ± 26.2 hours in those who did not.

**Conclusions.** Injected C1-INH concentrate is highly and rapidly effective in the treatment of laryngeal edema of HAE. Relief and resolution of symptoms begins 30 to 60 minutes after injection, and duration of the upper airway obstruction is substantially reduced.

**Reviewer’s Comments.** Injections of the C1-INH preparation, now available in Europe, has been successful in helping resolution of the episodic swelling of the skin and intestinal mucosa, which commonly occur in HAE. However, before this study the use of the C1-INH concentrate had not been assessed in laryngeal edema of HAE because of the rapid onset and potential fatality of this complication. Although this study is not carefully controlled, the results are encouraging, especially because emergency measures, such as tracheostomy, were never required. Hopefully, this C1-INH concentrate will soon be readily available in all countries.

**Allen Adinoff, MD**
Aurora, CO

**ATOPIC DERMATITIS**

**EFFECTIVENESS OF OCCLUSIVE BEDDING IN THE TREATMENT OF ATOPIC DERMATITIS—A PLACEBO-CONTROLLED TRIAL OF 12 MONTHS’ DURATION**

**Holm L, Ohman S, Bengtsson A, van Hage-Hamsten M, Scheynius A. Allergy. 2001;56:152–158**

**Purpose of the Study.** Allergen exposure in atopic dermatitis (AD) is a contributing factor in the pathogenesis of this multifactorial disease. This study addressed the effectiveness of allergen avoidance measures in patients with AD by utilizing mattress encasement.

**Study Population.** Forty adult patients with AD whose treatment consisted of low-potency topical steroids and emollients only.

**Methods.** Serum was obtained from each participant for total immunoglobulin E (IgE), CD30, IgE-specific antibody to house dust mites (HDM), cat, and *Pityrosporum orbiculare*. Each subject was evaluated by the Severity Scoring of Atopic Dermatitis (SCORAD) index to determine eczema severity as well as skin prick test (SPT) and atopy patch test (APT) for HDM. The active treatment group (n = 22) received occlusive mattress and pillow covers while the placebo group (n = 18) received cotton covers. Participants kept a symptom diary of itch severity. The above lab data and eczema severity were followed over a 12-month period. In addition, dust samples were analyzed for cat and HDM allergen at 3, 6, and 12 months.

**Results.** The eczema severity by SCORAD index and patient perception of itching was significantly reduced in both the active treatment and placebo groups. The serum CD30 significantly decreased in both groups and seemed to correlate with the eczema severity (P < .001). The HDM-specific IgE was also significantly decreased in both study populations in the last 6 months of the study (P < .05). Elevated HDM allergen concentration was not common in either group; however, for those with detectable levels, exposure significantly decreased in the active treatment group (P < .005). Patients with a positive APT to HDM had a more pronounced reduction of HDM-specific IgE in the active treatment group (P < .05).

**Conclusions.** Both groups had significant reduction in eczema severity and HDM-specific IgE. One explanation is that allergen reduction capacity of the cotton covers may be similar to occlusive covers in this population with low HDM concentrations. Also participant awareness of dust mite infestation may have altered the cleaning habits of placebo participants. Serum CD30 seemed to correlate with asthma severity suggesting that this may be a useful marker in AD. Sensitization and exposure did not appear to have an effect on the study outcome as nonsensitized and nonexposed individuals benefited equally as compared with sensitized and exposed individuals. This may be explained by reduction of other allergens or irritants.

**Reviewers’ Comments.** Although allergen exposure plays a role in AD, large studies have not been performed in this population to address the proposed benefits of
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Pediatrics 2002;110;437
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