



From the Pages of allergywatch®

Penicillin allergy



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The articles cited in this month's chapter of *From the Pages of AllergyWatch* focus on penicillin allergy. The literature has been rich with articles that cover this topic in very broad strokes from epidemi-

ology to outcomes measures. These articles complement those found in this month's emphasis for the *Annals* to update and expand the reader's knowledge in this important aspect of our practice base.

Inpatient Penicillin Allergy Testing Safety and Efficacy Data

True penicillin allergy in hospitalized patients carries risks, including longer hospital stay and a higher risk of resistant infections. Inpatient allergy testing can identify patients incorrectly labeled as allergic to penicillin. This meta-analysis evaluated the effects of inpatient allergy testing on clinical outcomes. A systemic review identified 24 studies of inpatient interventions to assess penicillin allergy during an index admission in which a penicillin antibiotic would be required. Sample size ranged from 24 to 252 patients; the main type of intervention was penicillin skin testing (PST), alone or with oral amoxicillin challenge. Change in antimicrobial therapy was the most commonly reported clinical outcome. The proportion of patients with negative PSTs ranged from 79% to 100%, with a population-weighted mean of 95.1%. The interventions consistently led to prescribing changes, including increased prescription of penicillin and cephalosporins and decreased use of vancomycin and fluoroquinolones. The changes in antibiotic prescribing were greater in intensive care unit settings: 77.97%, compared with 54.73% in other inpatient settings.

Some studies reported cost reductions; rates of adverse effects were very low. Available data suggest that inpatient penicillin allergy testing leads to favorable changes in antibiotic prescribing and other clinical outcomes. Rates of negative penicillin tests are similar to those reported in outpatient and perioperative studies; the benefits of inpatient testing appear largest in intensive care unit settings. The authors conclude, "Healthcare providers should be empowered to safely perform PST."

Comments from David Lang, MD: This meta-analysis provides additional evidence supporting the utility of immediate hypersensitivity skin testing as an important aspect of the management of hospitalized patients with a history of penicillin allergy. A substantial rise occurred in prescribing of penicillin and cephalosporin antibiotics in intensive care settings. Penicillin skin testing should be included as a component of a successful antibiotic surveillance program.

Sacco KA, Bates A, Brigham TJ, et al. Clinical outcomes following inpatient penicillin allergy testing: a systematic review and meta-analysis. *Allergy*. 2017;118:729-731.

Further Busting the Penicillin Allergy Mislabels

Many children seen in the emergency department (ED) are incorrectly reported as having penicillin allergy. Some reported

adverse drug reactions are not consistent with true allergic reactions. This study assessed the presence of high-risk and low-risk

Disclosures: Dr. Lang reports consulting fees from Genentech, GlaxoSmithKline, Hycor, and Novartis; consulting and contracted research for Genentech; and serving as a speaker and earning honoraria from Genentech and Novartis. Dr. Dinakar reports serving as a consultant and advisor for DBV Technologies and Teva, and as a clinical investigator for DBV Technologies and Abbott. Dr. Oppenheimer reports serving as a consultant and advisor for AstraZeneca, GlaxoSmithKline, Mylan, Novartis, and Teva; earning royalties from UpToDate; and receiving research funding from AstraZeneca, Medimmune, Novartis, and Sanofi. Dr. Hernandez-Trujillo reports serving as a consultant and advisor for CSL Behring; receiving honoraria from Bayer, Meda, and Merck; and receiving research funding from CSL Behring. Dr. Fineman reports serving as a speaker and teacher for AstraZeneca, Aimune, DBV Technologies, and Shire; and as a clinical investigator for Aimune, DBV Technologies, and Shire.

symptoms among pediatric ED patients labeled with penicillin allergy. The study included 500 children seen in a pediatric ED with parent-reported penicillin allergy. A parental questionnaire sought information on age at allergy diagnosis, allergy symptoms, and time from first dose to symptoms. Allergy symptoms were classified as high- or low-risk in consultation with a pediatric allergist, based on organ system involved and the potential for immunoglobulin E-mediated or T-cell-driven reaction. Median age at allergy diagnosis was 1 year, and younger than 3 years in three-fourths of children. Seventy-six percent of children had exclusively low-risk symptoms: most commonly rash (92.8%) and itching (40.6%). The remaining 120 patients had at least one high-risk symptom: most commonly facial swelling (10.0%) and difficulty breathing (7.4%). Symptoms occurred after first exposure to penicillin in 71% of children; ear infection was by far the most common indication. In 54.8% of cases, symptoms began within 24 hours of drug administration. Most pediatric ED patients with parent-reported penicillin allergy have only low-risk symptoms unlikely to reflect true penicillin allergy. In a subsequent study, the authors report the results of allergy testing in children with low-risk symptoms. Three-fourths of pediatric ED patients labeled with penicillin allergy have only “low-risk” symptoms for true allergic reactions. The authors report the results of penicillin allergy testing in children with such low-risk symptoms. The study included 100 children, aged 4 to 18 years, seen at a pediatric ED with parent-reported penicillin allergy. All had only low-risk symptoms for true penicillin allergy—mainly rash and itching—on a parental questionnaire. Penicillin allergy was assessed following a standard 3-tier testing process (percutaneous testing,

intracutaneous testing, and oral challenge). Median age was 1 year at allergy diagnosis and 9 years at allergy testing. As hypothesized, all children had negative results on penicillin allergy testing. This included 3 patients with positive results on percutaneous testing. In all 100 patients, the penicillin allergy label was removed from the medical record. Many pediatric ED patients are incorrectly reported and mislabeled as having penicillin allergy. Using a questionnaire to identify children with “low-risk” symptoms could promote increased use of first-line penicillin antibiotics.

Comments from Chitra Dinakar, MD: Wow, finally there are data that validate what allergists have known all along: most children who present to the ED with concerns of penicillin allergy have a low risk for true reaction! Also welcome is the creation of a risk stratification questionnaire for penicillin allergy that helps stratify patients as low risk and high risk. This excellent 3-tier study conducted at the Children's Hospital of Wisconsin convincingly demonstrates that low-risk allergy symptoms—most commonly rash and itching—likely do not represent true allergy in the pediatric ED. What a gigantic health care benefit to all stakeholders to have the penicillin allergy label removed from the medical records!

Vyles, D, Chiu A, Simpson P, et al. Parent-reported penicillin allergy symptoms in the pediatric emergency department. *Acad Pediatr*. 2017;17:251-255.

Vyles D, Adams J, Chiu A, et al. Allergy testing in children with low-risk penicillin allergy symptoms. *Pediatrics*. 2017;140:e20170471.

Allergists Can Lead in Inpatient Penicillin Allergy Testing

Most patients who report penicillin allergy can tolerate penicillin. Despite its impact on antibiotic prescribing, testing for penicillin allergy is infrequently performed in hospitals. This study reports a multidisciplinary approach to inpatient penicillin allergy testing. The program was implemented at an academic medical center, in a partnership between the allergy and pharmacy departments. Daily reports identified inpatients with reported penicillin allergy and prioritized them for evaluation. In appropriate cases, a specialty pharmacist performed diagnostic testing for penicillin allergy at the bedside. Of 1,203 patients screened over an 18-month period, 252 were interviewed by the allergy pharmacist. Penicillin allergy testing was performed in 247 patients and completed in 228. Just 5 patients had positive penicillin allergy test results. Overall, the program led to removal of reported penicillin allergy in 90.5% of cases; often, this was achieved just by taking a detailed history. Negative test results led to significant changes in antibiotic prescribing, including prescribing of a penicillin or cephalosporin in more than one third of cases. In approximately 7% of patients found not to have penicillin allergy, this label was added back on a later health care

encounter. In most cases, the allergy pharmacist was able to clear these incorrect reports. This experience shows that a dedicated inpatient penicillin allergy testing program is feasible and effective. The authors believe this is a practical and proactive approach to large-scale penicillin testing, which is readily adaptable to the needs of varying health care settings.

Comments from John J. Oppenheimer, MD: This very interesting study explored the use of a physician–pharmacist team to determine whether inpatients labeled with “penicillin allergy” could undergo a turnkey skin test and challenge protocol to remove this diagnosis when inaccurate. Recent studies have demonstrated increased morbidity and costs in hospitalized patients with a label of penicillin allergy. Through this program, more than 90% of patients were ultimately able to have the penicillin allergy label removed. The study provides a great framework for allergists to aid in improving antibiotic stewardship.

Chen JR, Tarver SA, Alvarez KS, et al. A proactive approach to penicillin testing in hospitalized patients. *J Allergy Clin Immunol Pract*. 2017;5:686-693.

Intrapartum Amoxicillin Does Not Increase Penicillin Allergy in Offspring

In pregnant women colonized with group B *Streptococcus* (GBS), intrapartum treatment with intravenous antibiotics is essential to prevent neonatal infection. Penicillin is the drug of choice. Previous studies have suggested increased rates of atopic diseases in children exposed to intrapartum antibiotics. The new study sought to determine whether intrapartum amoxicillin increases the risk of penicillin allergy in children. The retrospective analysis included a birth cohort of 804 children born at the Mayo Clinic in 2007. Eighty children were reported as having penicillin allergy. Intrapartum exposure to intravenous penicillin for GBS treatment was

evaluated for association with penicillin allergy. Nearly 80% of children with penicillin allergy were white, and more than 60% were boys. Reported penicillin allergy was unrelated to intrapartum exposure to penicillin, amoxicillin, or ampicillin. Nor did any of the other factors evaluated—including timing of antibiotic administration, maternal diagnosis of GBS, or mode of delivery—affect the children's risk of developing penicillin allergy. Children born to mothers receiving penicillin for treatment of GBS are not at increased risk of penicillin allergy. This risk is also unaffected by the presence of GBS, or by cesarean delivery.

Comments from Vivian Hernandez-Trujillio, MD: Increased interest in predicting which patients will develop allergies has led to studies looking at factors present at the time of childbirth. The authors studied mothers with GBS infection who received intrapartum antibiotics, including amoxicillin, ampicillin, and vancomycin. Unlike prior studies that have shown an association between intrapartum antibiotic use, cesarean delivery, and increased atopy in children, this study reassures us that neither treatment for GBS nor

cesarean delivery appears to increase the risk of penicillin allergy in offspring. Further studies would be helpful to explore whether this applies to other antibiotics as well.

May SM, Hartz MF, Joshi AY, Park MA. Intrapartum antibiotic exposure for group B Streptococcus treatment did not increase penicillin allergy in children. *Ann Allergy Asthma Immunol*. 2016;116:134-138.