

Penicillin Allergy Delabeling

Laura Kvenvold, MD
Ian Michelow, MD

Connecticut Children's

What is a Clinical Pathway?

An evidence-based guideline that decreases unnecessary variation and helps promote safe, effective, and consistent patient care.

Objectives of Pathway

- To standardize the process for identifying patients with low risk of true penicillin allergy
- To standardize the process for delabeling low-risk penicillin allergies in the inpatient setting

Why is Pathway Necessary?

- Inappropriate penicillin allergy labels (PAL) are very common
- Carrying a PAL can result in use of overly broad spectrum antibiotics which is associated with a variety of negative outcomes
- New practice parameters emphasize the need to proactively identify false labels and remove (delabel) them
- A direct oral challenge with amoxicillin is safe and effective in testing patients who are at a low risk of having a true, IgE-mediated reaction
- There is limited access to allergists nationwide. This pathway empowers all healthcare providers to safely delabel PAL, allowing more patients access to this important care

Background

- About 10% of the US population carries a penicillin allergy label; however only 1% are actually real IgE-mediated (or severe delayed hypersensitivity reactions; 75% of patients with a PAL receive it before the age of 3 years
- Avoidance of penicillins, which is often first line therapy, is associated with increased treatment failures, surgical site infections, adverse side effects, development of resistant infections, and healthcare costs
- Numerous studies indicate that people listed as having a “low risk” PAL are able to safely undergo a direct oral drug challenge rather than requiring specialized skin testing first
- Allergy specialty services are limited; enabling other non-allergy providers to delabel patients is necessary
- The most recent Drug Allergy Practice Parameters (2022) recommend pediatric patients be proactively delabeled as part of standard of care

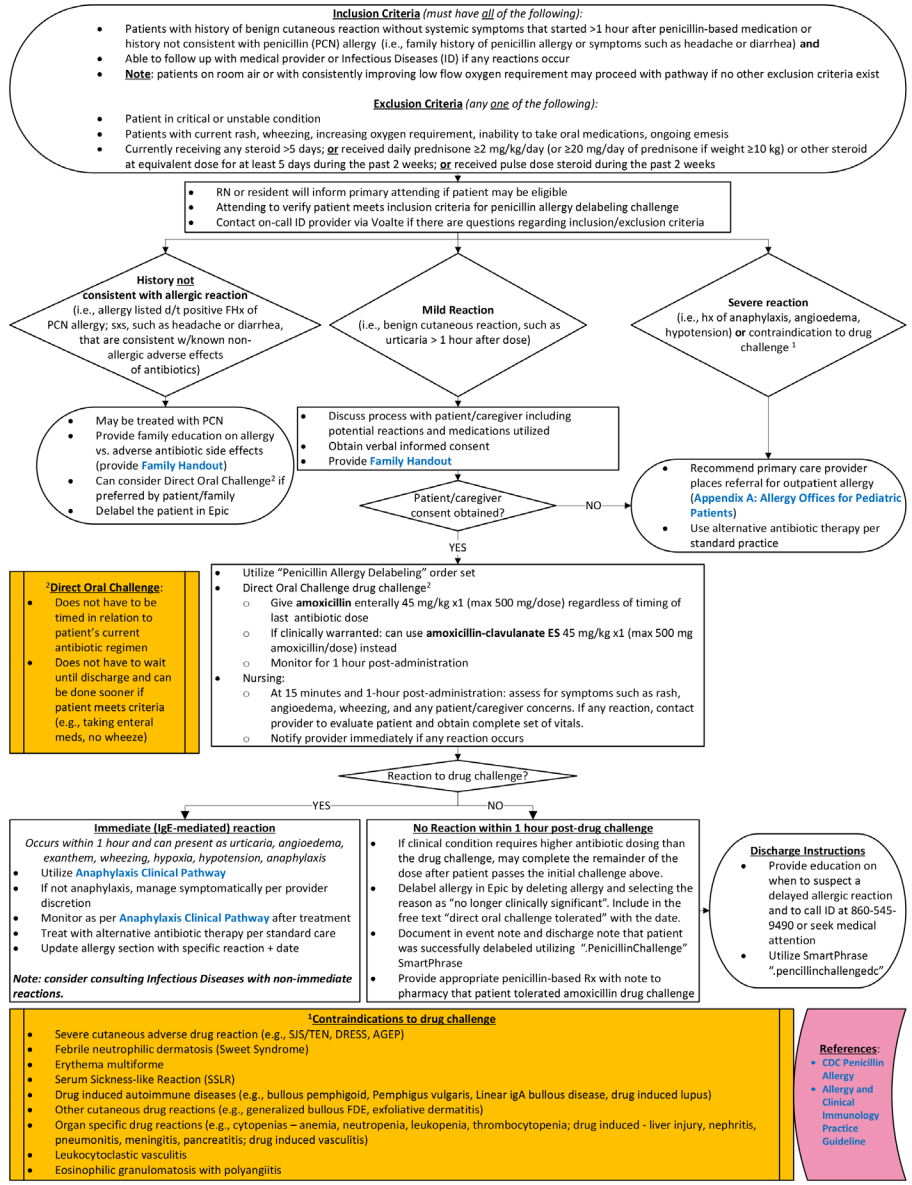
This is the Penicillin Allergy Delabeling Clinical Pathway.

We will be reviewing each component in the following slides.

CLINICAL PATHWAY:

Penicillin Allergy Delabeling

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.



CONTACTS: LAURA KVENVOLD, MD | IAN MICHELOW, MD

LAST UPDATED: 10.20.26

©2019 Connecticut Children's Medical Center. All rights reserved.

CLINICAL PATHWAY:

Penicillin Allergy Delabeling

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.

Inclusion Criteria *(must have all of the following):*

- Patients with history of benign cutaneous reaction without systemic symptoms that started >1 hour after penicillin-based medication or history not consistent with penicillin (PCN) allergy (i.e., family history of penicillin allergy or symptoms such as headache or diarrhea) **and**
- Able to follow up with medical provider or Infectious Diseases (ID) if any reactions occur
- **Note**: patients on room air or with consistently improving low flow oxygen requirement may proceed with pathway if no other exclusion criteria exist

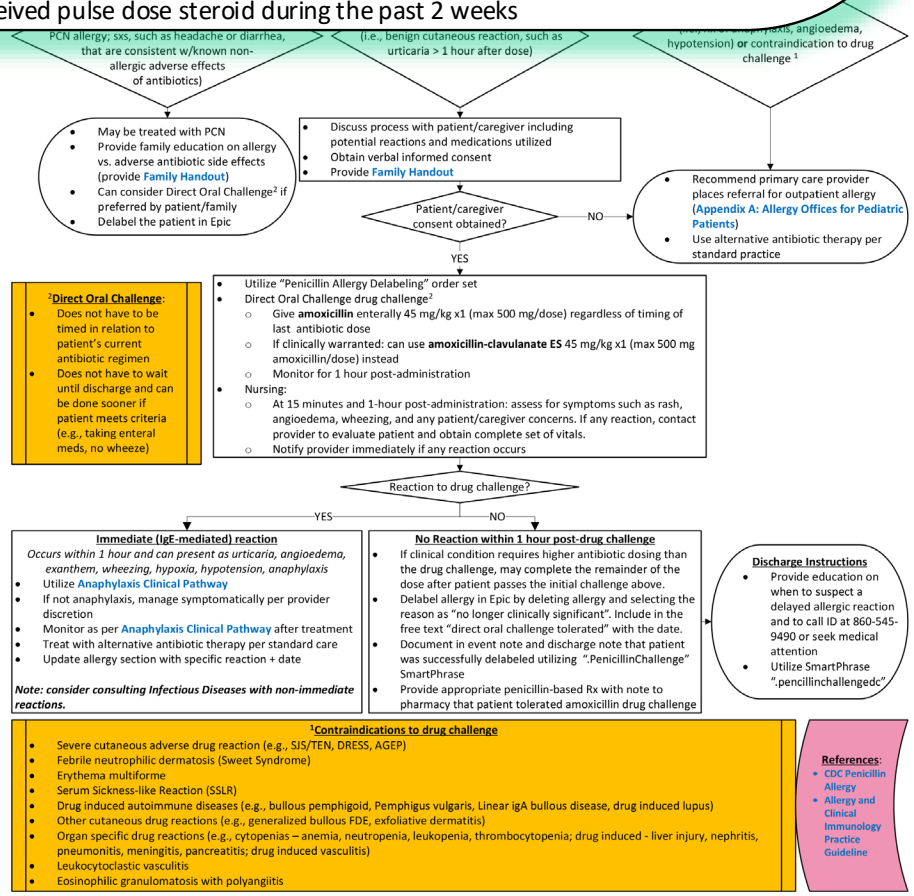
Exclusion Criteria *(any one of the following):*

- Patient in critical or unstable condition
- Patients with current rash, wheezing, increasing oxygen requirement, inability to take oral medications, ongoing emesis
- Currently receiving any steroid >5 days; **or** received daily prednisone ≥2 mg/kg/day (or ≥20 mg/day of prednisone if weight ≥10 kg) or other steroid at equivalent dose for at least 5 days during the past 2 weeks; **or** received pulse dose steroid during the past 2 weeks

Exclusion criteria were developed so that IF the patient has a reaction, the provider will be able to tell from signs or symptoms. The listed signs/symptoms could all mask an allergic reaction which could result in a false outcome.

Only clinically stable patients should be challenged; otherwise the risk may outweigh the benefits of challenge

Patients that are on oxygen (low flow, stable or improving) are safe to delabel as anaphylaxis may still be recognized by CHANGE in oxygen requirement.



CONTACTS: LAURA KVENVOLD, MD | IAN MICHELOW, MD

LAST UPDATED: 10.20.26

©2019 Connecticut Children's Medical Center. All rights reserved.

CLINICAL PATHWAY:

Penicillin Allergy Delabeling

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.

Inclusion Criteria *(must have all of the following):*

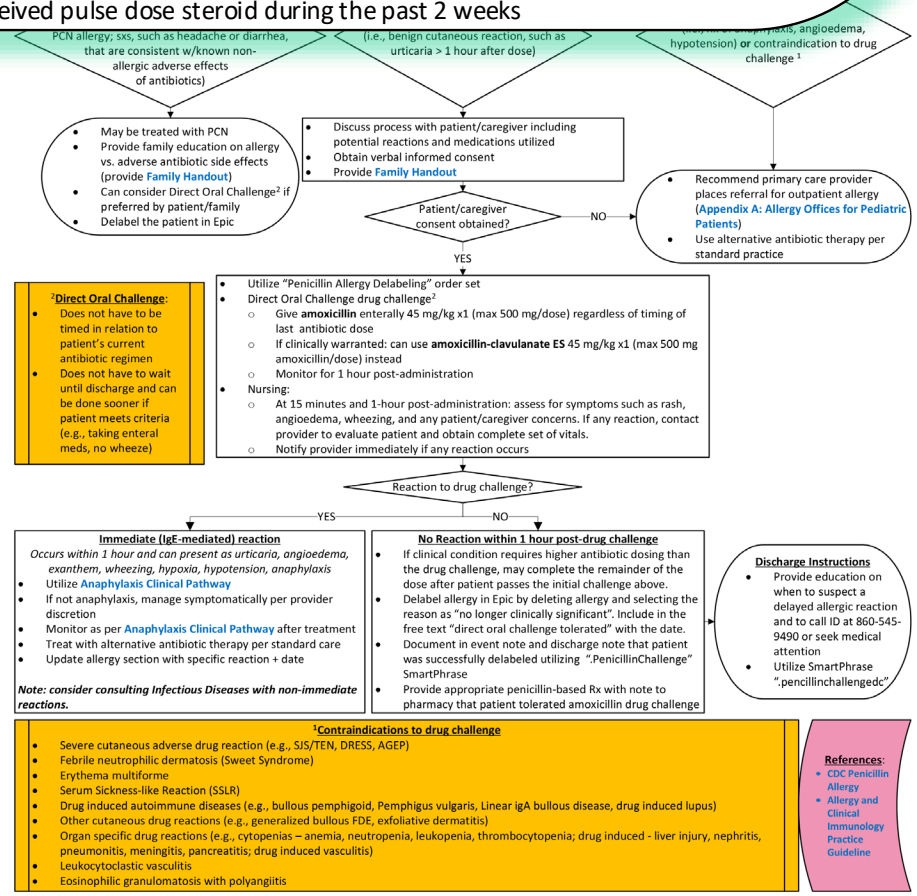
- Patients with history of benign cutaneous reaction without systemic symptoms that started >1 hour after penicillin-based medication or history not consistent with penicillin (PCN) allergy (i.e., family history of penicillin allergy or symptoms such as headache or diarrhea) **and**
- Able to follow up with medical provider or Infectious Diseases (ID) if any reactions occur
- **Note**: patients on room air or with consistently improving low flow oxygen requirement may proceed with pathway if no other exclusion criteria exist

Exclusion Criteria *(any one of the following):*

- Patient in critical or unstable condition
- Patients with current rash, wheezing, increasing oxygen requirement, inability to take oral medications, ongoing emesis
- Currently receiving any steroid >5 days; **or** received daily prednisone ≥2 mg/kg/day (or ≥20 mg/day of prednisone if weight ≥10 kg) or other steroid at equivalent dose for at least 5 days during the past 2 weeks; **or** received pulse dose steroid during the past 2 weeks

Direct oral challenge for patients with recent systemic steroid use is controversial. Use of steroids may mask the development of hives which could be a clue to an IgE-mediated reaction. If the patient is currently, or recently receiving steroids, see specific exclusion criteria parameters.

Inhaled and topical corticosteroid use is not an issue–these are NOT a contraindication to use of the pathway for delabeling.



CONTACTS: LAURA KVENVOLD, MD | IAN MICHELOW, MD

LAST UPDATED: 10.20.26

©2019 Connecticut Children's Medical Center. All rights reserved.

CLINICAL PATHWAY:

Penicillin Allergy Delabeling

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.

Inclusion Criteria *(must have all of the following):*

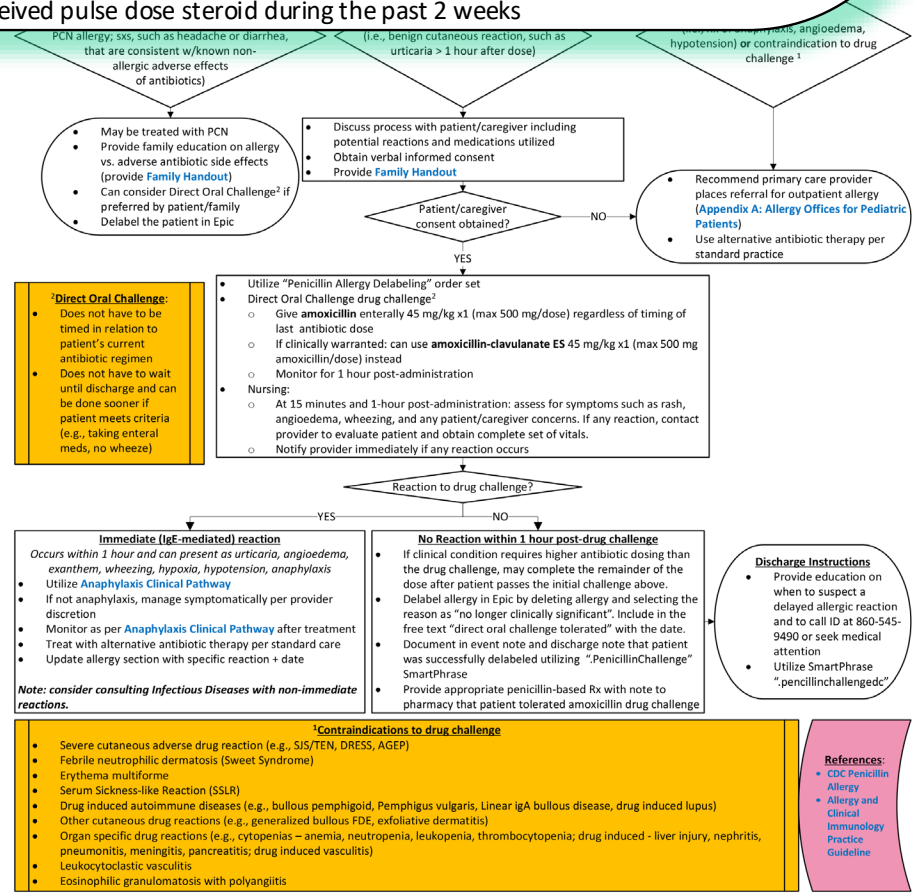
- Patients with history of benign cutaneous reaction without systemic symptoms that started >1 hour after penicillin-based medication or history not consistent with penicillin (PCN) allergy (i.e., family history of penicillin allergy or symptoms such as headache or diarrhea) **and**
- Able to follow up with medical provider or Infectious Diseases (ID) if any reactions occur
- **Note**: patients on room air or with consistently improving low flow oxygen requirement may proceed with pathway if no other exclusion criteria exist

Exclusion Criteria *(any one of the following):*

- Patient in critical or unstable condition
- Patients with current rash, wheezing, increasing oxygen requirement, inability to take oral medications, ongoing emesis
- Currently receiving any steroid >5 days; **or** received daily prednisone ≥2 mg/kg/day (or ≥20 mg/day of prednisone if weight ≥10 kg) or other steroid at equivalent dose for at least 5 days during the past 2 weeks; **or** received pulse dose steroid during the past 2 weeks

Other forms of immunosuppressive therapy and immunocompromising conditions are not strict contraindications for direct oral challenge for delabeling of penicillin allergy. There are studies that suggest that direct oral challenge is safe and effective in these patients.

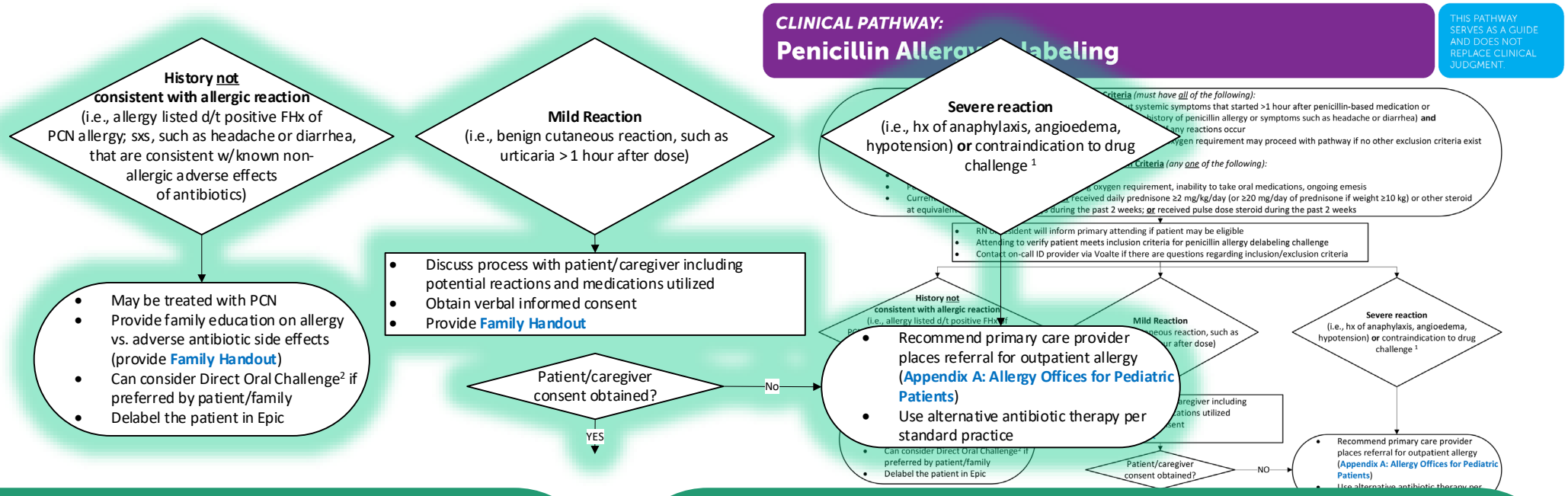
If you are unsure about whether a medication or condition limits use of the pathway, you can reach out to ID to discuss further.



CONTACTS: LAURA KVENVOLD, MD | IAN MICHELOW, MD

LAST UPDATED: 10.20.26

©2019 Connecticut Children's Medical Center. All rights reserved.



Getting an accurate allergy history is essential to determine the patient's risk level.

Tips: Get the STORY*

* Carter et al. (2023)

STORY mnemonic acronym

Symptoms	Describe the *symptoms* of the patient's reaction to penicillin.
Timing	Indicate how much *time* (in years) has passed since reaction.
Onset	Specify the *onset* of the reaction (e.g., started immediately after taking penicillin, within 24 hours of taking penicillin, etc.).
Resolution	Describe how symptoms *resolved* or went away.
Yet again	Specify whether the patient has received penicillin *yet again* since the reaction and it so, how penicillin was tolerated.

LAST UPDATED: 10.20.26

©2019 Connecticut Children's Medical Center. All rights reserved.

CLINICAL PATHWAY:
Penicillin Allergy Delabeling

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.

Lose the Label!

Get rid of your penicillin allergy for g

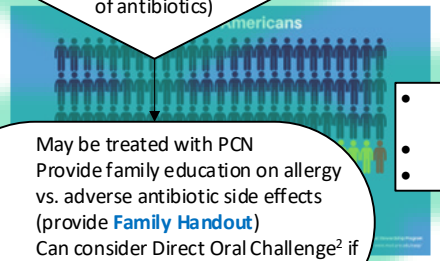
People are often labeled as "penicillin allergic" if they ha or penicillin. Most of the time, these reactions are not real allergies or dangerous.

Why does it matter?

Penicillin and amoxicillin often work better for certain infections. People who have a penicillin allergy may get different antibiotics that do not work as well. Sometimes these other antibiotics have more side effects. They can also cost more and taste worse.

Did you know?

- Many kids develop a rash when they get amoxicil an allergy
- Penicillin allergies are not passed down in families
- 80% of people with true allergy to penicillin grow out of it in 10 years



Remember, common side effects (like diarrhea) or a positive family history are not reasons to avoid using a penicillin antibiotic.

Penicillin allergies do NOT run in families.

Most people grow out of penicillin allergies within 10 years.

A family handout can be accessed on the pathway's internet homepage, and there are links to this on the pathway algorithm.

©2019 Connecticut Children's Medical Center. All rights reserved.

CLINICAL PATHWAY:
Penicillin Allergy Delabeling
Appendix A: Allergy Offices for Pediatric Patients

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.

Advanced Specialt
Dr. Yogen Da
Newtow
P: 203-830-470

Allergy Associates of Hartfo
21 Woodland St., Hartford, CT
(also offices in Glastonbury, Meriden, and Vernon)
59-8904

Massachusetts Allergy
rtson
90 Carew St
P: 413-707

Hartford H
Dr. Annya St
538 Litchfield St
P: 860-496-1790

Connecticut Asthma and Allergy Center (CAAC)
Multiple locations including West Hartford, Avon, amden, Middletown, Manchester
P: 860-232-9911

Allergy and Asthma Family Care
Dr. Shayna Burke
928 Farmington Ave, West Hartford, CT
P: 860-233-6293

Adult and Pediatric Allergy and Asthma of Connecticut
Dr. McGrath
12 Silas Deane Hwy, Wethersfield, CT
60-257-3535

ling Physicians, Allergy
Jigisha Morosky and colleagues
1260 Silas Deane Hwy, Wethersfield, CT
(also office locations in Enfield, Glastonbury)
P: 860-749-7001

Legal disclaimer:
This list of allergists is provided as an informational resource for patients and referring providers. Inclusion on this list does not constitute an endorsement, recommendation, or guarantee of the services or quality of care provided by any listed allergist. Connecticut Children's has compiled this list based on publicly available information and does not assume responsibility for verifying the credentials or capabilities of individual providers. Patients and referring providers are encouraged to perform their own due diligence when selecting a provider. This list is updated periodically; however, Connecticut Children's does not guarantee that the information is complete, accurate, or up-to-date.

CONTACTS: LAURA KVENVOLD, MD | IAN MICHELOW, MD

LAST UPDATED: 10.20.26

Connecticut Children's

©2019 Connecticut Children's Medical Center. All rights reserved.

CLINICAL PATHWAY:

Penicillin Allergy Delabeling

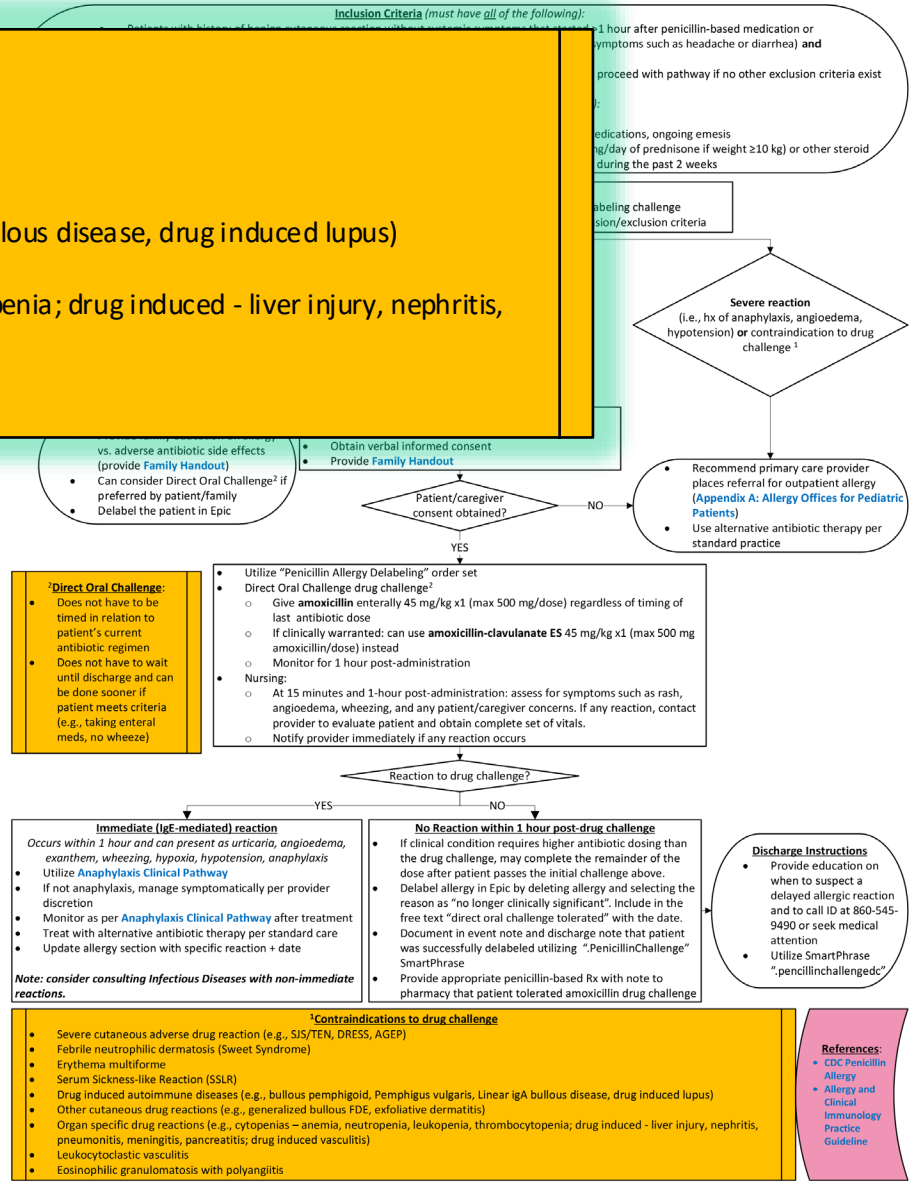
THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.

[1]Contraindications to drug challenge

- Severe cutaneous adverse drug reaction (e.g., SJS/TEN, DRESS, AGEP)
- Febrile neutrophilic dermatosis (Sweet Syndrome)
- Erythema multiforme
- Serum Sickness-like Reaction (SSLR)
- Drug induced autoimmune diseases (e.g., bullous pemphigoid, Pemphigus vulgaris, Linear igA bullous disease, drug induced lupus)
- Other cutaneous drug reactions (e.g., generalized bullous FDE, exfoliative dermatitis)
- Organ specific drug reactions (e.g., cytopenias – anemia, neutropenia, leukopenia, thrombocytopenia; drug induced - liver injury, nephritis, pneumonitis, meningitis, pancreatitis; drug induced vasculitis)
- Leukocytoclastic vasculitis
- Eosinophilic granulomatosis with polyangiitis

There are some reasons to avoid retrial of a penicillin that are NOT IgE-mediated. These reactions can be severe and are more likely to recur sooner with a retrial.

Luckily, these conditions are relatively uncommon in pediatric patients.



CONTACTS: LAURA KVENVOLD, MD | IAN MICHELOW, MD

LAST UPDATED: 10.20.26

©2019 Connecticut Children's Medical Center. All rights reserved.

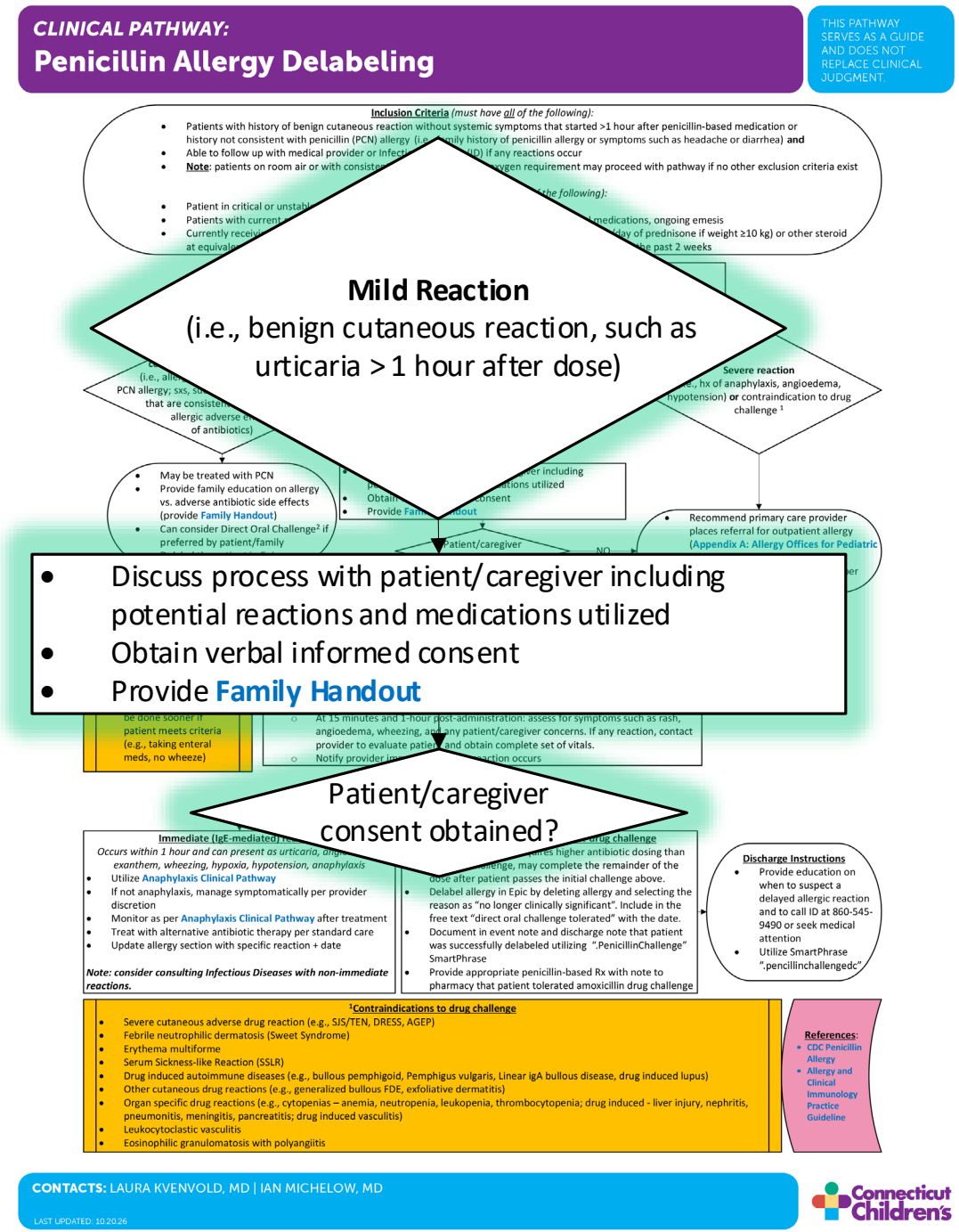
For a “mild reaction”, can discuss penicillin allergy delabeling with family.

While there is not a written consent form, you want to be sure the caregiver and patient are in agreement with the challenge and the potential for a reaction.

Please document in a note **using the SmartPhrase “.pencillinchallenge”**

There is a patient handout you can print from the pathway internet homepage for patients and caregivers.

Most patients and caregivers are excited to be “cured” of their allergy.

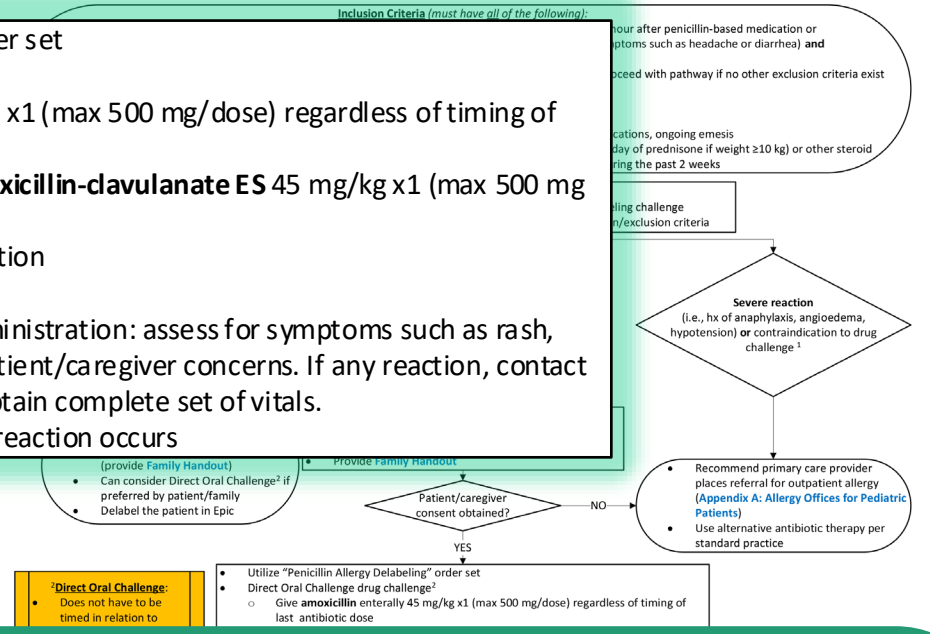


©2019 Connecticut Children's Medical Center. All rights reserved.

CLINICAL PATHWAY:
Penicillin Allergy Delabeling

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.

- Utilize "Penicillin Allergy Delabeling" order set
- Direct Oral Challenge drug challenge[2]
  - Give **amoxicillin** enterally 45 mg/kg x1 (max 500 mg/dose) regardless of timing of last antibiotic dose
  - If clinically warranted: can use **amoxicillin-clavulanate ES** 45 mg/kg x1 (max 500 mg amoxicillin/dose) instead
  - Monitor for 1 hour post-administration
- Nursing:
  - At 15 minutes and 1-hour post-administration: assess for symptoms such as rash, angioedema, wheezing, and any patient/caregiver concerns. If any reaction, contact provider to evaluate patient and obtain complete set of vitals.
  - Notify provider immediately if any reaction occurs



[2]**Direct Oral Challenge**:

- Does not have to be timed in relation to patient's current antibiotic regimen
- Does not have to wait until discharge and can be done sooner if patient meets criteria (e.g., taking enteral meds, no wheeze)

Please always **use the order set**. It is helpful for ordering the correct med/dose and the appropriate nursing orders.

Delabeling **does not** require cardiopulmonary monitoring.

Delabeling is proving that a suspected false allergy is in fact false and safe to remove from the patient's chart.

Delabeling is NOT the same as desensitization.

Desensitization is the medical process of providing increasingly larger doses of a medication under intensive medical supervision to allow temporary safe administration of a penicillin (e.g. in a pregnant patient with syphilis). This is a much riskier endeavor.

LAST UPDATED: 10.20.26

©2019 Connecticut Children's Medical Center. All rights reserved.

Immediate (IgE-mediated) reaction

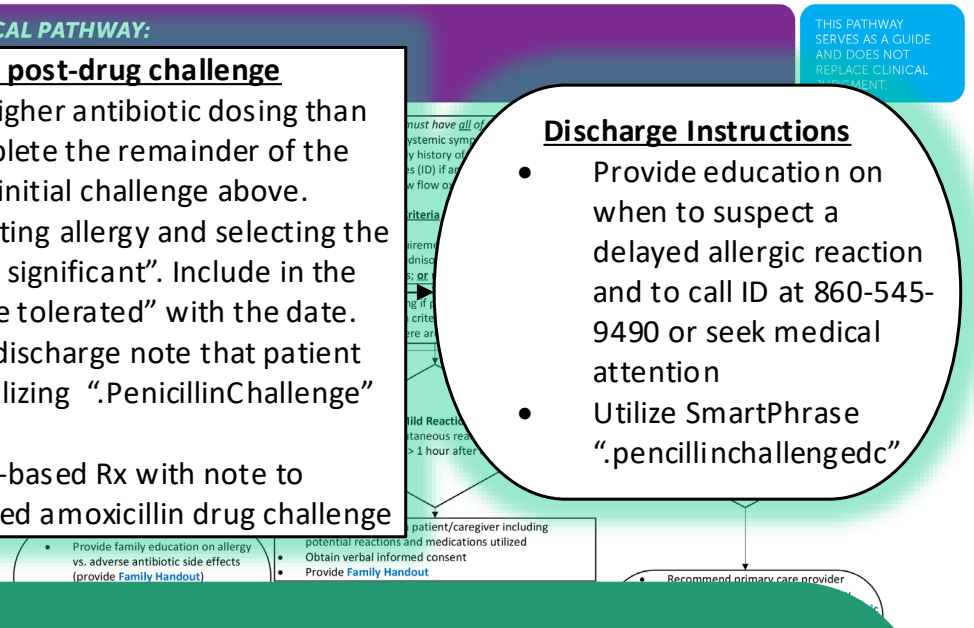
Occurs within 1 hour and can present as urticaria, angioedema, exanthem, wheezing, hypoxia, hypotension, anaphylaxis

- Utilize **Anaphylaxis Clinical Pathway**
- If not anaphylaxis, manage symptomatically per provider discretion
- Monitor as per **Anaphylaxis Clinical Pathway** after treatment
- Treat with alternative antibiotic therapy per standard care
- Update allergy section with specific reaction + date

Note: consider consulting Infectious Diseases with non-immediate reactions.

No Reaction within 1 hour post-drug challenge

- If clinical condition requires higher antibiotic dosing than the drug challenge, may complete the remainder of the dose after patient passes the initial challenge above.
- Delabel allergy in Epic by deleting allergy and selecting the reason as "no longer clinically significant". Include in the free text "direct oral challenge tolerated" with the date.
- Document in event note and discharge note that patient was successfully delabeled utilizing ".PenicillinChallenge" SmartPhrase
- Provide appropriate penicillin-based Rx with note to pharmacy that patient tolerated amoxicillin drug challenge



If the patient has ANY reaction, they should not not be delabeled.

There are not allergy reaction medications in the order set to have "just in case". If there is any concern for a reaction, the provider should promptly evaluate the patient and determine which medications, if any, are appropriate (see **Anaphylaxis Clinical Pathway** for guidance).

For non-immediate reactions, consider consulting ID to assist in evaluation and management.

If there is no reaction to the drug challenge:
- Give the rest of the antibiotic dose for the clinical condition
- Remove the allergy in Epic with documentation that the patient tolerated the direct oral challenge.
- Document in an event note **and** discharge note by utilizing ".PenicillinChallenge" SmartPhrase.

©2019 Connecticut Children's Medical Center. All rights reserved.

CLINICAL PATHWAY:

Penicillin Allergy Delabeling

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.

Immediate (IgE-mediated) reaction

Occurs within 1 hour and can present as urticaria, angioedema, exanthem, wheezing, hypoxia, hypotension, anaphylaxis

- Utilize **Anaphylaxis Clinical Pathway**
- If not anaphylaxis, manage symptomatically per provider discretion
- Monitor as per **Anaphylaxis Clinical Pathway** after treatment
- Treat with alternative antibiotic therapy per standard care
- Update allergy section with specific reaction + date

Note: consider consulting Infectious Diseases with non-immediate reactions.

No Reaction within 1 hour post-drug challenge

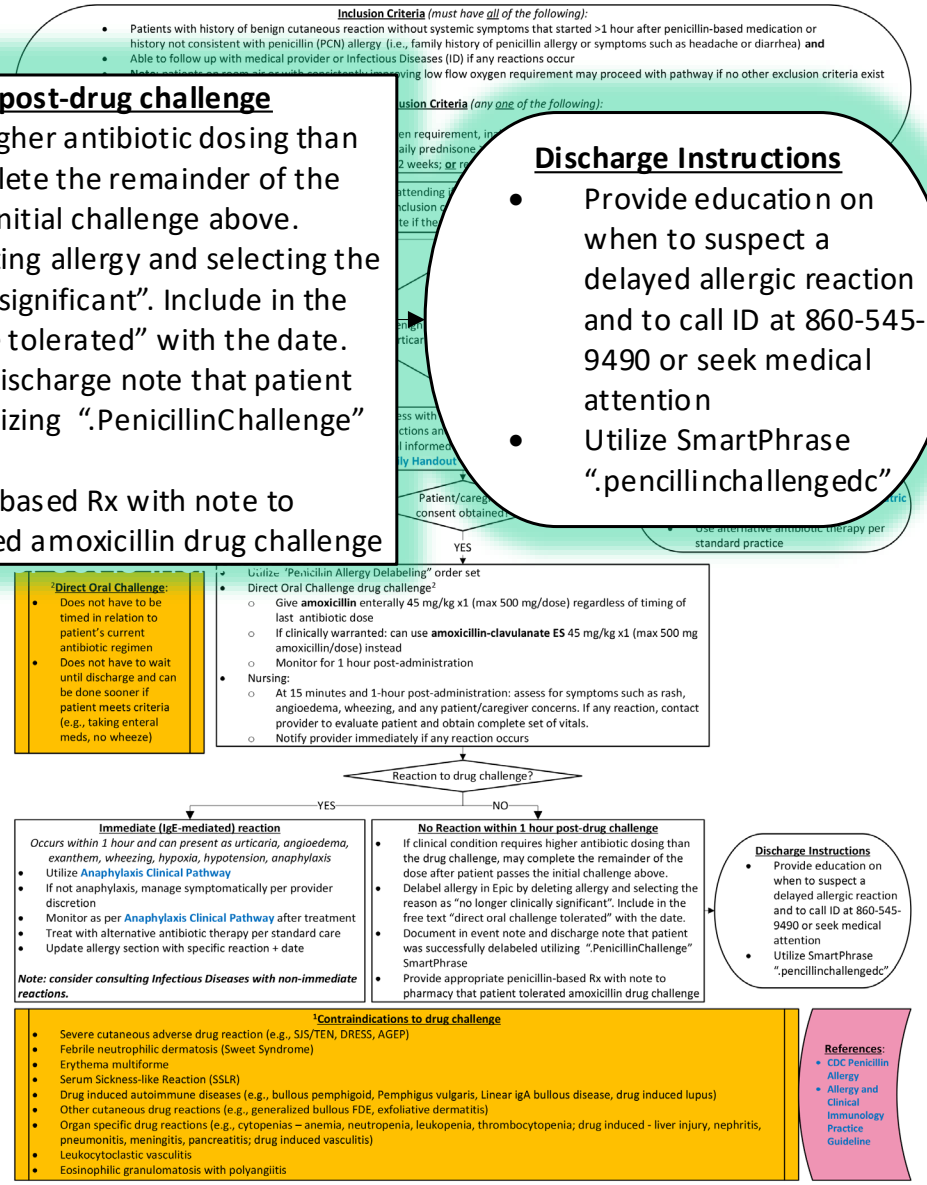
- If clinical condition requires higher antibiotic dosing than the drug challenge, may complete the remainder of the dose after patient passes the initial challenge above.
- Delabel allergy in Epic by deleting allergy and selecting the reason as "no longer clinically significant". Include in the free text "direct oral challenge tolerated" with the date.
- Document in event note and discharge note that patient was successfully delabeled utilizing ".PenicillinChallenge" SmartPhrase
- Provide appropriate penicillin-based Rx with note to pharmacy that patient tolerated amoxicillin drug challenge

Discharge Instructions

- Provide education on when to suspect a delayed allergic reaction and to call ID at 860-545-9490 or seek medical attention
- Utilize SmartPhrase ".pencillinchallengedc"

Rarely, late hypersensitivity reactions can occur after discharge. These are usually not severe.

Please be sure that the patient education is included in your discharge paperwork by using the **SmartPhrase ".pencillinchallengedc"**



CONTACTS: LAURA KVENVOLD, MD | IAN MICHELOW, MD

LAST UPDATED: 10.20.26

©2019 Connecticut Children's Medical Center. All rights reserved.

Use of Order Set and SmartPhrase

- In the pathway, there is guidance on the use of the Penicillin Allergy Delabeling order set for medication orders as well as nursing instructions for the trial. Use of this order set is encouraged to allow for standardization of dosing/monitoring.

- There is also a SmartPhrase to allow for easy documentation, "**.PenicillinChallenge"**. This contains drop down menus to ease documentation of infectious diagnosis, documented past reaction, medication used, caregiver/patient consent/assent, and challenge outcome. This SmartPhrase also allows for data gathering to monitor impact of the pathway for quality improvement purposes.

SmartPhrase Tips

- The SmartPhrase: .PenicillinChallenge includes drop down lists that aid in ease of documentation but also provides useful data to track the efficacy of the pathway

- Since the SmartPhrase includes a drop down list regarding **consent/assent**, it is ideal to utilize this SmartPhrase **even if caregiver/patients opt out** of a challenge after the delabeling conversation is had

- The SmartPhrase also includes a drop down list to document the **outcome** of the challenge; so it's best to use/complete AFTER the challenge is complete

Review of Key Points

- Inappropriate penicillin allergy labels are common and can be associated with negative patient outcomes and increased healthcare costs

- Direct oral challenge with amoxicillin is safe and effective in those patients with a low risk for true IgE-mediated reaction; proactive delabeling can be done by non-allergy providers

- Clear documentation of oral challenge when delabeling allergies is important to limit the chance that the patient will be relabeled as allergic in the future

Quality Metrics

- Percentage of patients with order set usage
- Percentage of patients with penicillin allergy that undergo a direct oral challenge (DOC)
- Percentage of patients challenged who are discharged on penicillin-class antibiotics
- Review of severity of reaction (if present)
- Percentage of challenged patients with documentation of DOC in the discharge note
- Percentage of patients with allergy appropriately delabeled in the allergy section of the medical record
- Service that performed challenge

Pathway Contacts

- Laura Kvenvold, MD
  - Infectious Diseases and Immunology
  - Infection Prevention and Control
- Ian Michelow, MD
  - Infectious Diseases and Immunology
  - Antimicrobial Stewardship Program

References

Anstey, K. M., Tsao, L., & Otani, I. M. (2022). Drug Allergy Delabeling Programs: Recent Strategies and Targeted Populations. In *Clinical Reviews in Allergy and Immunology* (Vol. 62, Issue 3, pp. 484–504). Springer. https://doi.org/10.1007/s12016-021-08913-x

Carter EJ, Schramm C, Baron K, Zolla MM, Zavez K, Banach DB. Perceived usefulness of a mnemonic to improve nurses' evaluation of reported penicillin allergies. *ASHE*. 2023;3(1):e124. doi:10.1017/ash.2023.177

Caubet, J. C., Kaiser, L., Lemaître, B., Fellay, B., Gervaix, A., & Eigenmann, P. A. (2011). The role of penicillin in benign skin rashes in childhood: A prospective study based on drug rechallenge. *Journal of Allergy and Clinical Immunology*, *127*(1), 218–222. https://doi.org/10.1016/j.jaci.2010.08.025

Khan, D. A., et al. (2022). Drug allergy: A 2022 practice parameter update. *Journal of Allergy and Clinical Immunology*, *150*(6), 1333–1393. https://doi.org/10.1016/j.jaci.2022.08.028

Nguyen, M., Parashar, S., Lee, B. R., Dowling, P., & Aljubran, S. (2022). *Twenty-year comparison of delabeling pediatric patients with penicillin allergy with and without prior skin testing*. https://doi.org/10.1016/j

Ray, K. M., Vyles, D. E., Zembles, T. N., & Mitchell, M. L. (2024). Successful pediatric inpatient penicillin allergy delabeling through direct oral challenges. *Journal of Allergy and Clinical Immunology: In Practice*, *12*(8), 2193–2195. https://doi.org/10.1016/j.jaip.2024.04.042

Staicu, M. L., Vyles, D., Shenoy, E. S., Stone, C. A., Banks, T., Alvarez, K. S., & Blumenthal, K. G. (2020). Penicillin Allergy Delabeling: A Multidisciplinary Opportunity. *Journal of Allergy and Clinical Immunology: In Practice*, *8*(9), 2858-2868.e16. https://doi.org/10.1016/j.jaip.2020.04.059

Waldron, J. L., & Trubiano, J. A. (2022). Antibiotic allergy labels in immunocompromised populations. *Transplant Infectious Disease*, *24*(5). https://doi.org/10.1111/tid.13955

Thank You!

About Connecticut Children's Pathways Program

Clinical pathways guide the management of patients to optimize consistent use of evidence-based practice. Clinical pathways have been shown to improve guideline adherence and quality outcomes, while decreasing length of stay and cost. Here at Connecticut Children's, our Clinical Pathways Program aims to deliver evidence-based, high value care to the greatest number of children in a diversity of patient settings. These pathways serve as a guide for providers and do not replace clinical judgment.