Addressing the Resurgence of Syphilis: PENICILLIN ALLERGY ASSESSMENT IN A CLINIC SETTING

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Disclosures

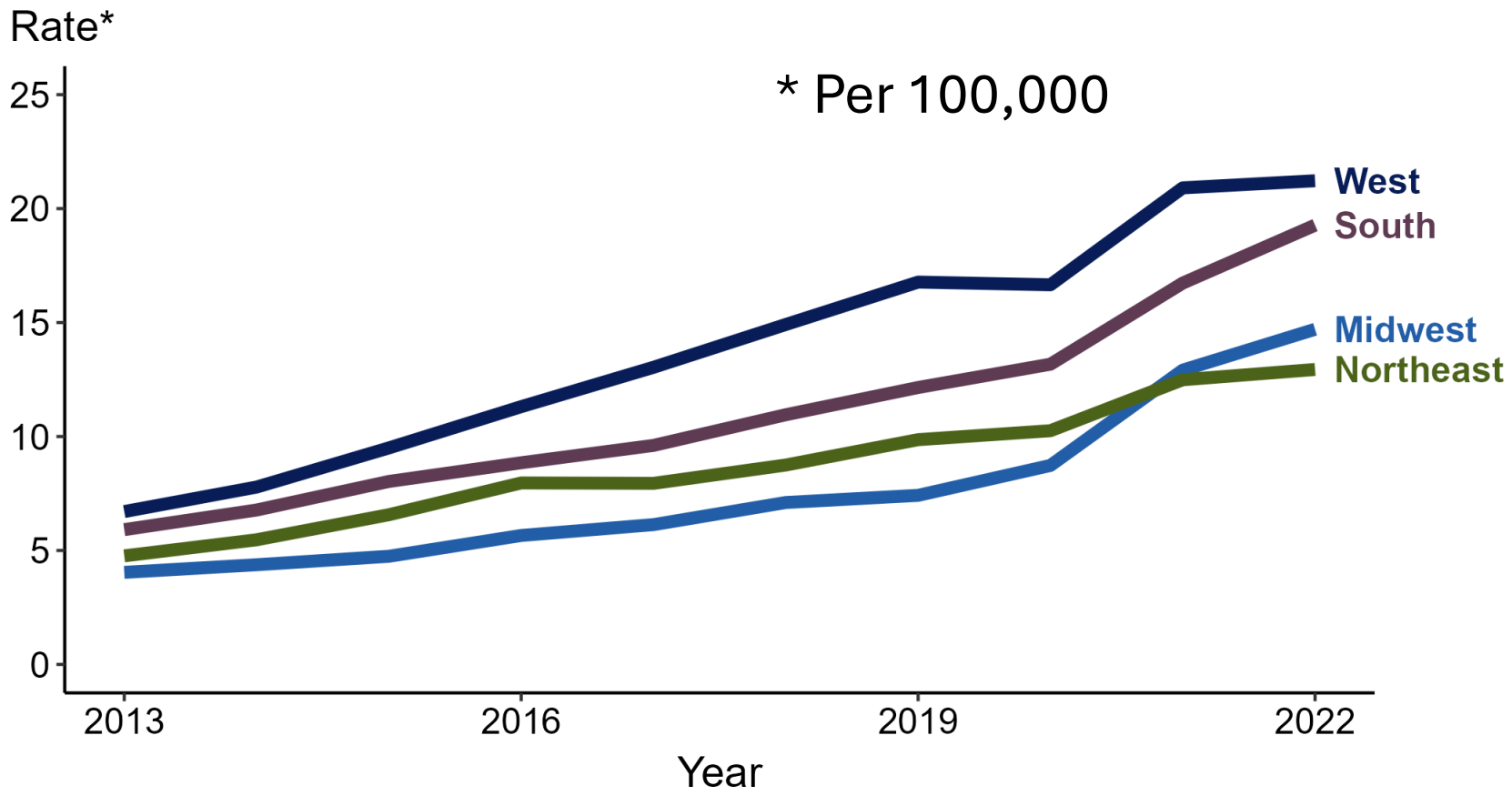
- I have NO financial or other associations with the manufacturers of commercial products, suppliers or commercial services, or commercial supporters. I will NOT discuss any use of unlabeled product(s) or products(s) under investigational use.

Learning Objectives

- Implement a facility level policy for penicillin allergy assessment
- Develop protocols for risk assessment and amoxicillin challenge
- Promote optimal treatment strategies for patients with syphilis

Syphilis cases have skyrocketed in the US.

Primary and Secondary Syphilis
Rates of Reported Cases by Region, United States, 2013–2022



Penicillin is the first-line treatment for syphilis.

"Penicillin is recommended for all clinical stages of syphilis, and no proven alternatives exist for treating neurosyphilis, congenital syphilis, or syphilis during pregnancy."

STI programs and clinicians should promote increased access to penicillin allergy testing.

Source: CDC STI Treatment Guidelines, 2021.

Reported penicillin allergy is common.

Actual penicillin allergy is uncommon.

Reported allergy to penicillin is approximately 10% among the U.S. population

Of those reporting PCN allergy, over 90% tolerate PCN when tested

80% of patients with a true IgE-mediated allergic reaction to penicillin have lost the sensitivity after 10 years

Source: CDC STI Treatment Guidelines, 2021

Patients with low-risk history can be given an oral challenge.

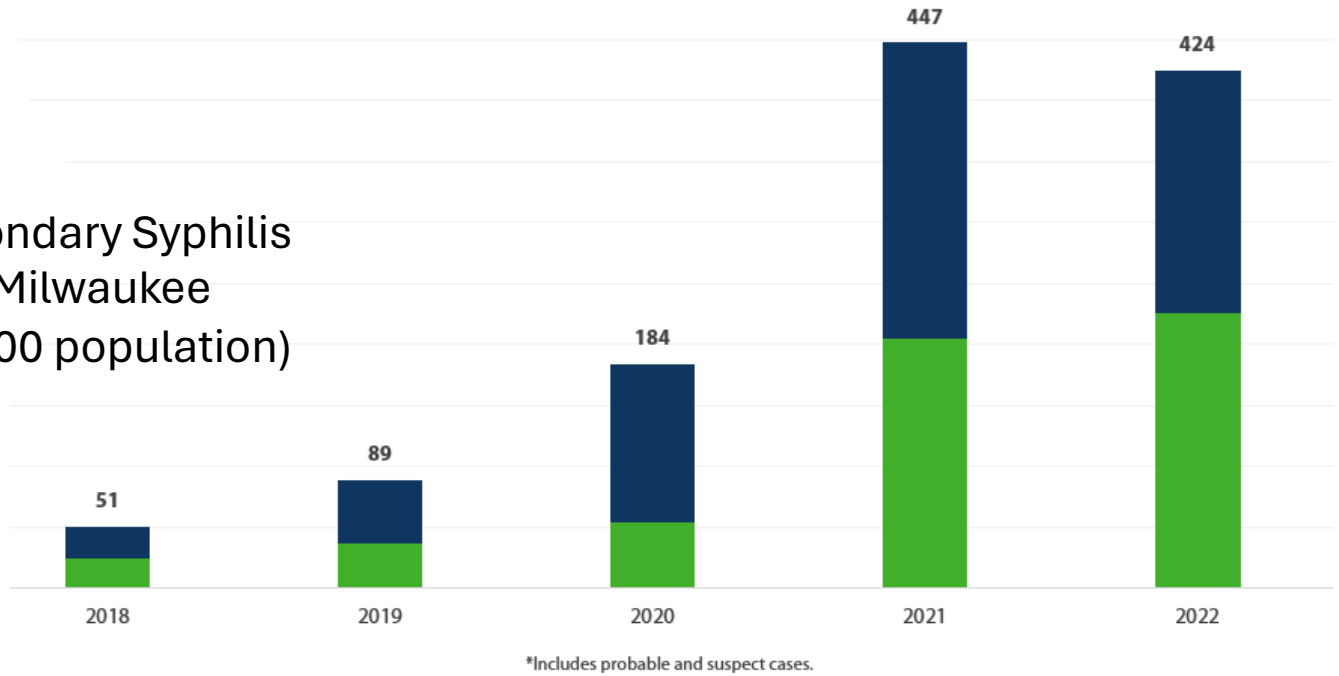
- If the patient gives only a low-risk history of IgE-mediated penicillin allergy, an oral challenge can be administered to document the absence of allergy. If the reaction occurred in the distant past (>10 years), the likelihood is reduced even further.

Managing Persons Who Have a History of Penicillin Allergy, CDC STI Treatment Guidelines 2021

Quality Improvement Initiative

City of Milwaukee Health Department: Keenan Sexual Health Center

Primary and Secondary Syphilis in the City of Milwaukee (Cases per 100,000 population)



Take a careful allergy history (MAST):

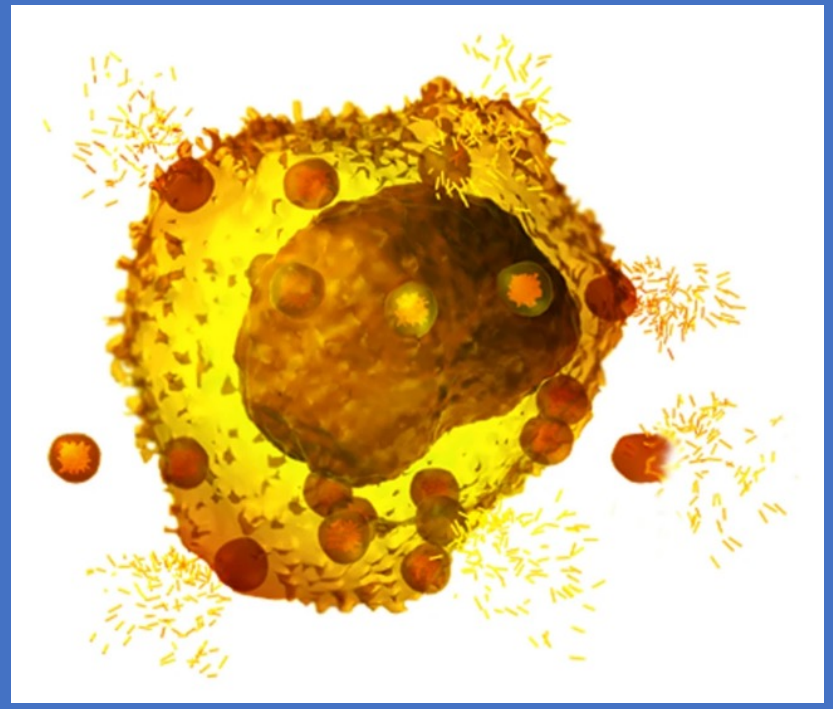


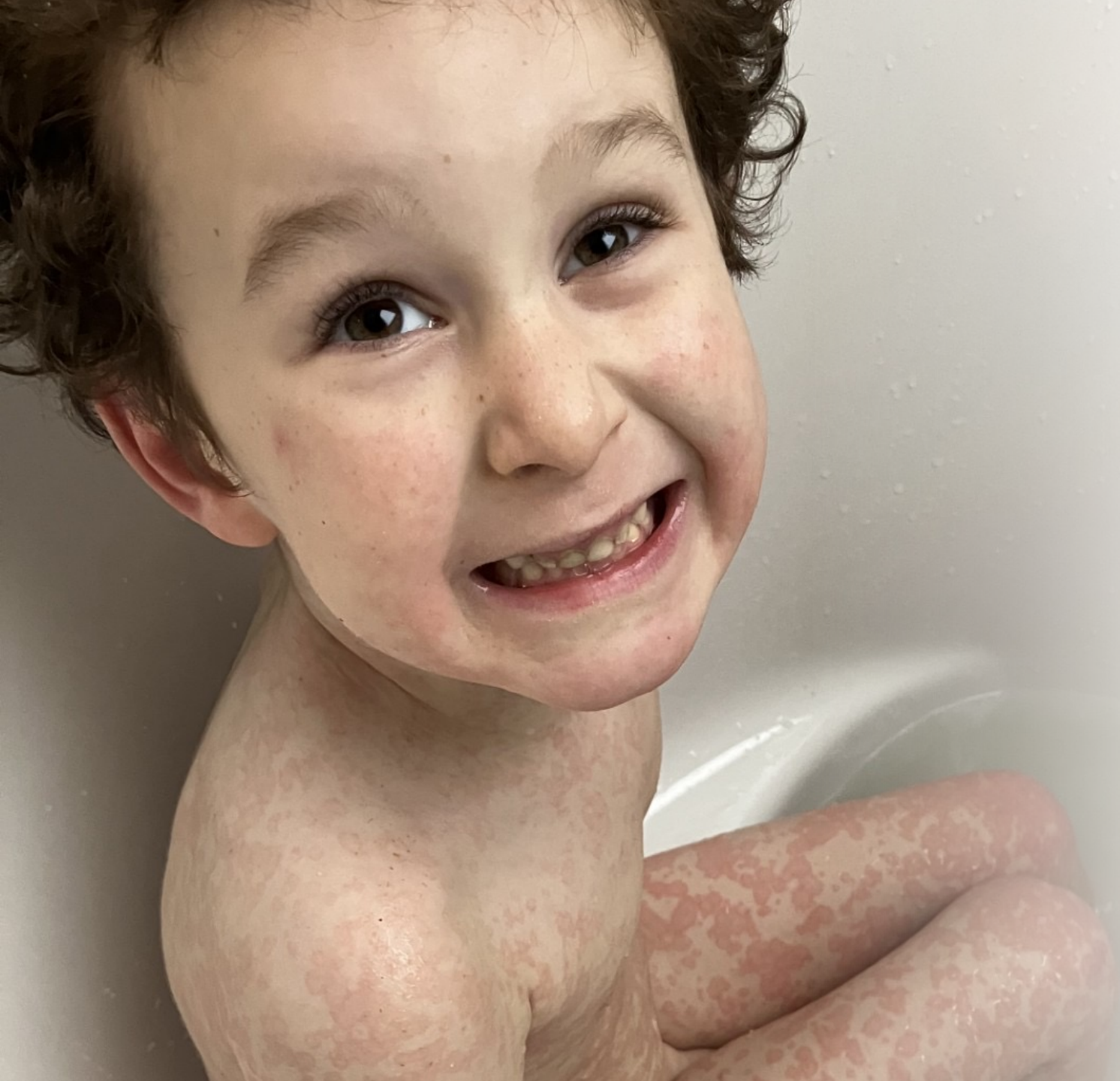
Image: https://doi.org/10.1038/s41598-020-71901-2

What **M**edication caused the reaction? Have they since tolerated any penicillin medications?

When did this occur (approximate **A**ge or year)?

What **S**ymptoms occurred?

What **T**reatment was needed? (Did it involve an ER/hospital setting?)



Identify a low-risk history :

- Delayed onset rash (>24 hours)
- Localized rash
- Pruritis without rash
- Symptoms unknown
- Family history of penicillin or other drug allergy
- Patient denies allergy, but it is on the medical record
- Gastrointestinal Symptoms
- Headache

Evaluating Risk of True Penicillin Allergy: PEN-FAST

Assess Risk Factors	Calculate Score	Estimate risk of a positive result on allergy testing
Allergy event occurring five or fewer years ago (2 points) Anaphylaxis/angioedema or severe cutaneous adverse reaction (2 points) Treatment required for the episode (1 point)	0 = Very Low	0.6% risk (1 out of 164)
	1-2 = Low	5% risk (16 out of 296)
	3 = Moderate	19% risk (25 out of 132)
	4-5 = High	53% risk (16 out of 30)

PENicillin allergy, Five or fewer years ago, **A**naphylaxis or angioedema, **S**evere, **T**reatment)

Trubiano JA, Vogrin S, Chua KYL, Bourke J, Yun J, Douglas A, Stone CA, Yu R, Groenendijk L, Holmes NE, Phillips EJ. Development and Validation of a Penicillin Allergy Clinical Decision Rule. JAMA Intern Med. 2020 May 1;180(5):745-752.
Whelan SO, Moriarty F. Predicting True Penicillin Allergy in Adults. Am Fam Physician. 2021 Jun 15;103(12):760-761.

Milwaukee Health Department Protocol

If PEN-FAST score is 0:

Direct oral amoxicillin challenge

If PEN-FAST score is 1-3:

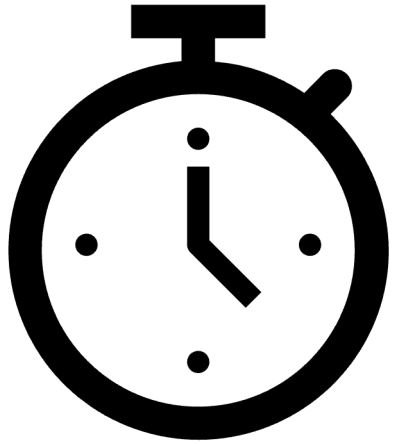
Referral to allergist (and give doxy)

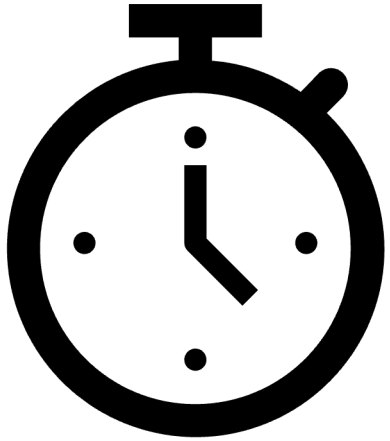
If PEN-FAST score is 4-5:

Give doxycycline or referral to allergist for desensitization

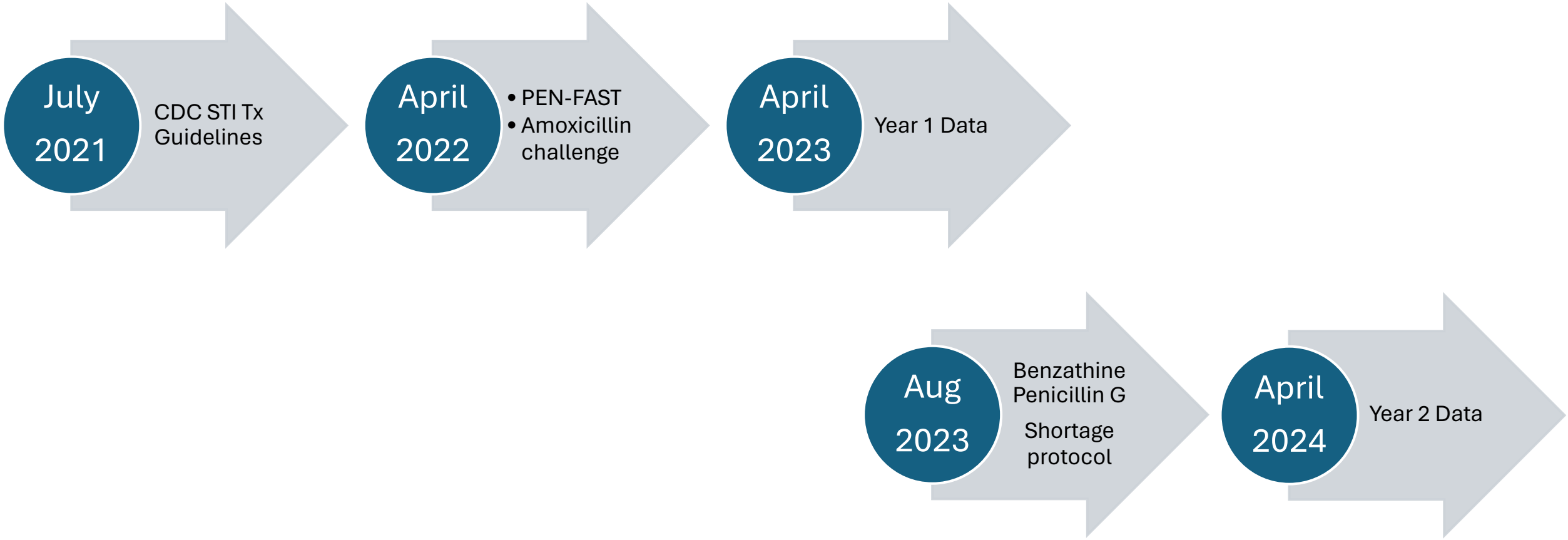
Oral Amoxicillin Challenge Protocol

- Amoxicillin 500mg PO
- Monitor 30 minutes
- Benzathine PCN G 2.4mU IM
- Monitor 30 minutes



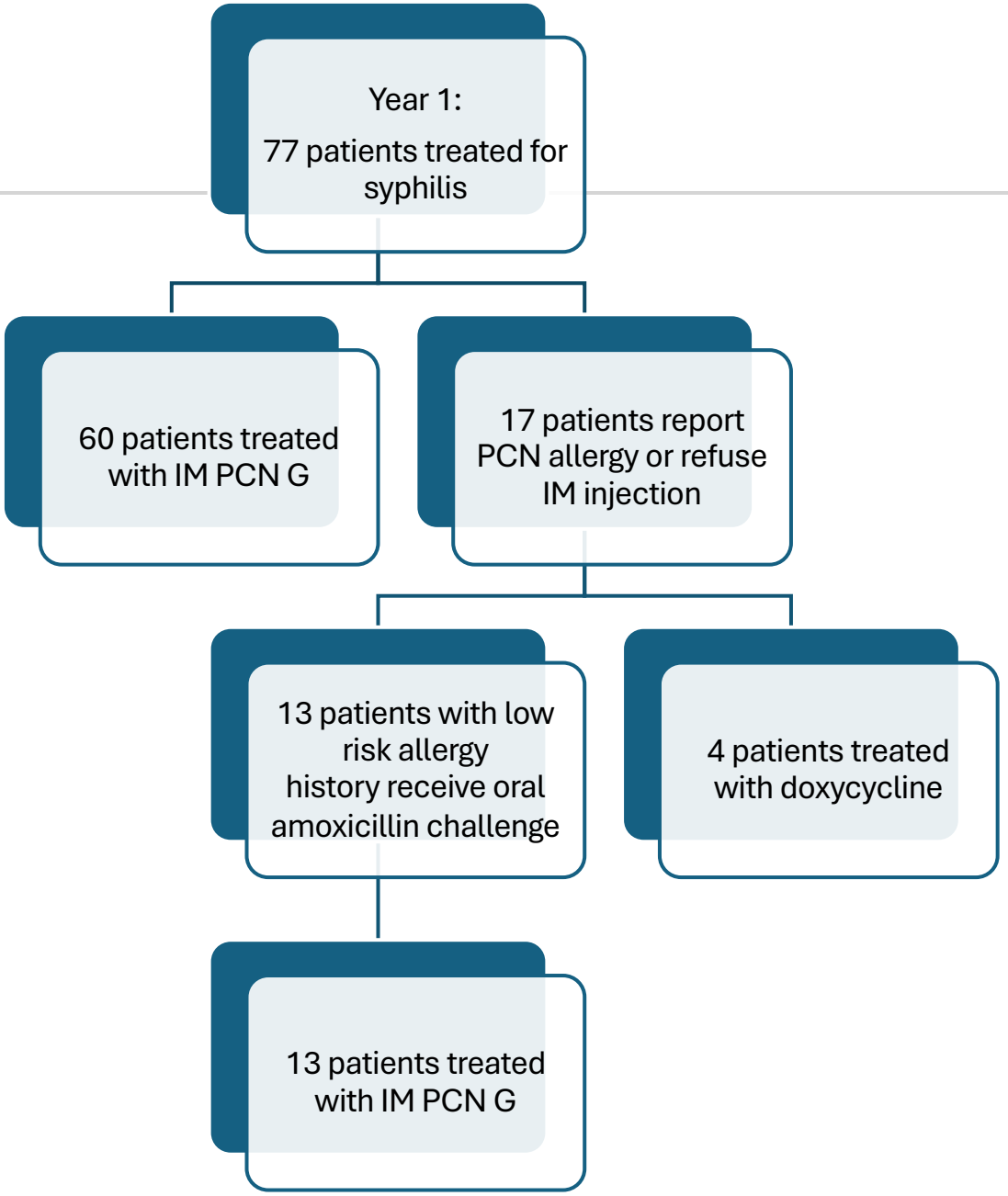


Timeline for PCN Allergy QI Initiative at MHD



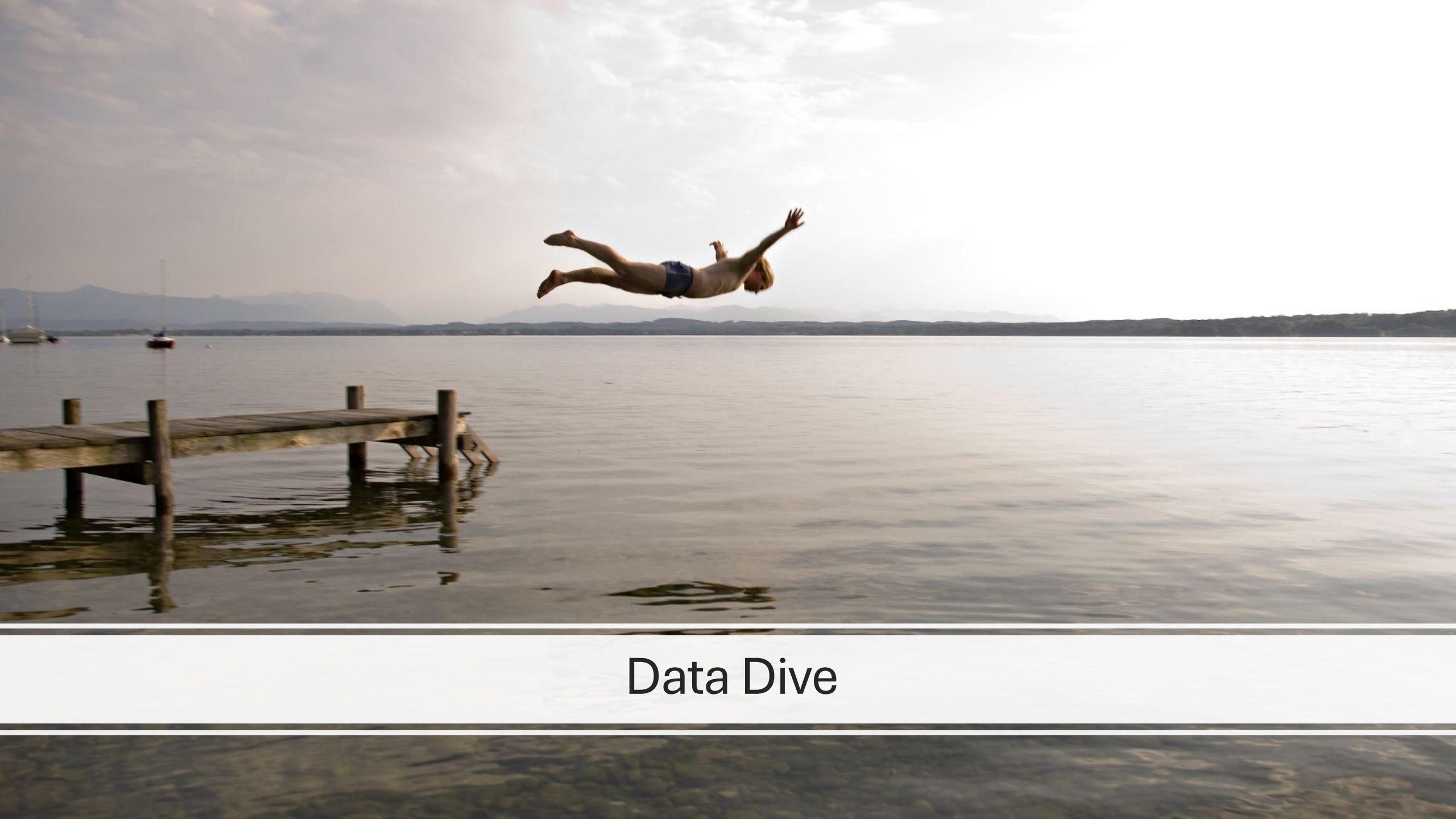
Outcomes

- No adverse reactions with Amoxicillin.
- All clients subsequently received IM benzathine penicillin G (PCN G).
- Year 1 (4/22-4/23): oral amoxicillin challenge reduced the use of alternative treatment by 17% (13/77).
- Year 2 (4/23-4/24): 10 patients received and passed oral amoxicillin challenge. Data collection was disrupted due to initiation of benzathine penicillin G shortage protocols in August 2022.



Conclusions

- We safely and effectively increased treatment with preferred penicillin regimens in clients with syphilis through nursing protocols for penicillin allergy assessment using a validated risk scoring tool (PEN-FAST) and implementation of in-clinic oral amoxicillin challenge.



Data Dive

Original Investigation

March 16, 2020

Development and Validation of a Penicillin Allergy Clinical Decision Rule

Jason A. Trubiano, MBBS, PhD[1,2,3]; Sara Vogrin, MBBS, MBiostat[4]; Kyra Y. L. Chua, MBBS, PhD[1]; et al

» Author Affiliations | Article Information

JAMA Intern Med. 2020;180(5):745-752. doi:10.1001/jamainternmed.2020.0403

"In this study, PEN-FAST was found to be a simple rule that accurately identified low-risk penicillin allergies that do not require formal allergy testing. The results suggest that a PEN-FAST score of less than 3, associated with a high negative predictive value, could be used by clinicians and antimicrobial stewardship programs to identify low-risk penicillin allergies at the point of care."

JOURNAL ARTICLE

Safety and efficacy of de-labelling penicillin allergy in adults using direct oral challenge: a systematic review

Lesley Cooper ✉, Jenny Harbour, Jacqueline Sneddon, R Andrew Seaton

JAC-Antimicrobial Resistance, Volume 3, Issue 1, March 2021, dlaa123,
https://doi.org/10.1093/jacamr/dlaa123

Published: 27 January 2021 **Article history** ▾

"Direct oral challenge is safe and effective for de-labelling patients assessed as low risk for true allergy. Non-specialist clinicians competent in using an assessment algorithm can offer evaluation of penicillin allergy labels using direct oral challenge in appropriate patients."

Original Investigation

September 16, 2024

Reaction Risk to Direct Penicillin Challenges

A Systematic Review and Meta-Analysis

Kimberly G. Blumenthal, MD, MSc[1,2,3]; Liam R. Smith, BS[2,3]; Jushin Teg S. Mann, BS[4]; et al

» Author Affiliations | Article Information

JAMA Intern Med. Published online September 16, 2024. doi:10.1001/jamainternmed.2024.4606

"These findings suggest that reactions to direct penicillin challenges in patients with penicillin allergy histories are infrequent, occurring at similar rates to challenges performed after negative results of allergy testing."

FULL TEXT ARTICLE

Safety of direct oral challenge to amoxicillin in pregnant patients at a Canadian tertiary hospital

Raymond Mak MD, Bei Yuan Zhang MPH, Vanessa Paquette PharmD, Stephanie C. Erdle MD, Julie E. Van Schalkwyk MD, Tiffany Wong MD, Melissa Watt CCRP and Chelsea Elwood MD

Journal of Allergy and Clinical Immunology: In Practice, 2022-07-01, Volume 10, Issue 7, Pages 1919-1921.e1,

CLINICAL IMPLICATIONS

Low-risk pregnant patients can safely receive direct oral challenge without preceding skin testing to rule out a penicillin allergy.

Research Letter | Allergy

September 19, 2022

Validation of the PEN-FAST Score in a Pediatric Population

Ana Maria Copaescu, MD[1]; Sara Vogrin, MBBS, MBiostat[2]; Greg Shand, MSc[3]; et al

» Author Affiliations | Article Information

JAMA Netw Open. 2022;5(9):e2233703. doi:10.1001/jamanetworkopen.2022.33703

"This previously validated tool in an adult population was not useful for risk stratification in children younger than 12 years."

Review

January 15, 2019

Evaluation and Management of Penicillin Allergy
A Review

Erica S. Shenoy, MD, PhD[1,2,3]; Eric Macy, MD, MS[4]; Theresa Rowe, DO, MS[5]; et al

» Author Affiliations | Article Information

JAMA. 2019;321(2):188-199. doi:10.1001/jama.2018.19283

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

[a] Vital signs should be checked every 15 minutes, but patients do not typically require continuous pulse oximetry or cardiac monitoring.
[b] Medication and dosages are provided in Toolkit E.

Questions?

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