

## PENICILLIN ALLERGY

### **-The Common Misconception-**

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Penicillin allergy is the most common allergy reported in children who present to the emergency department. It is estimated that > 90% of children who are labeled as “penicillin allergic” are actually able to tolerate penicillin when given the opportunity to undergo drug challenge/testing. Several recently published articles in 2018 address the issues of antibiotic allergy labeling and have gone so far as to discuss potential patient and public health consequences, as well as cost savings/benefits to healthcare institutions and families.

A recent review by Norton et al addresses antibiotic allergy labels in pediatrics patients. The authors conclude that improved patient and provider education related to drug allergies and reconciliation of allergy labels will prevent children from carrying false antibiotic allergies into adulthood. They also stress that education of providers on the differences between adverse drug reactions and hypersensitivity reactions is key to reducing incorrect allergy labeling.

### **Why It Matters:**

Labeling a child with a penicillin allergy without having a true allergic reaction has many negative effects including: increased cost (Rx costs are 30-40% higher), increased health risks, less efficacious treatments, longer hospital stays, and increased resistance to certain pathogens (23.4% more C. diff., 14.1% more MRSA, and 30.1% more VRE)<sup>1</sup>. As an example, if half of the children treated for otitis media received amoxicillin instead of cefdinir due to a reported penicillin allergy, annual savings would be \$34 million.

### **Understanding Different Drug Reactions:**

Approximately 35% of adverse drug events are reported as allergies in emergency departments and <10% of those are actually confirmed allergic reactions. True drug allergies are <15% of total adverse drug reactions overall. The most common drug allergy reported is delayed urticaria (occurring hours to days after exposure to an antibiotic) which usually occurs with a concomitant viral infection – it is not an IgE mediated reaction and should not be recorded as a drug allergy. It is important to understand the difference between an adverse drug reaction (side effect) and a true drug allergy.

<b><u>SIDE EFFECTS</u></b>	<b><u>TRUE ALLERGY</u></b>
<ul style="list-style-type: none"><li>• Do not involve anaphylaxis</li><li>• Not life-threatening</li><li>• Unwanted, but may be unavoidable</li><li>• Predictable</li><li>• Often dose dependent</li><li>• Onset occurs gradually (not immediately)</li><li>• Examples: nausea, vomiting, diarrhea, bleeding on warfarin</li></ul>	<ul style="list-style-type: none"><li>• Cause anaphylaxis</li><li>• Potential life-threatening reactions</li><li>• IgE-mediated response</li><li>• NOT dose dependent</li><li>• Occurs almost immediately (or within 1 hr of exposure)</li><li>• Symptoms: difficulty swallowing, hives, fever, shortness of breath</li></ul>

### **How to evaluate a patient labeled with an antibiotic allergy**

- Gather patient history (include subjective AND objective information).
- Get documentation of medications given, onset of reaction, and description of reaction that occurred.
- Obtain documentation of other exposures to the medication if possible.
- If provider is suspicious of a true allergic, IgE mediated reaction, a consult/referral to an allergist should be made for evaluation of possible skin testing and graded challenge.
- Immediate reactions (15-20 min after IV / 1 hr after PO) should always prompt further testing.

## **Skin Testing**<sup>1</sup>

- Skin prick / intradermal testing is a safe and efficacious method to diagnose intermediate reactions to antibiotics (mostly Beta-lactams).
- Guidelines recommend waiting 4-6 weeks after a reported reaction has completely resolved before performing skin test due to depleted mediators causing false positive.
- Can be performed in children at any age, even in infants.
- If patient passes a skin test, proceed to either a graded challenge or desensitization.
- If patient fails skin test, proceed to desensitization if that drug is required.

## **Graded Challenge**<sup>1</sup>

- Gold standard for drug allergy diagnosis.
- Used in patients with **low** probability for drug allergy (after negative skin test).
- Drug can be administered as a single dose or a weight based dose can be given in multiple intervals (ex: give 10% then the remaining 90% in 30-60 minutes).
- Used when skin test is negative to ensure there is no allergy to drug.
- If patient passes a graded challenge, then it is clinically reasonable they do not have drug allergy.

## **Desensitization**<sup>1</sup>

- Induced temporary drug tolerance by administering incremental doses of drug.
- Used in patients with proven or **high** risk for drug allergy when there is no alternative drug available.
- Must be performed in a monitored setting.
- Starting dose is usually in fractions of a milligram, which is doubled every 15-30 min until a cumulative therapeutic dose has been achieved.
- Once the drug is no longer in serum, the patient can no longer tolerate it and repeat desensitization is usually indicated if there is a delay of >2 half-lives.

## **Articles of reference:**

### ***Antibiotic Allergy in Pediatrics***<sup>1</sup>

A Norton, et al

It is estimated that 75% of children diagnosed with a penicillin allergy receive this allergy label before their third birthday and without confirmation by a physician. The authors hypothesize that the epidemiology of the penicillin allergy label can be traced back to the drug allergy box on medical forms. This box does not discriminate between predictable adverse drug reactions, true allergies, pharmacologic effects, and temporal observations, which leaves much room for interpretation by parents. A study found that out of 10,096 patients, 792 reported a drug allergy; 117 reports were consistent with actual IgE reaction, but only 7 tested positive for true drug allergy. Cross-reactivity is another area of concern for many patients. It is important to note that among the patients with a true, documented penicillin allergy; only 2% will also have a reaction to a cephalosporin. Drug challenging and desensitization are tools that should be utilized to guide therapy and ensure patients are receiving the standard of care. Although drug challenging is considered the gold standard in diagnosis, it is reported that 36-50% of patients with a negative challenge maintain documentation of still having the allergy. The authors here conclude that targeted, prospective antibiotic allergy management (similar to what has been studied in adult emergency departments) would lead to a positive impact on allergy de-labeling, as well as improve antimicrobial use and appropriateness. Education, promotion of allergy de-labeling and regularly reconciled interactive electronic medical records provide the best chance to avoid unnecessary allergy labeling.

## ***Antibiotic Use after the Removal of Penicillin Allergy Label***<sup>2,3</sup>

D. Vyles, et al

This is a follow-up case series following 100 children who tested negative for a penicillin allergy after receiving a 3-tiered challenge to a reported allergy. The series gathered data from parent and physician interviews after the children passed the penicillin challenge test. In this review, it was reported that 80% of parents have notified their PCP but also 84% of the PCPs reported they were not notified by the parents of their children passing the allergy test. This led to almost 52% of the children still having penicillin allergy in their PCP medical record after passing penicillin challenge. When parents were asked how comfortable they would be giving their child penicillin after passing the test, 24% said they would be “somewhat comfortable” and 4% would still be “uncomfortable.” Within 1 year of testing, 36 of the 100 children had received 26 penicillin derivatives and none suffered a serious reaction. The participants all had low-risk symptoms (if any) and were likely never allergic in the first place. This review demonstrates how crucial both education to parents and providers can be as well as comprehensive communication between parents, PCPs and subspecialty physicians.

A cost savings and avoidance analysis was performed on the same 100 children from the case series above. In the 36 children who received penicillin/derivative after passing the drug-challenge, only one patient had a reaction and it was a minor rash. The cost savings analysis found that not labeling the patients as penicillin allergic would save patients an estimated \$30 per prescriptions, and cost avoidance of \$1,812 per patient over the course of one year. The authors estimated a total potential savings to a pediatric ED was \$199,223 showing how significant the potential cost savings could be if low-risk patients are de-labeled and able to receive amoxicillin instead of cefdinir.

## References

1. Norton, A. et al (2018). Antibiotic Allergy in Pediatrics. *Pediatrics*, 141(5). [doi:10.1542/peds.2017-2497](https://doi.org/10.1542/peds.2017-2497)
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3. Paridon, B. (2018, May 21). Removing Low-Risk Penicillin Allergy Label Leads to Healthcare Cost Savings. Retrieved May 25, 2018, from <https://www.infectiousdiseaseadvisor.com/antibiotics-antimicrobial-resistance/removing-low-risk-penicillin-allergy-label-leads-to-healthcare-cost-savings/article/767517/>