INFECTIOUS DISEASES DEPARTMENT
GUIDELINE

ANTIBIOTIC ALLERGY ORAL CHALLENGE

Staff this document applies to:

- Infectious Diseases Department
- Austin Health nurses, doctors, and pharmacy staff

Related Austin Health policies, procedures or guidelines:

Austin Health Drug & Antibiotic Allergy Services (DAAS) Protocol

Antimicrobial Stewardship Antibiotic Allergy Ward Round

Drug Allergy Challenge HITH Admission Policy

Anaphylaxis – Initial Management

Purpose:

To provide guidance on antibiotic allergy assessment and management of an oral antibiotic challenge in patients who have an antibiotic allergy.

Background:

Adverse drug reactions to antibiotics can be divided into two broad categories:

- **Type A reactions**: Non-immune mediated – for example, cytopenia, increased serum creatinine and gastrointestinal intolerance.
- **Type B reactions**: Immune-mediated – for example, rash, anaphylaxis, urticaria, angioedema, acute interstitial nephritis and severe cutaneous adverse reaction (SCAR). SCAR refers to a distinct group of diagnoses including Stevens-Johnson syndrome (SJS), Toxic epidermal necrolysis (TEN), Drug reaction with eosinophilia and systemic symptoms (DRESS) and Acute generalised erythematous pustulosis (AGEP).

The most common antibiotic allergies are to penicillins and sulfonamides.

Penicillin Allergy

A patient-reported "penicillin" allergy is documented in 9-15% of hospitalised patients[1]. These penicillin allergies are associated with inappropriate prescribing and inferior patient outcomes [1, 2]. Protocolised oral antibiotic challenge has been successful in patients with remote and mild allergy histories[3, 4]. Austin Health experience with oral penicillin rechallenge has also been published[5]. Penicillin oral challenge should be considered in patients that currently need or may need beta-lactam based therapy in the future.

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Note:

- Penicillin allergy pre-1960 is likely due to phenoxymethylpenicillin or benzylpenicillin. Penicillin allergy post-1960 may be related to flucloxacillin/dicloxacillin or amoxicillin (post-1972).

Trimethoprim-sulfamethoxazole Allergy

Sulfonamide antibiotic allergy is the second most reported class of antibiotic allergy[6].

Patients with HIV are at a higher risk for developing allergic reactions to sulfonamide antimicrobials.

Due to molecular structure differences, there is a very low risk of cross-allergenicity between sulfonamide antibiotics and sulfonamide non-antibiotic agents (e.g.; furosemide, sulfonylureas).

Protocolised direct oral challenge in patients with a low to moderate risk trimethoprim-sulfamethoxazole allergy has been demonstrated to be a safe and effective alternative to trimethoprim-sulfamethoxazole desensitisation protocols[6,7]. Trimethoprim-sulfamethoxazole oral challenge should be considered in patients that currently need or may need sulfonamide antibiotic -based therapy in the future. Delabeling of low to moderate risk sulfonamide antibiotic allergy labels enables optimal antibiotic prescribing, particularly in immunocompromised patients who may require trimethoprim-sulfamethoxazole treatment or prophylaxis therapy.

Definitions and Abbreviations:

- **Penicillin –** Phenoxymethylpenicillin, benzylpenicillin, benzathine penicillin, penicillin "unspecified"
- **Aminopenicillin** – Amoxicillin, ampicillin, amoxicillin-clavulanate
- **TMP-SMX** – Trimethoprim-sulfamethoxazole
- **ADR** – Adverse drug reaction
- **MPE** – Maculopapular exanthema (rash without angioedema, urticaria, blistering, desquamation, internal organ involvement and/or mucosal involvement).
- **SCAR** – Severe cutaneous adverse reaction (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms, acute generalised exanthematous pustulosis)
- **Type A** – Non-immune mediated pharmacologically predictable side effect (e.g., headache, gastrointestinal upset)
- **Type B** – Immune mediated ADR (e.g., anaphylaxis, urticaria, angioedema, rash, SCAR, acute interstitial nephritis, drug induced liver injury)

Oral Antibiotic Challenge - Inclusion & Exclusion criteria (Inpatient/ Outpatient):

Inclusion criteria:

1. Age > 16 years
2. Active Infectious Diseases inpatient/consult patient or patient identified by antimicrobial stewardship or Drug and Antibiotic Allergy Service (DAAS)
3. **For an INPATIENT oral challenge,** history of penicillins, aminopenicillin, TMP-SMX, or unspecified "sulfa" or sulfonamide allergy that is **low risk.** (See Figure 1)
   - **Low risk** allergy criteria (either/or) - Use Appendix 1 and Appendix 2 to assess antibiotic allergy risk:
     a. Unknown reaction > 5 years previous or date that can't be recalled
     b. Type A ADR reaction where direct delabeling is not accepted by the patient
     c. History of benign childhood rash, non-urticarial rash, MPE or rash unspecified > 5-10 years previous*
     d. Local IM penicillin injection site reaction (only)

   **Patients reporting a benign childhood exanthem that is described as isolated urticaria may be challenged on a case-by-case basis*

   - The PEN-FAST (Penicillin Allergy Clinical Decision Rule) or SUL-FAST (Sulfonamide Allergy Clinical Decision Rule) (Appendix 3) may be used in lieu of the Antibiotic Allergy Assessment Tool Appendix 2) to guide a risk assessment and consideration of oral challenge in patient-reported penicillin and trimethoprim-sulfamethoxazole, unspecified 'sulfa' or sulfonamide allergies.

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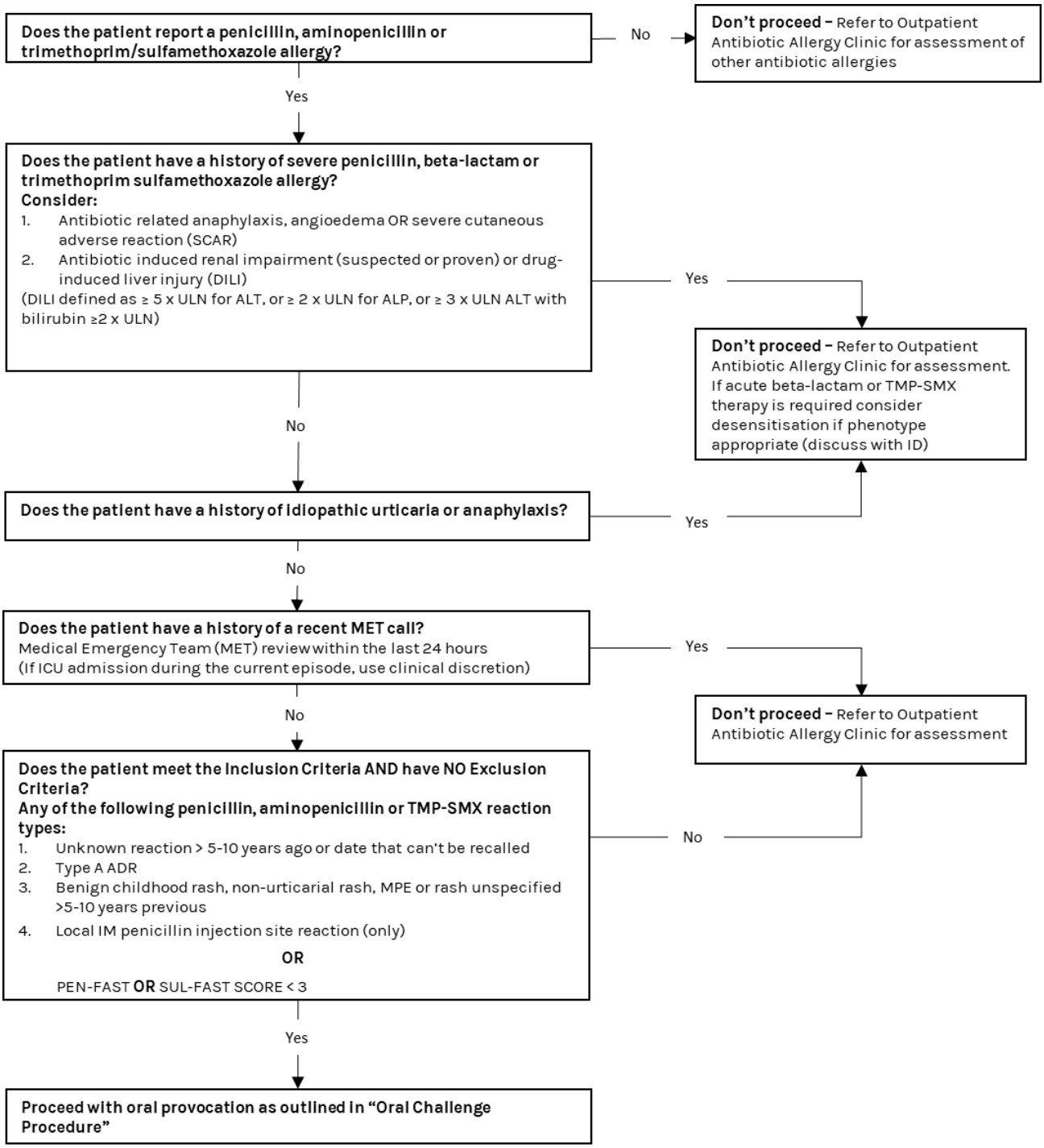
Exclusion criteria:

1. Haemodynamically unstable patients
2. Pregnancy
3. Allergy history unavailable due to patient cognitive impairment and no collateral history
4. History of antibiotic-associated anaphylaxis
5. History of antibiotic-associated Severe Cutaneous Adverse Reactions (SCAR)
6. History of acute kidney injury or severe liver impairment associated with antibiotic therapy
7. If ICU admission during current episode (relative contraindication) – use clinical discretion
8. Currently prescribed: prednisolone > 25 mg daily (or equivalent) or H1-antagonist antihistamines.
    a. Note: If patient has a clinical need for trimethoprim-sulfamethoxazole treatment or prophylaxis and if prescribed concomitant high-dose corticosteroids that cannot be weaned in the near future, safe to proceed to oral challenge as per standard testing schedule. If possible, withhold the daily corticosteroid dose on the day of oral challenge. If the corticosteroid is dosed weekly, schedule the oral challenge on a day most remote from the weekly corticosteroid dose.

If the patient does not meet inclusion/exclusion criteria, they can be referred to the Outpatient Antibiotic Allergy Clinic if likely to require future antibiotic therapy.

Figure 1: Flow chart for determining suitability of patients for INPATIENT antibiotic oral challenge



Oral challenge procedure

Inpatient antibiotic oral challenge

Inpatient oral challenge to be performed only after consultation with and consent by the Infectious Diseases Department, with infectious diseases medical or allergy nursing staff on site and available to be in attendance in the setting of an acute adverse event**.**

1. Ensure patient meets the criteria for antibiotic oral challenge (See Figure 1)

If the patient does not meet the criteria for inpatient antibiotic oral challenge, see Appendix 4 for antibiotic recommendations for patients who report a penicillin allergy.

For recommendations on alternative agents in patients with trimethoprim-sulfamethoxazole allergy, consult ID.

2. Obtain verbal consent from patient's treating Unit to perform inpatient antibiotic oral challenge.

3. Patient to be consented by Infectious Diseases / Immunology Consultant, Fellow or Registrar, or delegate as per Infectious Diseases advice.

4. Oral challenges may be undertaken on any day or at any time at the directive of medical staff from the Department of Infectious Diseases and Immunology.

5. Drug order to be charted by Infectious Diseases / Immunology Consultant, Fellow or Registrar, or delegate as per Infectious Diseases / Immunology advice, using Cerner "ID Oral" Antibiotic Challenge Careset.

Oral Penicillin Challenge

Single dose (**immediate phenotype**): phenoxymethylpenicillin 250 mg or amoxicillin 250 mg or flucloxacillin 250 mg or amoxicillin-clavulanate 500 mg-125 mg.

Single dose (**delayed or unknown phenotype**): phenoxymethylpenicillin 500 mg or amoxicillin 500 mg or flucloxacillin 500 mg or amoxicillin-clavulanate 500 mg-125 mg.

- If reported allergy is phenoxymethylpenicillin or benzylpenicillin – give phenoxymethylpenicillin
- If reported allergy is amoxicillin or ampicillin – give amoxicillin
- If reported allergy is flucloxacillin – give flucloxacillin
- If reported allergy is amoxicillin-clavulanate – challenge with amoxicillin first. If amoxicillin challenge is negative, proceed to amoxicillin-clavulanate challenge.
- If reported allergy is "unknown penicillin" – give amoxicillin. Phenoxymethylpenicillin may be considered if patient reports "unknown penicillin" prior to 1970.
- If reported allergy is a Type A ADR (with clear history) and acute beta-lactam therapy required, administration of full treatment dose can proceed without test dose.

Oral Trimethoprim-Sulfamethoxazole Challenge

- SUL-FAST < 3 and delayed phenotype: Single dose oral challenge -
  - ½ x Trimethoprim-sulfamethoxazole 160/800 mg tablet. (This is half a "double strength" tablet).
- SUL-FAST < 3 and immediate phenotype: Split-dose oral challenge -
  - 1 mL trimethoprim-sulfamethoxazole 40 mg-200 mg/5 mL oral suspension, then if no reaction after 30 minutes
  - 9 mL trimethoprim-sulfamethoxazole 40 mg-200 mg/5 mL oral suspension

6. Medical or specialised allergy nursing staff to be available during 1 hour of oral challenge observation period and available thereafter to attend patient immediately if required.

7. Resuscitation equipment must be available on the ward, however PRN prescription NOT required.

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8. NURSING requirements:

    a. Immediately prior to oral challenge, perform baseline patient observations (HR, BP, Sats, RR)
    b. Administer **orally** either a single dose of phenoxymethylpenicillin or amoxicillin or flucloxacillin or amoxicillin-clavulanate (dosed according to protocol) or ½ x trimethoprim-sulfamethoxazole 160/800 mg tablet as charted in Cerner (unscheduled order) by Infectious Diseases / Immunology, or charted by delegate as per Infectious Diseases / Immunology advice
    c. Perform 30 minutely observations for 1 hour post oral challenge.

9. If there is a history of delayed MPE and no current antibiotic requirements, consider additional testing with a 3-day oral challenge (phenoxymethylpenicillin 500 mg BD or amoxicillin 500 mg BD or flucloxacillin 500 mg BD or amoxicillin-clavulanate 500 mg-125 mg DAILY or trimethoprim-sulfamethoxazole 160/800 mg DAILY) to exclude delayed hypersensitivity.

10. If no evidence of reaction, Infectious Diseases / Immunology Department to remove penicillin, aminopenicillin or trimethoprim-sulfamethoxazole allergy from electronic medical record (Cerner) immediately post challenge. A letter will be sent to the patient, their other treating clinicians and general practitioner to notify them of the allergy removal.

11. If the patient is still an inpatient 24 hours post oral challenge, specialised allergy nursing review is recommended to ensure a missed delayed reaction has not occurred.

12. The patient is to be provided with Drug and Antibiotic Allergy Service (DAAS) dedicated 24-hour phone contact details to report any symptoms of a delayed reaction after the initial monitoring period.

Outpatient antibiotic oral challenge (at Antibiotic Allergy Clinic)

Internal referrals can be made by paper referral - email: antibiotic.allergy@austin.org.au or via the EMR Specialist Clinics pathway - Select 'Infectious Diseases', then 'Drug Allergy'.

As per Inpatient antibiotic oral challenge procedure above, with the following modifications:

Oral Penicillin Challenge

- Oral challenge may be preceded by skin testing.

Patients with a history of **low-risk immediate allergy** symptoms receive a single dose challenge: phenoxymethylpenicillin 250 mg or amoxicillin 250 mg or flucloxacillin 250 mg or amoxicillin-clavulanate 500 mg-125 mg.

Patients with a history of **moderate to severe immediate allergy** symptoms or PEN-FAST score >2 [8] (see Appendix 3) receive a two-dose oral challenge:

- 50 mg phenoxymethylpenicillin /amoxicillin /flucloxacillin or 1 mL amoxicillin-clavulanate 400 mg-57 mg/5 mL oral suspension, then if no reaction after 30 minutes;
- 200 mg phenoxymethylpenicillin /amoxicillin /flucloxacillin or 9 mL amoxicillin-clavulanate 400 mg-57 mg/5 mL oral suspension.

- Monitoring period:
    - Anaphylaxis as phenotype: patients can be discharged 1.5 hours post the first dose of the oral challenge.
    - All other immediate phenotypes: patients can be discharged 1 hour post the first dose of the oral challenge

Patients with a history of **moderate to severe delayed (or unknown) allergy** symptoms receive a single dose oral challenge:

- 500 mg phenoxymethylpenicillin /amoxicillin /flucloxacillin or 500 mg-125 mg amoxicillin-clavulanate, with nursing observations for 1 hour, then;
    - Non-SCAR phenotypes: 3-day course oral challenge phenoxymethylpenicillin /amoxicillin/ flucloxacillin, 500 mg orally BD, or amoxicillin-clavulanate 500 mg-125 mg orally DAILY.
    - SCAR phenotypes: 5-day course oral challenge with dosing as specified above
- If a patient has received skin testing, routine follow-up photographs of the skin testing site are taken by the patient at 24 hours and 48 hours. Verbal and written instructions are provided to the patient to send skin testing site photographs to the DAAS phone which are then reviewed by DAAS Medical staff.
- Patients may also send photographs of a delayed rash or other reaction (regardless of prior skin testing) to the DAAS phone for Medical review*.

Oral Trimethoprim-Sulfamethoxazole Challenge

- **SUL-FAST score < 3 and delayed phenotype:** Single dose oral challenge -
    - ½ x Trimethoprim-sulfamethoxazole 160/800 mg tablet. (This is half a "double strength" tablet).
- **SUL-FAST score < 3 and immediate phenotype:** Split-dose oral challenge -
    - 1 mL trimethoprim-sulfamethoxazole 40 mg-200 mg/5 mL oral suspension, then if no reaction after 30 minutes
    - 9 mL trimethoprim-sulfamethoxazole 40 mg-200 mg/5 mL oral suspension
- **SUL-FAST score > 3:** testing plan to be discussed at Clinic.
- Monitoring period:
    - Anaphylaxis as phenotype: patients can be discharged 1.5 hours post the first dose of the oral challenge.
    - All other phenotypes: patients can be discharged 1 hour post the first dose of the oral challenge
- If not requiring acute trimethoprim-sulfamethoxazole therapy, consider 3-day course of oral trimethoprim-sulfamethoxazole 160/800 mg, 1 tablet DAILY.
- If a patient has received skin testing, routine follow-up photographs of the skin testing site are taken by the patient at 24 hours and 48 hours. Verbal and written instructions are provided to the patient to send skin testing site photographs to the DAAS phone which are then reviewed by DAAS Medical staff.
- Patients may also send photographs of a delayed rash or other reaction (regardless of prior skin testing) to the DAAS phone for Medical review*.

**Some patients may be referred to Hospital in the Home (HITH) for observation of prolonged oral challenge procedures – see:* Drug Allergy Challenge HITH Admission Policy

Outpatient antibiotic oral challenge (Remote oral challenge)

As per outpatient oral challenge procedure above, with the following modifications:

- Patients with penicillin or trimethoprim/sulfamethoxazole allergy will be identified via weekly review of non-allergy specialist clinic bookings (e.g. haematology, liver transplant, ID vaccine clinic).
- Patients will be referred for antibiotic allergy telehealth clinic assessment prior to their non-allergy specialist clinic appointment.
- Patients with a low-risk penicillin or trimethoprim/sulfamethoxazole allergy according to Appendix 2 and/or Appendix 3 will be consented for oral challenge
- Oral challenge will be undertaken during next routine non-allergy specialist clinic appointment.
- Oral challenge will be administered by allergy nursing staff attending the non-allergy specialist clinic or by non-allergy specialist clinic nursing staff with allergy nursing supervision.

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Updated September 2024

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Legislation/References/Supporting Documents:

1. Trubiano JA, Chen C, Cheng AC, Grayson ML, Slavin MA, Thursky KA, et al. Antimicrobial allergy 'labels' drive inappropriate antimicrobial prescribing: lessons for stewardship. The Journal of Antimicrobial Chemotherapy. 2016; 71(6): 1715-22

2. Macy E, Contreras R. Healthcare use and serious infection prevalance associated with penicillin "allergy" in hospitalised patients: A cohort study. The Journal of Allergy and Clinical Immunology. 2015; 133(3): 790-6.

3. Bourke J, Pavlos R, James I, Phillips E. Improving the effectiveness of penicillin allergy de-labeling. The Journal of Allergy and Clinical Immunology in Practice. 2015; 3(3): 365-34 e1.

4. Blumenthal KG, Shenoy ES, Varughese CA, Hurwitz S, Hooper DC, Banerji A. Impact of a clinical guideline for prescribing antibiotics to inpatents reporting penicillin or cephalosporin allergy. Annals of allergy, asthma and immunology: official publication of the Americna College of Allergy, Asthma & Immunology. 2015; 11(4): 294-300 e2.

5. Trubiano J, Vogrin S, Copaescu A, Nasra M, Douglas A, Holmes N, et al. Direct oral penicillin challenge for penicillin allergy delabelling as a health services intervention: A multicentre cohort study. Allergy. 2021. https://doi.org/10.1111/all.15169

6. Krantz S, Stone, C, Abreo A, Phillips E. Oral challenge with trimethoprim-sulfamethoxazole in patients with "sulfa" antibiotic allergy. The Journal of Allergy and Clinical Immunology: In Practice. 2020; 8(2): 757-760

7. Rose M, Vogrin S, Chua K, Drewett G, Douglas A, Slavin M et al. The safety and efficacy of direct oral challenge in trimethoprim-sulfamethoxazole antibiotic allergy. The Journal of Allergy and Clinical Immunology: In Practice. 2021; 9(1): 3847-3849

8. 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. doi: 10.1001/jamainternmed.2020.0403.

9. Devchand M, Urbancic K, Khumra S, Douglas A, Smibert O, Cohen E et al. Pathways to improved antibiotic biotic allergy and antimicrobial stewardship practice – The validation of a beta-lactam antibiotic allergy assessment tool. The journal of allergy and clinical immunology in practice. 2018

10. Krantz M, Stone C, Abreo A, Phillips E. Reply to "the safety and efficacy of direct oral challenge in trimethoprim-sulfamethoxazole antibiotic allergy". The Journal of Allergy and Clinical Immunology: In Practice. 2021; 9(10): 3849-3850

11. Waldron J, Rose M, Vogrin S, Krantz M, Bolotte R, Phillips E, Trubiano J. Validation of an Allergy Clinical Decision Rule for "Sulfa" antibiotic allergy label – S-FAST. 2023. JACI. 151(2)

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Appendix 1: Clinical assessment of a patient's antibiotic allergy history

Antibiotic allergy assessment questions

1. What is the name of the antibiotic you are allergic to? .....
2. Please describe the details of this reaction? (*"assessment of type" – overleaf for suggestions*)

   .....
3. How many years ago did the reaction occur? (*"assessment of timing"*) .....

   (circle the timing)

   Less than 5 years ago 5-10 years ago More than 10 years ago
4. How long after having the first antibiotic dose did the reaction occur? (*"assessment of timing"*)

   .....
5. How was this reaction managed? (*"assessment of type and severity"*)

   .....
6. Were you hospitalised as a result of this reaction? Yes ☐ No ☐
7. Which other antibiotics have you safely taken since the reaction? (*"assessment of tolerance"*)

Use the above answers to tick the correct allergy phenotype on the Antibiotic Allergy Assessment Tool (Appendix 2)

Following antibiotic allergy assessment (tick off completed tasks):

Cerner allergy updated (substance, reaction description, severity)? Yes ☐ No ☐

For **low risk allergies ("green"** OR **"white")** contact Antibiotic Allergy Services via RBC

Yes ☐ No ☐

Name..... **Signature**.....

Designation..... **Date**.....

Appendix 2: Austin Health Antibiotic Allergy Assessment Tool

Dermatological

Skin manifestation		Recommendation & Resultant allergy type	
Childhood exanthem (unspecified) *Mild rash with no severe features*		☐	Unlikely to be significant (non-severe)
Immediate diffuse rash ("itchy immediate rash") *<2 hours post dose*		☐	Immediate hypersensitivity (non-severe)
Diffuse rash or localized rash/swelling with no other symptoms *(non-immediate or unknown timing)*	> 5 years ago; or unknown	☐	Delayed hypersensitivity (non-severe)
	≤ 5 years ago	☐	Delayed hypersensitivity (non-severe)
Angioedema ("lip, facial or tongue swelling")		☐	Immediate hypersensitivity (severe)
Generalized swelling (outside of angioedema)		☐	Immediate hypersensitivity (severe)
Urticaria ("wheals and hives") **isolated childhood urticaria may be challenged on a case-by-case basis*		☐	Immediate hypersensitivity (non-severe)
Mucosal ulceration ("mouth, eye or genital ulcers")		☐	Delayed hypersensitivity (severe)
Pustular, blistering or desquamating rash ("skin shedding")		☐	Delayed hypersensitivity (severe)

Respiratory or Systemic

Clinical manifestation	Recommendation & Resultant allergy type	
Laryngeal involvement ("throat tightness" or "hoarse voice")	☐	Immediate hypersensitivity (severe)
Respiratory compromise ("shortness of breath")	☐	Immediate hypersensitivity (severe)
Fever ("high temperature") *Not explained by infection*	☐	Delayed hypersensitivity (severe)
Anaphylaxis or unexplained collapse	☐	Immediate hypersensitivity (severe)

Haematological

Low platelets < 150 x10^9/L or unknown	☐	Potential immune mediated (severe)
Low neutrophils < 1x10^9/L or unknown	☐	Potential immune mediated (severe)
Low haemoglobin < 100 g/L or unknown	☐	Potential immune mediated (severe)
Eosinophilia (>0.7 x 10^9/L or unknown)	☐	Delayed hypersensitivity (severe)

Unknown

Clinical manifestation		Recommendation & Resultant allergy type
Unknown reaction ≤ 5 years ago	☐	Unknown (non-severe)
Unknown reaction > 5 years ago or **family history** of penicillin allergy only	☐	Unlikely to be significant (non-severe)

Renal

Severe renal injury, failure or AIN (>50% reduction in eGFR from baseline or absolute serum creatinine increase of ≥26.5µmol/L, or transplantation, or dialysis)	☐	Potential immune mediated (severe)
Mild renal impairment (Does not meet criteria in box above)	☐	Unlikely immune mediated (non-severe)

Liver

Severe liver injury, failure or DILI (≥5x upper limit of normal (ULN) for ALT or AST, or ≥3x ULN for ALT with ≥2x ULN for bilirubin, or ≥2x ULN for ALP, or transplant)	☐	Potential immune mediated (severe)
Mild hepatic enzyme derangement (Does not meet criteria in box above)	☐	Unlikely immune mediated (non-severe)

Gastrointestinal, Neurological or Infusion-related

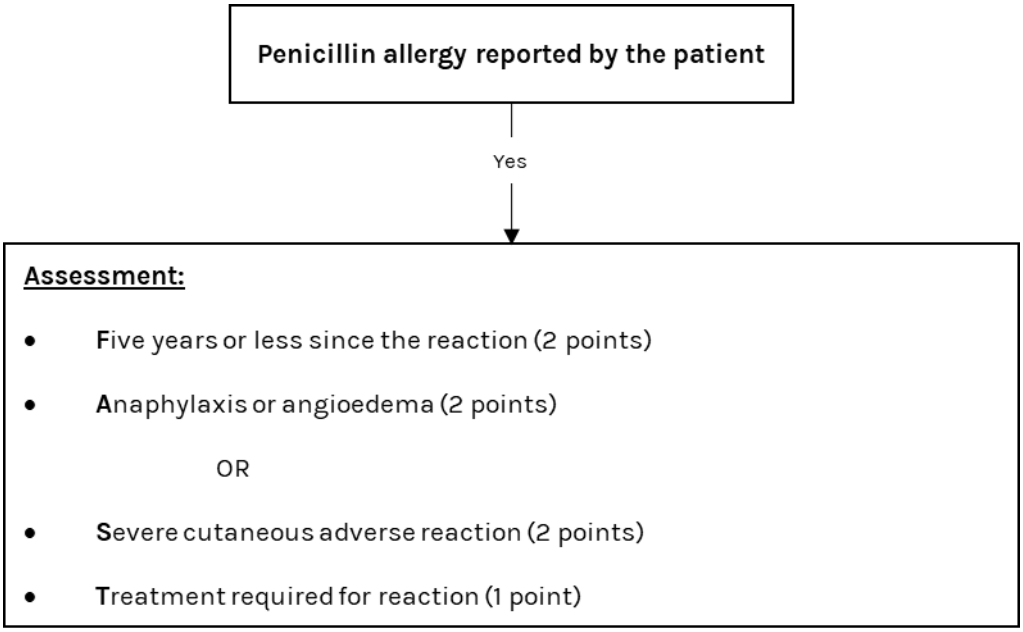
Gastrointestinal symptoms ("nausea, vomiting, diarrhoea")	☐	Unlikely immune mediated (non-severe)
Mild neurological manifestation ("headache, depression, mood disorder")	☐	Unlikely immune mediated (non-severe)
Severe neurological manifestation ("seizures or psychosis")	☐	Unknown or unclear mechanism
Anaphylactoid/infusion reaction (e.g. red man syndrome)	☐	Unknown or unclear mechanism

Appropriate for supervised direct oral rechallenge (or direct de-labelling) - Refer to ID, Pg 1547	☐ Low risk
Appropriate for supervised direct oral rechallenge – Refer to ID	☐ Low risk
May be appropriate for referral for specialized skin testing - Refer to OP antibiotic allergy service	☐ Moderate risk
May be appropriate for referral for specialized skin testing - Refer to antibiotic allergy service	☐ High risk

Appendix 3: PEN-FAST and SUL-FAST– Penicillin / Sulfonamide Allergy Clinical Decision Rule

PEN-FAST: designed for point-of-care risk assessment of patient-reported penicillin allergies.

SUL-FAST: the PEN-FAST Clinical Decision Rule criteria may be applied to identify appropriate low-risk oral challenge candidates in patients with a self-reported trimethoprim-sulfamethoxazole or unspecified 'sulfa' or sulfonamide allergy.



Interpretation:

0 points: **Very low risk** of positive penicillin allergy test , <1% (<1 in 100 patients reporting penicillin allergy)

1-2 points: **Low risk** of positive penicillin allergy test, 5% (1 in 20 patients)

3 points: **Moderate risk** of positive penicillin allergy test, 20% (1 in 5 patients)

4-5 points: **High risk** of positive penicillin allergy test, 50% (1 in 2 patients)

1. 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. doi: 10.1001/jamainternmed.2020.0403.
2. Waldron J, Rose M, Vogrin S, Krantz M, Bolotte R, Phillips E, Trubiano J. Validation of an Allergy Clinical Decision Rule for "Sulfa" antibiotic allergy label – S-FAST. 2023. JACI. 151(2)

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Appendix 4: Recommendations for antibiotic therapy in patients with a reported penicillin allergy

Table 1. Recommendations for antibiotic use in patients with a primary reported penicillin allergy.

Allergy Phenotype	Recommendation
Immediate Penicillin Hypersensitivity (non-severe) *IgE-mediated* E.g: urticaria	Avoid penicillins and 1st generation cephalosporins (except cefazolin) Consider ≥ 2nd generation cephalosporin if history of remote immediate hypersensitivity or mild presentation (urticaria only) Safe for carbapenem Safe for monobactams (aztreonam)
Immediate Penicillin Hypersensitivity (severe) *IgE-mediated* E.g: anaphylaxis	Avoid penicillins, 1st and 2nd generation cephalosporins Consider ≥ 3rd generation cephalosporin Consider carbapenem Safe for monobactams (aztreonam)
Delayed Penicillin Hypersensitivity (non-severe) *T-cell-mediated* E.g: mild rash	Avoid penicillins Avoid aminocephalosporins (cefalexin/cefaclor) only if primary allergy to aminopenicillins (amoxicillin/ampicillin) Safe for cefazolin Safe for ≥ 2nd generation cephalosporins Safe for carbapenems and monobactams
Delayed Penicillin Hypersensitivity (severe) *T-cell-mediated* E.g: SCAR	Avoid all beta-lactams (penicillins, cephalosporins) Consider carbapenem Safe for monobactams (aztreonam)

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