



INTRODUCTION TO PENICILLIN ALLERGY DELABELING

Antibiotic Awareness Week 2023
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Outline

- Facts About Penicillin Allergies and Testing
- Why Delabel?
- Penicillin Allergy Delabeling Intervention Types
 - History-taking
 - PO Challenges
 - Skin Testing
- Where Do I Start?
- Takeaways



This presentation is intended to give guidance, but does not replace clinical judgement



U.S. Antibiotic Awareness Week: Nov. 18 - 24, 2023

- **Now available from WA DOH:**
 - [New subpage dedicated to penicillin allergy delabeling resources](#)
 - 2 brand-new general patient educations each focused on the following topics:
 - Penicillin allergies vs. side effects
 - PO challenge and skin testing
 - 1 brand-new specialized patient education
 - Desensitization (use as part of an established desensitization program)

Facts About Penicillin Allergy

Approx. 10% of patients report a history of penicillin allergy...However...Up to 90% of these individuals can tolerate penicillin

80% of patients with IgE-mediated penicillin allergy lose their sensitivity after 10 years

Family history of penicillin allergy does not mean that a patient is allergic to penicillin

Side effects are often confused with allergic reactions, leading to incorrect allergy labels

[Khan D et al. J Allergy Clin Immunol. 2022 Dec;150\(6\):1333-1393](#)
[CDC. Is it Really a Penicillin Allergy?](#)

Facts About Penicillin Allergy Delabeling

Some very minor risk reactions can be delabeled by taking a detailed history (see Slide #11)

Severe reactions following penicillin allergy testing in eligible patients are rare, estimated at a frequency of 0.06%

Negative penicillin skin testing results carry a predictive value for anaphylaxis that exceeds 95% and that approaches 100% when combined with oral amoxicillin challenge

PO amoxicillin challenges are safe and effective for delabeling low-risk patients

There are different protocols for testing that combine or separately utilize skin testing and PO challenges

[Khan D et al. J Allergy Clin Immunol. 2022 Dec;150\(6\):1333-1393](#)

[Shenoy et al. JAMA. 2019 Jan 15;321\(2\):188-199](#)

[Chang, K & Guarderas, J. Am Fam Physician. 2018 Jul 1;98\(1\):34-39](#)

[Cardosos-Fernandes, A et al. Clin Transl Allergy. 2021 Jun; 11\(4\): e12008](#)

[Cooper, L et al. JAC Antimicrob Resist. 2021 Jan 27; 3\(1\)](#)

Why Delabel?

Penicillin and other beta-lactam allergies are associated with:

- Increased use of broad-spectrum and non-preferred antibiotics
- 23% increased odds of *C. difficile* infection
- 14% increased odds of methicillin-resistant *Staphylococcus aureus* colonization or infection
- 30% increased odds of vancomycin-resistant *Enterococcus* colonization or infection
- 50% increased odds of surgical site infections
- Longer lengths of stay, higher mortality, higher readmission rates, and higher costs

Penicillins are first-line therapies for certain disease states, including:

- Syphilis
- Community-acquired pneumonia (outpatient)
- Otitis media
- Group B *Streptococcus* infection
- Dental infections
- And more!



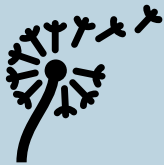
ACOG Opinion #797

- “Penicillin allergy testing...is safe during pregnancy”



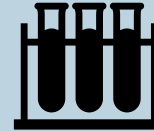
CDC's STI Treatment Guidelines

- “If appropriate, STI programs and ambulatory settings should consider developing expanded access to penicillin...allergy assessment”



AAAAI's Drug Allergy Practice Parameter

- “We recommend that a proactive effort should be made to delabel patients with reported penicillin allergy”



AAFP's Allergy Testing: Common Questions and Answers

- “Testing can be helpful in patients with a history of allergy to antibiotics when there are limited alternative treatments”



CDC

- “...Evaluate the patient for a true penicillin allergy...by conducting a history and physician, and, when appropriate, a skin test and challenge dose”



IDSA: Implementing an Antibiotic Stewardship Program

- “In patients with a history of beta-lactam allergy, we suggest that [antibiotic stewardship programs] promote allergy assessments and penicillin...skin testing when appropriate.”

Give your patients the gift of the best antibiotic choice to treat their bacterial infection!

Who Can Play a Role in Delabeling?

- Allergists
- Pharmacists
- Infectious diseases providers
- Emergency clinicians
- Internists
- Intensivists
- Advanced practice providers
- Nurses
- Outpatient providers
- Pediatricians



Washington State Data

- NHSN Patient Safety Component - Annual Hospital Survey:

*44. Our facility has a policy or formal procedure for other interventions to ensure optimal use of antibiotics: (Check all that apply.)

- Early administration of effective antibiotics to optimize the treatment of sepsis
- Treatment protocols for *Staphylococcus aureus* bloodstream infection
- Stopping unnecessary antibiotic(s) in new cases of *Clostridioides difficile* infection (CDI)
- Review of culture-proven invasive (for example, bloodstream) infections
- Review of planned outpatient parenteral antibiotic therapy (OPAT)
- The treating team to review antibiotics 48-72 hours after initial order (specifically, antibiotic time-out).
- Assess and clarify documented penicillin allergy
- Using the shortest effective duration of antibiotics at discharge for common clinical conditions (for example, community-acquired pneumonia, urinary tract infections, skin, and soft tissue infections)
- None of the above

CDC 57.103 (Front) Rev. 14, v11.1

15 of 21

- **Percentage of hospitals in WA answering “Yes” in 2022 = 29%**
 - 26% of critical access hospitals
 - 18% of all other acute care facilities
 - Survey had a 92% response rate from all WA hospitals

Delabeling Interventions

- 3 intervention types that address different reaction risk levels



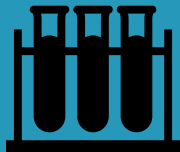
History

- Asking questions to assess and clarify the penicillin allergy



PO drug challenge

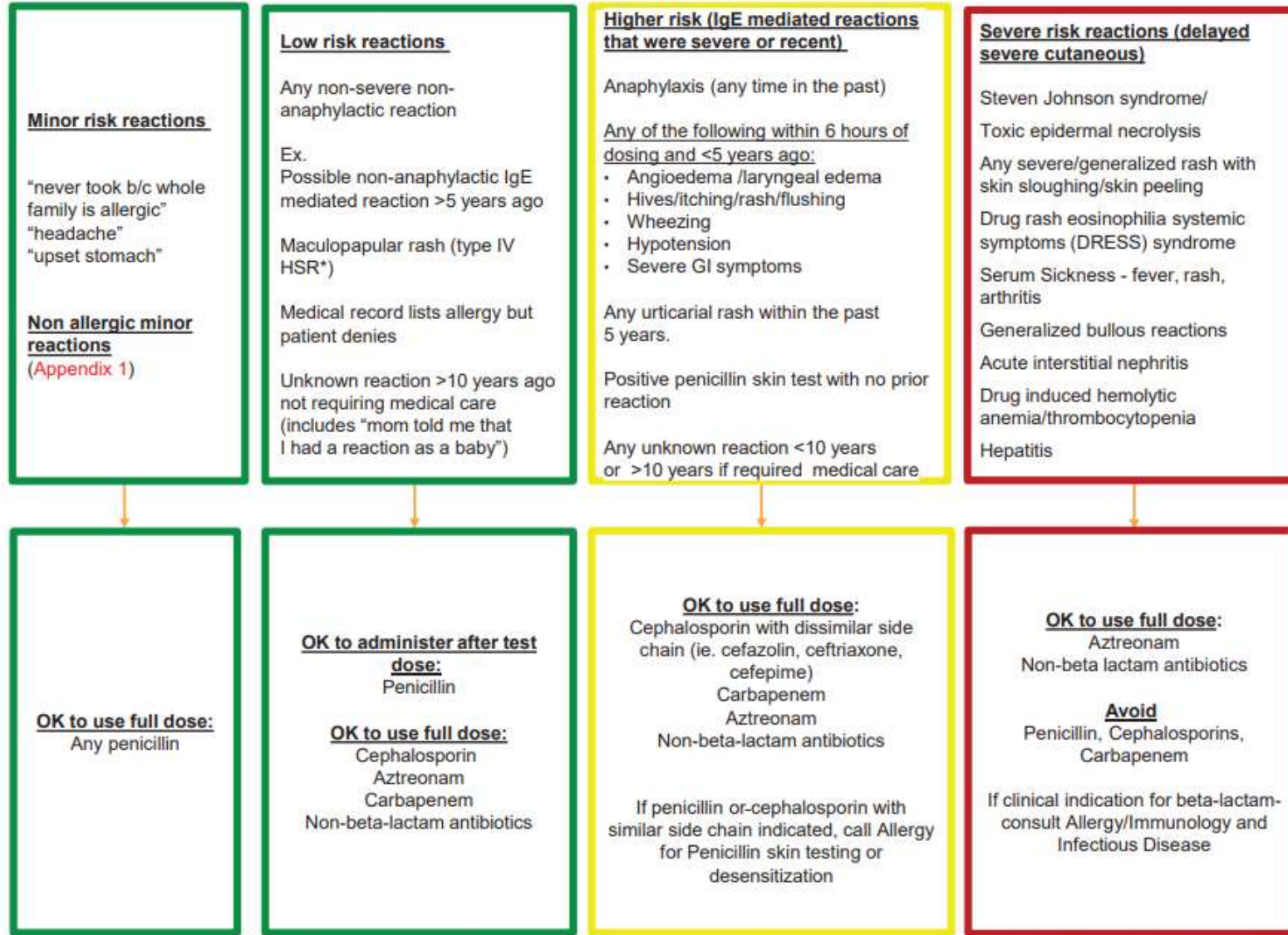
- Small, PO test dose(s) of amoxicillin



Skin testing

- Scratch testing
- Intradermal testing

Figure 1: Assessment of a Patient Reported Penicillin Allergy



*HSR: Hypersensitivity reaction. **See below for inpatient test dose procedure. For outpatient test dose and skin testing, refer to allergy clinic. Cefazolin in Penicillin allergy - see reference 13 and 14. ** See beta lactam cross-reactivity table

Who Should **NOT** Be Delabeled?

- These patients **should not receive drug challenges**
- Consult an allergist for guidance if a beta-lactam is indicated in a patient who meets these criteria

TABLE IV. Contraindications to drug challenges

Severe cutaneous adverse drug reactions
SJS/TEN
DRESS
AGEP
Drug-induced neutrophilic dermatosis
Sweet's syndrome
Drug-induced autoimmune diseases
Bullous pemphigoid
Pemphigus vulgaris
Linear IgA bullous disease
Drug induced lupus
Other cutaneous drug reactions
Generalized bullous FDE
Exfoliative dermatitis
Severe drug anaphylaxis*
Organ-specific drug reactions
Cytopenias (anemia, neutropenia, leukopenia, thrombocytopenia)
Drug induced liver injury
Nephritis
Pneumonitis
Meningitis
Pancreatitis
Drug-induced vasculitis
Leukocytoclastic vasculitis
Eosinophilic granulomatosis with polyangiitis
Angiotensin-converting enzyme inhibitor angioedema

*In the absence of reliable skin testing or when the benefit does not outweigh the risk.

Delabeling Using History

- Side effects can frequently be mislabeled as allergies!
- [American Academy of Allergy, Asthma, and Immunology's Drug Allergy Primer](#):
 - “We recommend against any testing in patients with a history inconsistent with penicillin allergy (such as headache, family history of penicillin allergy, or diarrhea...)”
- Take a detailed history, review patient’s medication history for evidence of recently tolerated penicillins
- See [CDC's Is It Really a Penicillin Allergy Factsheet](#) for questions that can be asked as part of the history



[Khan D et al. J Allergy Clin Immunol. 2022 Dec;150\(6\):1333-1393](#)
[CDC. Is it Really a Penicillin Allergy?](#)

Delabeling Using History

- [Chua, K et al. Clin Infect Dis. 2021 Aug 2;73\(3\):487-496](#)
 - Study: Multicenter whole-of-hospital intervention assessing the efficacy of inpatient delabeling for low-risk penicillin allergies using history or oral challenge in non-critically-ill adult patients
 - Results: Out of 355 patients who were delabeled, 161 or 45% of these were delabeled via history taking and review of medication history. This led to an increase in use of preferred antibiotics.
- [Turner, N et al. JAMA Netw Open. 2021 May 3;4\(5\):e219820](#)
 - Study: Longitudinal cross-sectional study assessing the efficacy of structured allergy history alone (phase 1) and assessment + skin testing (phase 2)
 - Results: Out of 273 who underwent assessment, 47 (17.2%) were considered to have no penicillin allergy based on history alone.

Delabeling Using History

- [Devchand, M et al. J Antimicrob Chemother. 2019 Jun 1;74\(6\):1725-1730](#)
 - Study: Prospective audit of pharmacist-led AMS penicillin allergy-delabeling ward rounds
 - Result: Out of the 106 adult patients meeting inclusion criteria, 13% of patients were directly delabeled using a detailed history and a medication review. This led to an increase in use of preferred antibiotics.

Delabeling Using PO Challenge

- Low-risk reactions (refer to chart on Slide #11)
- Small test dose(s) of amoxicillin taken by mouth
- Have supportive care measures on hand

One-Step

- 1 tab PO dose observed over 30-60 min
- May use single-dose challenge for patients at very low-risk without significant comorbidities

Two-Step

- ¼ tab PO dose observed over 30-60 min followed by 1 tab PO dose observed over 30-60 min
- Consider in patients with a history of more severe reaction or higher pre-test probability

[Khan D et al. J Allergy Clin Immunol. 2022 Dec;150\(6\):1333-1393](#)

Delabeling Using PO Challenge

- [Cooper, L et al. JAC Antimicrob Resist. 2021 Jan 27; 3\(1\)](#)
 - Study: Systematic review to assess the efficacy and safety of direct PO challenge in adult inpatients or outpatients without prior skin testing
 - Results: When conducted in conjunction with an allergy history process, validated tools, training, & clear guidelines, direct PO challenges in low-risk patients are safe and effective for delabeling patients. This can be performed by non-specialists.
- [Chua, K et al. Clin Infect Dis. 2021 Aug 2;73\(3\):487-496](#)
 - Study: Multicenter whole-of-hospital intervention assessing the efficacy of inpatient delabeling for low-risk penicillin allergies using history or oral challenge in non-critically-ill adult patients
 - Results: 194 patients had a negative PO challenge and 6 of them had a positive challenge. There were no acute-onset hypersensitivity reactions reported & 3 patients experienced a delayed reaction that did not require treatment.

Delabeling Using Skin Testing

- Higher-risk reactions (see chart on Slide #11)
- Perform a skin prick test first – if negative, perform an intradermal test
- PO challenge sometimes performed after skin testing
- Have supportive care on hand in case of reaction



Delabeling Using Skin Testing

- [Torney, N et al. Am J Health-Syst Pharm. 2021;78:1066-1073](#)
 - Study: Single-center observational cohort study describing the framework and results of a pharmacist-managed and pharmacist-administered penicillin allergy skin testing (PAST) service
 - Results: 85/90 adult patients who completed PAST were negative for a penicillin allergy. 1 patient developed a rash 24 hrs after being started on piperacillin-tazobactam. All other patients tolerated at least 1 dose of a penicillin antibiotic after PAST.
- [Turner, N et al. JAMA Netw Open. 2021 May 3;4\(5\):e219820](#)
 - Study: Longitudinal cross-sectional study assessing the efficacy of structured allergy history alone (phase 1) and assessment + skin testing (phase 2)
 - Results: 187/193 patients tested negative. No patients were documented to have subsequent reactions to penicillin-based antibiotic therapy.

Desensitization or Induction of Tolerance

- Performed in the acute care setting by trained health care providers
- Induces a temporary state of tolerance to a medication
- Typically performed when a penicillin is the only therapy choice available (i.e., syphilis in pregnancy)
- **Consider if the patient can benefit from a graded drug challenge instead**
- Do not desensitize patients reporting a history of SJS/TENS/DRESS!



[Chastain, D et al. Pharmacy \(Basel\). 2019 Sep; 7\(3\): 112](#)

Where Do I Start?

1. Start with implementing a process to assess and clarify penicillin allergies

- Start with [this CDC resource](#) that contains history questions and education for providers
- Partner with an allergist or other provider trained in penicillin allergy delabeling (physician, pharmacist) – [toolkits & resources also available here](#)
- Provide education to key stakeholders
- Post an antibiotic cross-reactivity chart ([Page 36 of this toolkit](#)) in the pharmacy and applicable clinical areas
- Network with other facilities to learn from their experiences
- Perform a Plan, Do, Study, Act (PDSA) cycle of the new change
- Collect data
- **Start small (1 department, 1 floor, or a certain # of patients)**

2. Assess your efforts

- Analyze internal data, lessons learned, perform another PDSA cycle if needed
- Share data with stakeholders

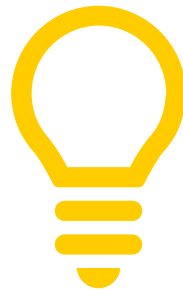
3. Grow your program

- Expand to another department/floor
- Consider offering PO challenges for eligible patients
- Consider offering skin testing for eligible patients after (if resources allow)

Small steps lead to big leaps!

Takeaways

- Penicillin allergy delabeling practices decrease the use of broad-spectrum and less efficacious antibiotics
- There are 3 intervention types that address different reaction risk levels: direct delabeling via history, PO challenges, and skin testing.
- Penicillin allergy delabeling practices can be safely performed by many different roles
- Start with implementing a process to take detailed histories of penicillin allergies and grow your program from there!



Resources

Getting Started

- [CDC's Is It a Penicillin Allergy?](#)
 - Contains questions that can be asked as part of a detailed allergy history assessment
- [PACE's Beta-Lactam Allergy Delabeling Guideline and Toolkit](#)
 - Provides guidance and contains templates to assist facilities who are just getting started
 - This resource contains a beta-lactam cross-reactivity chart on Page 36

Assessment Tools

- [University of WA's Penicillin Allergy Assessment Tool](#)
 - Provides clinical decision support to assist with assessing & clarifying penicillin allergies
- [PEN-FAST – Penicillin Allergy Risk Tool](#)
 - Enables point-of-care risk assessment of patient-reported penicillin allergies



U.S. Antibiotic Awareness Week: Nov. 18 - 24, 2023

Thank you!

Please enjoy the rest of our webinar mini-series!

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[Penicillin Allergy Delabeling | Washington State Department of Health](#)



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