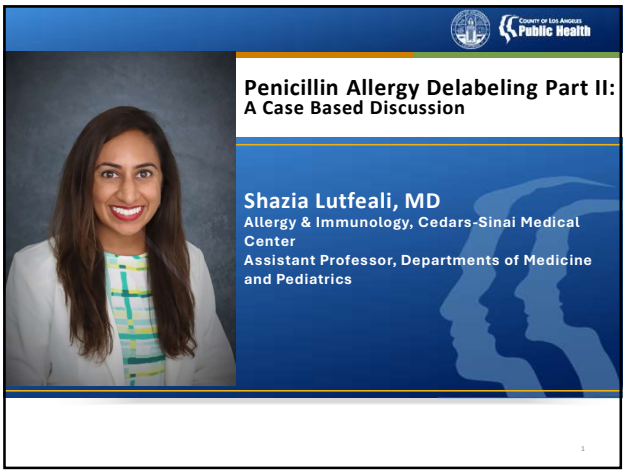

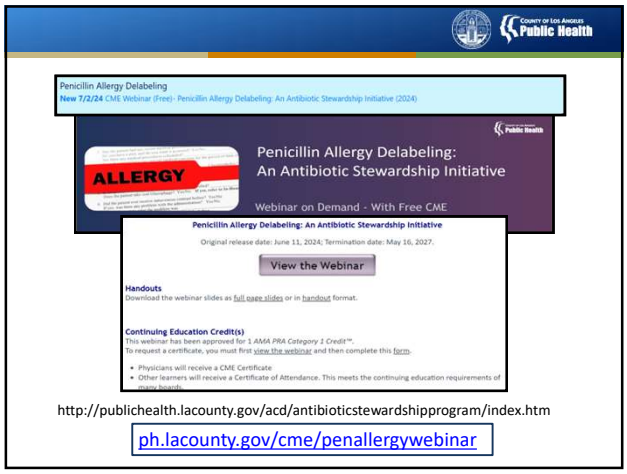

http://publichealth.lacounty.gov/acd/antibioticstewardshipprogram/index.htm

ph.lacounty.gov/cme/penallergywebinar

Key Points from "Penicillin Allergy Delabeling: An Antibiotic Stewardship Initiative"

LET'S REWIND

- 10-20% of the US population reports a penicillin allergy, but >90% are not allergic
  - True penicillin-associated anaphylaxis is very rare
- Reasons for inaccurate penicillin allergy labels:
  - Mislabeling of adverse effects
  - Initial misdiagnosis (viral exanthem)
  - Waning sensitivity (every year, ~10% of patients lose their penicillin sensitivity)

Case #6

A 43 year old female presents for penicillin allergy delabeling. Her history reveals that she took a course of amoxicillin as a teenager and within several hours of the first dose experienced scattered hives to her torso and extremities. She took a diphenhydramine tablet, took a nap, and the hives resolved by the end of the day.

Question: What is her PEN-FAST score?

A) 1
B) 2
C) 3
D) 4

PEN	Penicillin allergy reported by patient	If yes, proceed with assessment
F	Five years or less since reaction[a]	2 points
A	Anaphylaxis or angioedema	2 points
or		
S	Severe cutaneous adverse reaction[b]	
T	Treatment required for reaction[a]	1 point
		Total points

Trubiano et al. JAMA Intern Med 2020

Case #6 (cont.)

Utilization of PEN-FAST

Answer: 1 (Treatment required)

- Internationally validated clinical decision rule for adult patients
- Score <3 associated with low risk of true penicillin allergy (negative predictive value of 96.3%)
- Also validated in special populations (pregnancy, emergency department, intensive care unit)

PEN	Penicillin allergy reported by patient	If yes, proceed with assessment
F	Five years or less since reaction[a]	2 points
A	Anaphylaxis or angioedema	2 points
or		
S	Severe cutaneous adverse reaction[b]	
T	Treatment required for reaction[a]	1 point
		Total points

Interpretation

Points	
0	**Very low risk** of positive penicillin allergy test <1% (<1 in 100 patients reporting penicillin allergy)
1-2	**Low risk** of positive penicillin allergy test 5% (1 in 20 patients)
3	**Moderate risk** of positive penicillin allergy test 20% (1 in 5 patients)
4-5	**High risk** of positive penicillin allergy test 50% (1 in 2 patients)

Trubiano et al. JAMA Intern Med 2020

Case #7

A 33 year old female is questioned about her penicillin allergy history. She states she took amoxicillin several years ago and recalled feeling very nauseous afterwards. She also recalled needing to use her albuterol inhaler for some chest tightness. At the time, her primary care physician switched her to another antibiotic. Looking back, though, she is unsure if the asthma symptoms she experienced were related to amoxicillin ingestion or not. What would be the most appropriate next step in penicillin allergy delabeling?

A) Graded amoxicillin challenge
B) Full dose amoxicillin challenge
C) Penicillin skin testing

Case #7 (cont.)

When to Refer for Penicillin Skin Testing

Answer: Penicillin skin testing

Skin testing recommended for:
- Patients with a history of anaphylaxis
- Reactions occurring < 5 years ago (adult patients)
- Symptoms suggestive of an IgE-mediated reaction (other than benign cutaneous symptoms)

(-) skin test → Oral amoxicillin challenge

(+) skin test → Continued avoidance and/or Desensitization

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Case #8

A 57 year old male undergoes a graded oral amoxicillin challenge in your office. You decide to give him 50mg (1mL of 250mg/5mL solution) and intend to follow this up with a 450mg (9mL of 250mg/5mL solution) dose after a 30 minute monitoring period in between. However, about 15 minutes after taking the 50mg dose, the patient notes itching to his lower lip. A few minutes later, his lip is mildly but visibly swollen. His vital signs are stable and he has no other symptoms.

Question: How should this patient be treated?

A) Oral antihistamine

B) Intramuscular epinephrine

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Case #8 (cont.)

Management of Acute Reactions

Answer: Oral antihistamine (for presumed allergic angioedema)

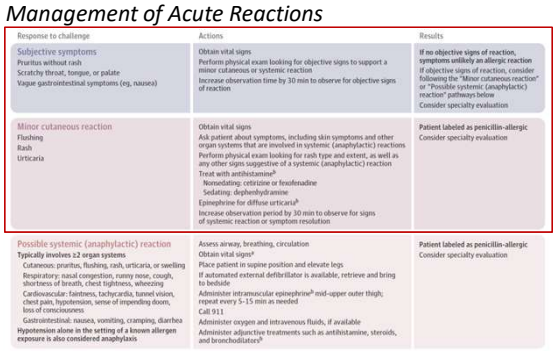
- Most reactions consist either of subjective symptoms or minor cutaneous reactions
- Standby medications:
  - Intramuscular and/or intranasal epinephrine
  - Oral antihistamine (2nd generation non-sedating preferred)
  - Inhaled/nebulized bronchodilator
  - H2 blocker
  - Steroids (oral and/or parenteral)

	Drug	Pediatric dosing	Adult dosing
Intramuscular (IM) epinephrine	Epinephrine 1 mg/mL (1: 1000)	**<10 kg:** 0.1 mg **10-25 kg:** 0.15 mg **Children >25 kg:** use Adult dosing	0.30 mg
Antihistamines	Diphenhydramine	1 to 2 mg/kg/dose (IM or PO); **Maximum:** 50mg/dose	25-50 mg
	Cetirizine	**6m to <2 years:** 2.5 mg **2 to 5 years:** 2.5-5 mg **Children ≥6 years:** use Adult dosing	10-20 mg
	Fexofenadine	**2 to 11 years:** 30-60 mg **Children ≥12 years:** use Adult dosing	90-360 mg
Glucocorticoids	Prednisone	1-2 mg/kg	20-60 mg
Bronchodilators	Albuterol inhaler	1 inhalation **Anaphylaxis:** 4-8 inhalations every 20 minutes for 3 doses	2 inhalations **Anaphylaxis:** 4-8 inhalations every 20 minutes for up to 4 hrs
	Albuterol nebulized	0.15 mg/kg (minimum dose: 2.5 mg) in 3 mL saline, inhaled via nebulizer **>12 years old:** use Adult dosing	2.5-5 mg every 20 minutes for 3 doses

Adapted from Shenoy ES et al. JAMA. 2019

Case #8 (cont.)

Management of Acute Reactions



Response to challenge	Actions	Results
Subjective symptoms Pruritus without rash Scratchy throat, tongue, or palate Vague gastrointestinal symptoms (eg, nausea)	Obtain vital signs Perform physical exam looking for objective signs to support a minor cutaneous or systemic reaction Increase observation time by 30 min to observe for objective signs of reaction	**If no objective signs of reaction, symptoms unlikely an allergic reaction** If objective signs of reaction, consider following the "Minor cutaneous reaction" or "Possible systemic (anaphylactic) reaction" pathways below Consider specialty evaluation
Minor cutaneous reaction Flushing Rash Urticaria	Obtain vital signs Ask patient about symptoms, including skin symptoms and other organ systems that are involved in systemic (anaphylactic) reactions Perform physical exam looking for rash type and extent, as well as any other signs suggestive of a systemic (anaphylactic) reaction Treat with antihistamine[b] Nonsedating: cetirizine or fexofenadine Sedating: dephenhydramine Epinephrine for diffuse urticaria[b] Increase observation period by 30 min to observe for signs of systemic reaction or symptom resolution	**Patient labeled as penicillin-allergic** Consider specialty evaluation
Possible systemic (anaphylactic) reaction **Typically involves ≥2 organ systems** Cutaneous: pruritus, flushing, rash, urticaria, or swelling Respiratory: nasal congestion, runny nose, cough, shortness of breath, chest tightness, wheezing Cardiovascular: faintness, tachycardia, tunnel vision, chest pain, hypotension, sense of impending doom, loss of consciousness Gastrointestinal: nausea, vomiting, cramping, diarrhea **Hypotension alone in the setting of a known allergen exposure is also considered anaphylaxis**	Assess airway, breathing, circulation Obtain vital signs[a] Place patient in supine position and elevate legs If automated external defibrillator is available, retrieve and bring to bedside Administer intramuscular epinephrine[b] mid-upper outer thigh; repeat every 5-15 min as needed Call 911 Administer oxygen and intravenous fluids, if available Administer adjunctive treatments such as antihistamine, steroids, and bronchodilators[b]	**Patient labeled as penicillin-allergic** Consider specialty evaluation

Shenoy ES et al. JAMA. 2019

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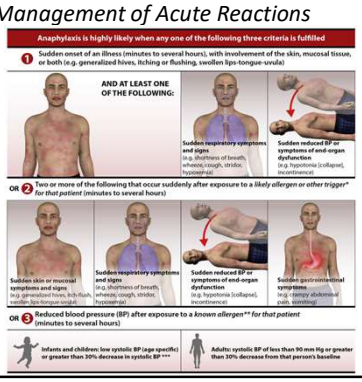
Case #8 (cont.)

Management of Acute Reactions



NIAID/FAAN Anaphylaxis Criteria

Shaker MS. J Allergy Clin Immunol. 2020

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Case #8 (cont.)

Management of Acute Reactions

- Severe reactions are extremely rare
  - Meta-analysis of 56 studies evaluating direct penicillin challenges showed that severe reactions occurred in only 5 of 9225 patients (0.05%)

Blumenthal KG et a. JAMA Intern Med. 2024

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Case #9

A 19 year old M presents for a scheduled surgical procedure. He is in need of perioperative antibiotics, and cefazolin is the preferred choice. However, he has a history of penicillin allergy listed in his chart.

Question: Can he safely receive cefazolin without any special precautions?

A) Yes

B) No

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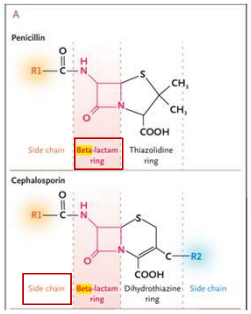
Case #9 (cont.)

Cross-Reactivity Between Penicillin and Cefazolin

Answer: Yes – patient can safely receive cefazolin

- Overall ~2% cross-reactivity between penicillins and cephalosporins
- BUT cefazolin has even lower cross-reactivity with penicillins (due to unique side chain)
  - 0.7% reaction rate to cefazolin among patients with unverified penicillin allergy
  - 0.8% reaction rate to cefazolin among patients with confirmed penicillin allergy



Castells M et al. N Engl J Med. 2019

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Case #9 (cont.)

Cross-Reactivity Between Penicillin and Cefazolin

Cefazolin Administration to Patients with History of Penicillin Hypersensitivity

Recommended Option: Administer cefazolin normally

Other Option: Administer cefazolin via drug challenge/test dose

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"Prospective, Multicenter, Head-to-Head Comparison Between Allergists Versus Nonallergists in Low-Risk Penicillin Allergy Delabeling"

- No difference in delabeling rates between allergist and nonallergist cohorts (93.3% vs. 94.1%)
- Similar improvements reported in health-related quality of life
- Waiting times (referral to penicillin allergy evaluation) significantly shorter for nonallergist vs. allergist cohorts (0.57 vs. 15.7 months)

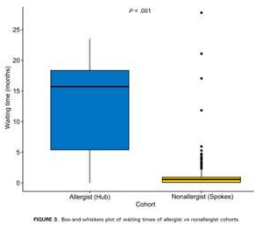

FIGURE 3. Box-and-whiskers plot of waiting times of allergist vs nonallergist cohorts.

Wong JCY et al. J Allergy Clin Immunol Pract. 2024

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"Delabeling penicillin allergy in a pediatric primary care clinic"

Direct amoxicillin graded challenge and observation performed by a trained pediatric nurse

During observation, patients completed routine healthcare maintenance visit with pediatrician

Outcomes:

- 100% of caregivers reported satisfaction with the challenge
- All delabeled patients reported they would use penicillins when prescribed
- None of the caregivers expressed a preference to have completed testing at an allergist's vs. pediatrician's office

Chow TG et al. Ann Allergy Asthma Immunol. 2023

17

"Oral Amoxicillin Challenges in Low-Risk Children During a Pediatric Emergency Room Visit"

MRN sticker

Penicillin Allergy Questionnaire

1) What age was your child at time of diagnosis? ☐ Years Months

2) What symptoms did your child have to the penicillin medication?

LOW risk symptoms	HIGH risk symptoms
Cough	Blisters (mouth)
Diarrhea	Blood pressure drop
Dizziness	Difficulty breathing
Family history of penicillin allergy	Seizures
Headache	Skin peeling
Itching (isolated / with only low risk)	Syncope
Nausea	Swelling (face)
Runny nose	Swelling (lips)
Vomiting (single episode)	Swelling (throat)
	Wheezing

3) Did any of these symptoms occur within 6 hrs of giving the medication?

Other symptoms	No	Unsure	Yes
Abdominal pain			
Itching (with rash)			
Rash			
Vomiting (multiple episodes)			

4) Is this patient low or high risk? Low High (One or more high risk symptoms = high risk)

5) Document low or high risk in Epic

Children 2-16 yrs with history of parent-reported penicillin allergy given a risk-stratifying questionnaire

Randomized to "No Oral Challenge" or "Oral Challenge" (500mg amoxicillin tablet or 520mg liquid)

1 hour observation period

Exclusion criteria:

- Developmental delay
- Contraindication to allergy testing
- Presenting symptoms of rash, vomiting, or asthma
- Admission to hospital (or too acutely ill to participate)

Vyles et al. J Allergy Clin Immunol Pract. 2020

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"Oral Amoxicillin Challenges in Low-Risk Children During a Pediatric Emergency Room Visit" (cont.)

40 children randomized to receive oral challenge → 37 children completed challenge* → 36 children (97.3%) passed challenge and successfully delabeled*

- 1 child refused to take medication
- 1 family did not want to wait
- 1 family decided not to participate

- 1 child developed mild urticaria after 40min which resolved with antihistamine

Vyles et al. J Allergy Clin Immunol Pract. 2020

Opportunities for Penicillin Allergy Delabeling

- Ambulatory care
- Hospitalized patients
- Preoperative evaluations
- Pediatric patients
- Pregnant patients
- Long-term care facilities
- Oncology patients
- Sexually transmitted infection clinics

Summary

- Inappropriate penicillin allergy labels pose a significant public health concern
- Delabeling can be performed by trained nurses, pharmacists, advanced practice providers, and non-allergist physicians
- Direct amoxicillin challenges are safe and effective for low risk patients

Resources To Aid with Implementation of Delabeling

- Los Angeles County Department of Public Health

Los Angeles County Department of Public Health Antibiotic Stewardship Program
Adult Low-Risk Penicillin Allergy Delabeling Toolkit for Hospitals

- American Academy of Allergy, Asthma, & Immunology

https://www.aaaai.org/tools-for-the-public/video-library/penicillin-allergy-videos

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