PAF levels increased from 4% in the control groups to 20% in the group with grade 1 anaphylaxis, 71% in the group with grade 2 anaphylaxis, and 100% in the group with grade 3 anaphylaxis. There was an inverse correlation between PAF levels and serum PAF acetylhydrolase activity. The proportion of patients with low PAF acetylhydrolase activity increased with the severity of anaphylaxis. Serum PAF acetylhydrolase activity was significantly lower in patients with fatal peanut anaphylaxis than in control patients.

CONCLUSIONS. Serum PAF levels were directly correlated and serum PAF acetylhydrolase activity was inversely correlated with the severity of anaphylaxis. PAF acetylhydrolase activity was significantly lower in patients with fatal anaphylactic reactions to peanuts than in patients in any of the control groups. Failure of PAF acetylhydrolase to inactivate PAF may contribute to the severity of anaphylaxis.

REVIEWER COMMENTS. PAF is 1 of the proinflammatory mediators that are released systemically by the degranulation of mast cells and basophils. Although PAF is not the only mediator that plays a role in anaphylaxis, these results suggest that PAF is very important. Therefore, it may be useful to develop new pharmaceutical agents that block its actions. Additional research is also needed to determine if PAF and PAF acetylhydrolase measurements may be used as a screening tool to select patients at highest risk for fatal anaphylaxis.

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Brian A. Smart, MD, FAAP
Glen Ellyn, IL

DRUG HYPERSENSITIVITY

Drug Allergy Claims in Children: From Self-reporting to Confirmed Diagnosis

PURPOSE OF THE STUDY. To assess the prevalence of self-reported adverse drug reactions and drug allergy in a pediatric population and confirm the diagnosis in children with suspected drug allergy.

STUDY POPULATION. Patients (n = 1426) responded to an initial cross-sectional survey. A total of 60 of 67 patients with reported drug allergy were evaluated at an allergy clinic.

METHODS. The first phase included a cross-sectional survey that assessed the life occurrence of adverse drug reactions and self-reported drug allergy in the outpatient clinic of a pediatric hospital. The second phase involved a diagnostic workup in children with parent-reported drug allergy, including detailed clinical history and in vitro and in vivo investigations. Specific immunoglobulin E (IgE) level determination for β-lactams, prick and intradermal skin testing for β-lactams, local anesthetics and sulfonamides, and patch tests (if a delayed reaction was reported) were performed. If all other investigations were inconclusive and a provocation test was not contraindicated, this test was performed.

RESULTS. The prevalence of self-reported adverse drug reactions and drug allergy were 10.2% and 6.0%, respectively. The frequency of a medical diagnosis of drug allergy was 3.9%. The majority of the suspected allergic reactions were noninmediate cutaneous events attributed to β-lactam antibiotics in younger children. Of 60 patients evaluated in the allergy clinic, 39 patients had a plausible clinical history, and additional investigation including a skin test, IgE-level measurement, and possible provocation tests were conducted. Drug allergy was diagnosed in 3 children on the basis of positive responses in skin (n = 1) and oral provocation (n = 2) tests.

CONCLUSIONS. Although adverse drug reactions and suspected drug allergy are frequently reported in children, after a complete evaluation, only a few of these reactions can be attributed to immediate and noninmediate drug allergy. Overall, 94% of the patients could tolerate the initially suspected drug.

REVIEWER COMMENTS. This study underscores a serious problem: patients who experience or perceive a drug reaction are often classified as being truly allergic when this may not be the case. Such overdiagnosis and misdiagnosis may result in suboptimal medication choices. These results show that only 6% of the patients with initially suspected drug allergy were truly allergic. This study demonstrates the importance of a complete and detailed history, with consideration of additional testing including skin-prick tests, specific IgE-level determination, and provocation tests. It should be noted that for nonimmediate drug allergy, an oral provocation test may require prolonged treatment to observe for symptoms. Such provocation tests would not be undertaken for severe previous reactions (eg, toxic epidermal necrolysis).

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Faith Huang, MD
Anna Nowak-Wegrzyn, MD
New York, NY

HLA-B*5701 Screening for Hypersensitivity to Abacavir

PURPOSE OF THE STUDY. Abacavir is associated with severe and potentially life-threatening hypersensitivity reactions in up to 8% of the white population. In 2002, HLA-B*5701
was noted to be highly associated with this hypersensitivity reaction. The purpose of this study was to evaluate the effectiveness of prospective HLA-B*5701 screening to avoid these reactions.

STUDY POPULATION. A total of 1956 HIV-infected patients from 19 countries who had not previously received abacavir were enrolled.

METHODS. Individual patients were randomly assigned to undergo prospective HLA-B*5701 screening, with exclusion of previously known HLA-B*5701 positive patients from abacavir treatment, or to undergo a standard approach of abacavir use without screening. All subjects who started abacavir were observed for 6 weeks, the time frame in which a large majority of hypersensitivity reactions occur. The clinical diagnosis of hypersensitivity reaction to abacavir was assessed further by epicutaneous patch testing.

RESULTS. The prevalence of HLA-B*5701 was 5.76% (109 of 1956 subjects) of the subjects assigned to receive abacavir. Seventy-two percent were men, 84% were white, and 18% had not received antiretroviral therapy previously. Screening effectively eliminated patch-test–confirmed hypersensitivity. None of the subjects in the prospectively screened group had reactions, compared with 2.7% in the control group. This yielded a negative predictive value of 100% and a positive predictive value of 47.9%. Hypersensitivity reactions to antiretroviral therapy were clinically diagnosed in 93 patients, with a significantly lower incidence in the prospectively screened group (3.4%) than in the control group (7.8%) (P < .001).

CONCLUSIONS. HLA-B*5701 screening dramatically reduced the risk of immunologically confirmed hypersensitivity to abacavir. This pharmacogenetic test is useful for reducing the incidence of immunologically mediated hypersensitivity reactions to abacavir.

REVIEWER COMMENTS. This expansive study demonstrated the clinical usefulness of pharmacogenomics testing for immunologically mediated hypersensitivity to a particular drug. This is the first such demonstration for reactions to antiretroviral agents. A major limitation in the use of abacavir has been the concern for a severe hypersensitivity reaction. The availability of this inexpensive test (approximately $80 at our institution) substantially reduces that potential and allows antiretroviral therapy selection to be based on the drug’s merit as an effective antiretroviral agent. A unique feature of hypersensitivity to this particular drug is that it is a true T-cell–mediated reaction. Patch testing has been used for many decades to identify offending contact hypersensitivity allergens (eg, nickel). The search for additional biomarkers that would reflect a potential for adverse reactions to other drugs is ongoing. This type of study leads the way in demonstrating clinical effectiveness of such an approach.

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Joseph A. Church, MD
Los Angeles, CA

**ATOPIC DERMATITIS AND ALLERGIC SKIN DISEASE**

**Pollen Grains Induce a Rapid and Biphasic Eczematous Immune Response in Atopic Eczema Patients**


**PURPOSE OF THE STUDY.** To investigate the relationship between eczematous reactions in subjects with immunoglobulin E–mediated allergy to pollen grains.

**STUDY POPULATION.** Two populations were evaluated: one population included subjects with atopic eczema who were sensitized to grass or birch pollen and who had a positive atopy patch test, and the second population included subjects without atopic eczema or atopy but who had a positive atopy patch test to nickel. In addition, as control populations, healthy volunteers and atopic subjects with eczema and sensitization to grass or birch but without a positive atopy patch test were included.

**METHODS.** Atopy patch tests with native pollen grains were performed to delineate the effect of native pollen grains on human skin of healthy and atopic individuals. A nickel patch test served as an established model of contact dermatitis. Skin-site samples were taken for biopsy 6 to 96 hours after allergen application and investigated immunohistochemically.

**RESULTS.** Histology of positive patch tests showed an influx of mononuclear cells (predominantly CD4+, CD25+, and CD45RO+). This influx was detected earlier in the pollen patch-test reactions compared with the immune response to nickel. A biphasic cytokine response could be detected in skin samples from the pollen patch test: interleukin 5 dominated in the early phase, and interferon γ dominated in the late phase. The nickel patch test was continuously dominated by interferon γ.

**CONCLUSIONS.** Pollen grains induce eczematous reactions in susceptible individuals. This reaction seems clinically and immunohistochemically similar to the contact hypersensitivity reaction to nickel but follows a faster kinetic and a biphasic course: T-helper 2 and immunoglobulin E in the early (24-hour) phase and T-helper 1 predominance in the late (96-hour) phase.

**REVIEWER COMMENTS.** This article highlights the importance of understanding that type 1 allergy-inducing antigens...
# HLA-B*5701 Screening for Hypersensitivity to Abacavir

Joseph A. Church

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