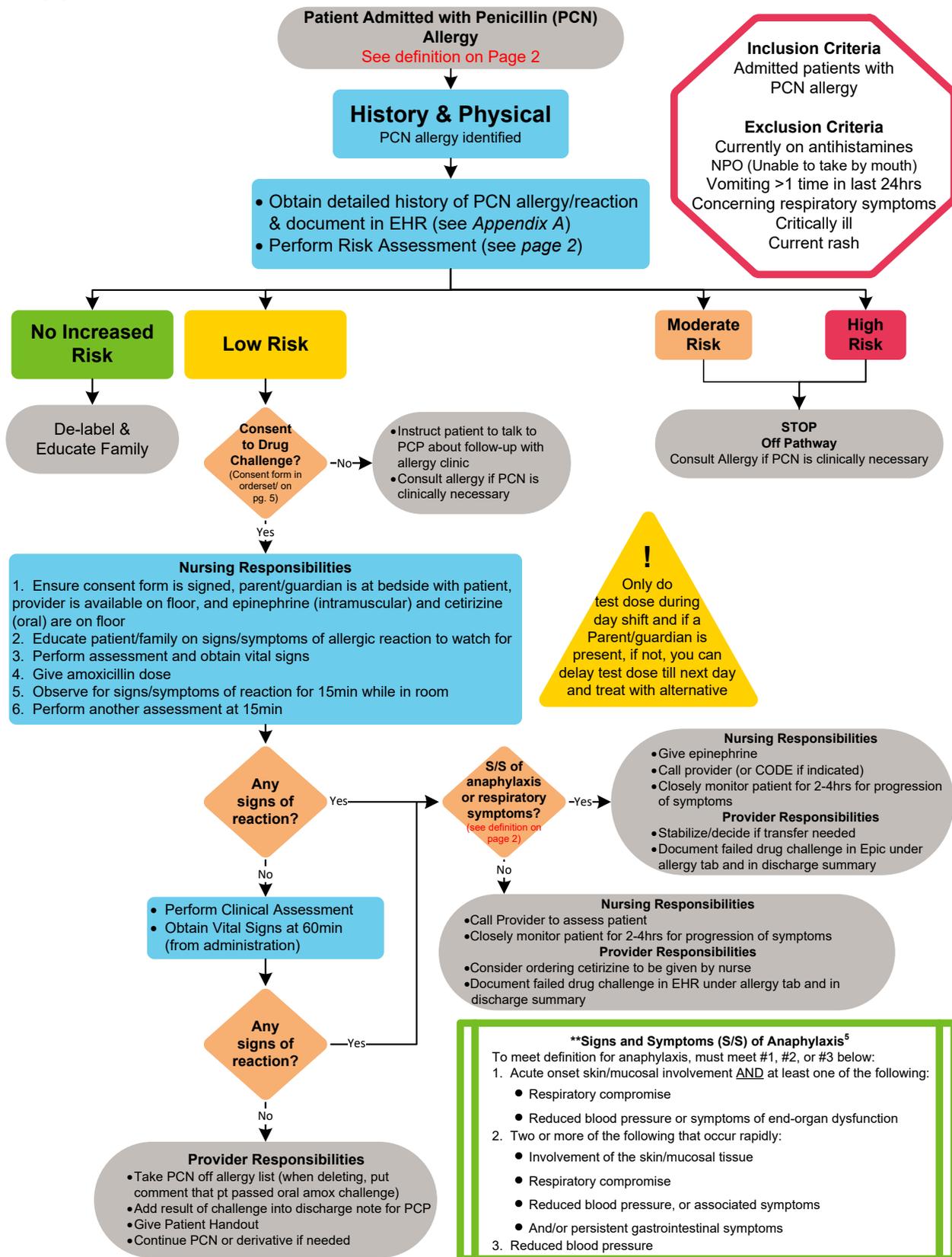


# PENICILLIN ALLERGY DELABELING

## ALGORITHM



Algorithm: Risk Assessment Based on Clinical History

- \*\*Allergies that qualify patient for oral amoxicillin challenge**
- Penicillin
  - Amoxicillin
  - Ampicillin
  - Ampicillin-sulbactam
  - Amoxicillin Clavulanic Acid

**No Increased Risk**  
*(Can simply de-label patient, no drug challenge needed)*

- Avoidance based on family history alone
- Has tolerated PCN since concerning incident without reaction

**Low Risk**  
*(Could consider oral challenge)*

- Delayed onset (greater than 24 hours after first dose) onset of isolated, non-progressive symptoms (such as gastrointestinal symptoms or rash/hives alone)

**Moderate Risk**  
*(Allergy consult needed if PCN desired based on primary team and ID consult for possible skin testing and/or desensitization)*

NOT To be given without Allergy and Infectious Disease input

- Unknown Clinical History
- Symptoms concerning for anaphylaxis
- Any symptoms requiring hospitalization
- Immediate symptoms (less than 24 hours after first dose of PCN)
- Progressive/worsening symptoms (within 60 minutes of dose)
- Reaction to intravenous/intramuscular formulation (within 60 minutes of dose)
- Primarily nasogastric tube (NG), gastric tube (GT), or jejunostomy tube (JT)

**High risk**  
*(PCN should be avoided. Skin prick testing and desensitization not recommended)*

Serious Cutaneous or Systemic Adverse Reactions concerning for but not limited to:

- Stevens-Johnson Syndrome (SJS) or Toxic Epidermal Necrolysis (TEN)
- Drug reaction with eosinophilia and systemic symptoms (DRESS)
- Acute Interstitial Nephritis (AIN)
- Serum Sickness

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## TARGET POPULATION

### Inclusion Criteria

- **No increased risk** for allergic reaction: Patient is avoiding penicillin based on family history alone, or has tolerated penicillin since the concerning incident without reaction.
- **Low risk** for allergic reaction: Patients who have delayed onset (greater than 24 hours after the first dose) of isolated symptoms (such as gastrointestinal symptoms or rash alone).

### Exclusion Criteria

- **Moderate risk** and **High risk** patients will continue to require formal evaluation through the allergy consult service should a penicillin be desired.
- Currently on antihistamines
- Vomiting more than 1 time in past 24 hours
- Concerning respiratory symptoms (wheezing, requiring oxygen, etc.)
- Critically ill
- Current rash
- Unable to take anything by mouth (NPO)

## BACKGROUND | DEFINITIONS

Penicillin allergy is reported in up to 10% of the general population, however, over 90% of patients reporting such an allergy tolerate penicillin without incident<sup>1</sup>. Common reasons for this include the previous reaction being attributed to penicillin when in fact it was more likely due to the infectious agent (i.e. a delayed viral exanthem) or a common side effect of the medication (i.e. diarrhea)<sup>1</sup>. True penicillin induced anaphylaxis is exceedingly rare (0.015%-0.04% of patients)<sup>1</sup>. Inappropriate penicillin allergy labeling has negative impacts on health care. Patients labeled as penicillin allergic have longer hospital stays and increased exposure to suboptimal antibiotics<sup>2</sup>. This use of suboptimal antibiotics leads to increase costs, contributes to antimicrobial resistance and increased side effects<sup>2</sup>. Specifically, having a penicillin allergy label has been associated with a 69% increased risk of *Methicillin Resistant Staph Aureus* (MRSA) and a 26% increased risk for *Clostridium Difficile* (C.diff)<sup>3</sup>. Due to the negative impact of a penicillin allergy label on patient outcomes, evaluation of penicillin allergy is considered an essential component of comprehensive antimicrobial stewardship programs<sup>4</sup>.

## Definitions

### Penicillin

Includes: penicillin, amoxicillin, amoxicillin-clavulanic acid, ampicillin, ampicillin-sulbactam

### De-labeling

The process of challenging the no-increased-risk or low-risk patient to amoxicillin. If this oral challenge is successful, de-labeling then requires removal of the penicillin allergy label in the patient's chart and providing education for the patient/parent and communication with primary providers regarding future use of penicillin and related antibiotics.

### Risk Categories

[See Definitions on Page 2](#)

### Anaphylaxis

NIH 2006 definition<sup>5</sup>: one of the 3 following scenarios:

1. Acute onset of a reaction (minutes to hours) with involvement of the skin/mucosal tissue AND at least one of the following:
  - Respiratory compromise
  - Reduced blood pressure or symptoms of end-organ dysfunction
2. Two or more of the following that occur rapidly after exposure to a likely allergen for that patient:
  - Involvement of the skin/mucosal tissue
  - Respiratory compromise
  - Reduced blood pressure, or associated symptoms
  - And/or persistent gastrointestinal symptoms
3. Reduced blood pressure after exposure to a known allergen

## INITIAL EVALUATION

### Penicillin allergy delabeling risk assessment

Patient with penicillin allergy listed when taking history. Detailed history obtained, and patient stratified into risk category based on the clinical history.

- See [Penicillin Allergy Screening Survey \(Appendix A\)](#)
- See [Algorithm: Risk Assessment Based on Clinical History](#)

If patient is at no increased risk or low risk, determine if any exclusion criteria apply

If patient does not fit exclusion criteria, discuss with team providers and parents the benefits and risks of performing a test dose for the patient.

- See [Family Decision Aid](#)– If team and parents agree to go ahead, proceed to Clinical Management section.

**Note: this pathway can be used to evaluate patients who require a penicillin while inpatient, but also to evaluate patients who are admitted with any diagnosis with a recorded PCN/derivative allergy.**

## CLINICAL MANAGEMENT/ THERAPEUTICS

There have been numerous publications indicating that patients with a history of delayed and non-life threatening reactions to penicillin (ie not consistent with an IgE mediated cause), can undergo an oral challenge with amoxicillin to safely and effectively rule out a penicillin allergy<sup>6-11</sup>. These studies together comprised a total of 3,299 patients who were low risk for penicillin allergy and underwent direct oral challenge to amoxicillin. Only 42/3299 patients (1.3%) had a reaction to their oral challenge, all of which were mild cutaneous reactions only<sup>6-12</sup>. It is currently endorsed to proceed directly to oral amoxicillin challenge in patients whose reactions to penicillin were described as benign rash, gastrointestinal symptoms, headaches or other benign somatic symptoms alone<sup>12</sup>. Other institutions have implemented penicillin allergy de-labeling protocols similar to this pathway which have demonstrated high rates of success<sup>13</sup>.

### Amoxicillin Test Dose

- Test dose only performed when the following criteria are met:
  - During day shift (if inpatient)
  - A parent or guardian is present
  - A provider is available on the floor
  - Rescue medications (epinephrine and cetirizine) are ordered and immediately available
- [Consent](#) obtained
- “Penicillin Allergy Delabeling” Epic order set used for ordering
- Amoxicillin 45mg/kg/dose (max 1000mg) orally, once
  - Indication: “Challenge Dose Amoxicillin”
  - Do not give amoxicillin dose until IM epinephrine (1mg/mL) and cetirizine are available on floor
  - Notify Provider/Escalate Care: If patient develops signs of acute anaphylaxis call provider; call Code Blue if signs of cardiopulmonary compromise. If patient develops minor allergic reaction only (hives, vomiting) call provider.
- Rescue medications
  - Epinephrine (1mg/mL formulation) INTRAMUSCULARLY in anterolateral middle third of thigh every 5 to 15 minutes.
    - <50Kg: 0.01 mg/kg/dose (1mg/mL formulation)
    - >50kg: give 0.5 mg/dose (1mg/mL formulation)
  - Cetirizine oral solution
    - Note: When given orally, a low or non-sedating anti- histamine (eg, cetirizine) is preferred over a sedating antihistamine (eg, diphenhydramine or chlorpheniramine) to avoid somnolence<sup>14</sup>
      - 6-23 months – 2.5mg po once
      - 2-5 years – 5mg po
      - Over 6 years – 10mg po
- Procedure
  - Nursing Responsibilities
    - Ensure consent form is signed, parent/guardian is at bedside with patient, provider is available on floor, and epinephrine (intramuscular) and cetirizine (oral) are on floor
    - Educate patient/family on signs/symptoms of allergic reaction to watch for
    - Perform assessment and obtain baseline vital signs
    - Give oral dose of amoxicillin as ordered

- Nurse should stay with patient for 15 minutes and perform another assessment at the end of the first 15 minutes. If stable, frequently check in on patient for the following 45 minutes
- Perform another assessment and obtain vital signs at 60 minutes after amoxicillin dose given
- If at any time there are signs or symptoms of a reaction:
  - For anaphylaxis ([see definition](#))
    - Nursing Responsibilities
      - Give IM epinephrine
      - Call provider (or CODE if indicated for cardio-pulmonary compromise)
      - Closely monitor patient for 2-4 hrs for progression of symptoms
    - Provider Responsibilities
      - Stabilize/decide if a transfer is needed
      - Document failed drug challenge in electronic health record (EHR) under allergy tab and in discharge summary
  - For isolated non-respiratory symptoms
    - Nursing Responsibilities
      - Call provider to assess patient
      - Closely monitor patient for 2-4 hrs for progression of symptoms
    - Provider Responsibilities
      - Consider ordering cetirizine to be given by nurse
      - Document failed drug challenge in EHR under allergy tab and in discharge summary
- If no reaction after 1 hour, nursing should notify provider that test dose is complete
  - Provider needs to delete allergy label from the patient's chart, with a notation of "patient had test dose of amoxicillin with no reaction on (date)"
  - Provider should then update the after visit instructions (AVS) or other discharge instructions (including d/c note for PCP) to include "patient had test dose of amoxicillin with no reaction on (date). Allergy label to penicillin removed from chart. Patient and parent educated that they may use this drug in the future."
  - Provider should discuss result with family and give family handout
  - Provider should change antibiotic regimen if warranted

## LABORATORY STUDIES | IMAGING

- Serum tryptase, if patient develops anaphylaxis:
  - Obtain within an hour of the start of symptoms
  - This will not influence acute management, but can be useful for the allergist who should see this patient in followup as an outpatient.

## PARENT | CAREGIVER EDUCATION

- See [Patient Education Handout](#) and [Family Algorithm](#)

## APPENDIX A: PENICILLIN ALLERGY SCREENING SURVEY

To help guide history taking (NOT intended for parent/caregiver to fill out)

### 1. Why is the patient currently avoiding penicillins?

- My child had a reaction to penicillin or a penicillin related-antibiotic
- Someone in my child's family is allergic to penicillins
- I don't remember
- Other reason (Please explain):

### 2. What was the name of the medicine the patient received?

- Penicillin
- Amoxicillin or amoxicillin-clavulanate
- Ampicillin or ampicillin-sulbactam
- Piperacillin or piperacillin-tazobactam
- Nafcillin, oxacillin, dicloxacillin

### 3. How was the medication given?

- By mouth
- Intravenously
- By a shot in the arm or buttocks

### 4. How soon after starting the medication did the symptoms start?

- Within 30 minutes of taking the first dose
- More than 30 minutes but less than 24 hours after the first dose
- Greater than 24 hours after the first dose
- Greater than 7 days after the first dose

### 5. How was the reaction treated?

- It gradually went away without any intervention or medication
- It went away with an oral antihistamine (Benadryl, Zyrtec, etc.)
- Epinephrine Administration

### 6. Did patient have to receive medical care from any of the following for the reaction?

- Pediatrician's Office
- Allergist's Office
- Urgent Care or Emergency Room
- Overnight Hospitalization

Continued on next page...

**APPENDIX A: PENICILLIN ALLERGY SCREENING SURVEY (CONTINUED)****7. Which of the following symptoms did the patient have to the medication:**

- Rash or hives alone (no other allergic symptoms)
- Nausea, vomiting or diarrhea alone (no other allergic symptoms)
- Lesions or ulcers involving the lips, mouth or eyes
- Peeling of the skin
- “Steven’s Johnson Syndrome (SJS)” or “Toxic Epidermal Necrolysis (TEN)”
- Involvement of the kidney or liver
- “Drug Rash with eosinophilia and systemic symptoms (DRESS)”
- Anemia or low blood counts
- Joint pains/swelling and fevers or “Serum sickness”
- Immediate respiratory symptoms (such as wheezing, cough, trouble breathing)
- Immediate swelling of the lips or tongue
- Blood pressure changes
- Anaphylaxis
- Other (Please explain)

**8. Has the patient had Penicillin or a Penicillin-related antibiotic since the initial reaction?**

- No
- Yes

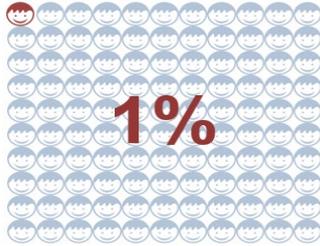
**9. If Yes to Question 8 above, what happened with these other exposures to penicillins?**

PATIENT EDUCATION HANDOUT

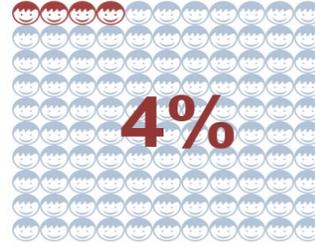
Your doctor has determined your child is eligible to take amoxicillin to see if they are allergic to it during their visit today. Here is some important information to consider:

In 100 children who report a penicillin/amoxicillin allergy:

1 will have an allergic reaction after taking a penicillin antibiotic



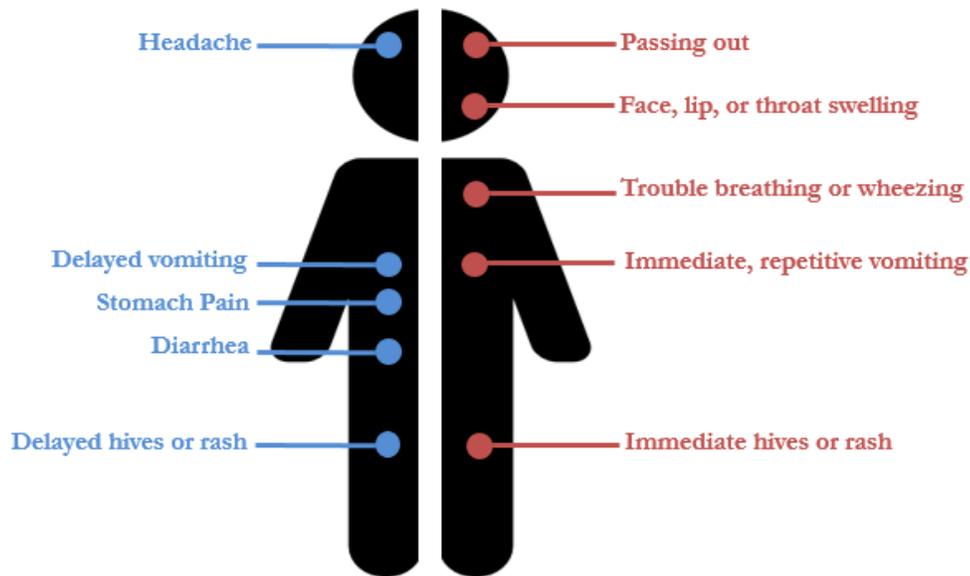
4 will have a rash that is not from an allergy and 95 will not have any reaction



Your child's reaction was likely NOT an allergy. It was probably a side effect or NOT due to the medicine.

SIDE EFFECTS

ALLERGIC SYMPTOMS



What are the Benefits of Testing My Child for an Allergy to this Medicine?

- Your child will be able to take penicillin/amoxicillin to treat common infections
- This medicine costs less money
- This medicine treats lots of infections
- This medicine has less severe side effects
- This medicine allows more options for treating common infections

Family Algorithm

### Testing for a Penicillin/Amoxicillin Allergy

Your child has penicillin or amoxicillin listed as an allergy in his/her chart. There is a very low chance your child actually has this allergy. During this visit, we will test your child to see if he/she has a reaction to the medication.

- Step 1:**
- Your doctor will answer any questions
  - Your nurse will take vital signs, perform an assessment, and give the medication
  - After 15 minutes another assessment will be performed to monitor for any symptoms
  - If your child is doing well, the nurse will come back in 45 minutes to re-check your child

**!**  
If your child is having trouble breathing, gets a rash, throws up, or if you are concerned, please tell your nurse right away.

**Step 2:  
Any Signs of Reaction?**

**DID NOT PASS**

- Your doctor will treat the reaction
- We will NOT remove the allergy from your child's chart
- They should NOT receive this medication in the future

- Passed**
- We will remove the penicillin/amoxicillin allergy from your child's chart
  - We will let your pediatrician's office know
  - You can tell your doctors and pharmacies that they can remove this allergy from your list
  - Your child CAN now take penicillin/amoxicillin unless he/she has a new reaction in the future

## REFERENCES

1. Solensky et al. Drug Allergy: An Updated Practice Parameter. *Annals of Allergy, Asthma and Immunology*. 2010
2. Macy, Contreras. Health care use and serious infection prevalence associated with penicillin “allergy” in hospitalized patients: A cohort study. *JACI* 2014;133(3):790-796
3. Blumenthal et al. Risk of methicillin resistant *Staphylococcus aureus* and *Clostridium difficile* in patients with a documented penicillin allergy: population based matched cohort study. *BMJ* 2018; 361:k2400.
4. <http://www.qualityforum.org/Publications/2016/05/AntibioticStewardshipPlaybook.aspx>
5. Sampson HA, Munoz-Furlong A, Campbell RI, et al. Second symposium on the definition and management of anaphylaxis: Summary report – second National Institutes of Allergy and Infectious Disease/Food Allergy and Anaphylaxis network symposium. *JACI* 2006; 117:391-7.
6. Mill C, Primeau MN, Medoff E, et al. Assessing the diagnostic properties of a graded oral provocation challenge for the diagnosis of immediate and nonimmediate reactions to amoxicillin in children. *JAMA Pediatr*. 2016;170:e160033.
7. Tucker MH, Lomas CM, Ramchandar N, Waldram JD. Amoxicillin challenge without penicillin skin testing in evaluation of penicillin allergy in a cohort of Marine recruits. *J Allergy Clin Immunol Pract*. 2017;5:813–815.
8. Labrosse R, Paradis L, Lacombe J, et al. Efficacy and safety of 5-day challenge for the evaluation of nonsevere amoxicillin allergy in children. *J Allergy Clin Immunol Pract*. 2018; 6(5) 1673-1680.
9. Lammatteo M, Alvarez A, Ferastraoaru D, et al. Safety and outcomes of oral graded challenges to amoxicillin without prior skin testing [published online May 23, 2018]. *J Allergy Clin Immunol Pract*. doi:10.1016/j.jaip.2018.05.008.
10. Ibanez MD, Del Rio PR, Lasa EM, et al. Prospective assessment of diagnostic tests for pediatric penicillin allergy, from clinical history to challenge tests. *Ann Allergy Asthma Immunol*. 2018;121. 235-244.e3.
11. Confino-Cohen R, Rosman Y, Goldberg A, et al. Oral challenge without skin testing safely excludes clinically significant delayed-onset penicillin hypersensitivity. *J Allergy Clin Immunol Pract*. 2017;5:669–675.
12. Macy E, Vyles D. Who needs penicillin allergy testing? *Ann Allergy Immunol* 2018;121:523-529.
13. Blumenthal KG et al. Addressing Inpatient Beta-Lactam Allergies: A Multihospital Implementation. *J Allergy Clin Immunol Pract*. 2017 May - Jun;5(3):616-625.e7.
14. Lieberman et al. Anaphylaxis: A Practice Parameter Update 2015. *Ann Allergy Asthma Immunol* 2015; 115 :341-384.

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