Penicillin Allergy Diagnosis and Documentation in Primary Care

1 in 10 people report a penicillin allergy. But less than 10% of those are likely to be truly penicillin allergic.

Why worry about incorrect penicillin allergy labels?

Penicillin allergy labels are linked to:

- An extra 6 deaths per 1000 adult patients in the year after receiving an antibiotic.[1]
- 26% more C. difficile infections and 70% more MRSA colonisation/infections.[2]
- Increased risk of antimicrobial resistance and use of watch/reserve antibiotics, e.g. fluoroquinolones.
- Increased treatment costs and hospital stays, with poorer clinical outcomes.

Alternatives to penicillins often have more potentially harmful side effects and/or may be less effective.

BUT:

- True penicillin allergy can cause anaphylaxis, which may be fatal.
- Penicillin causes 0.7% - 10% of all anaphylaxis cases and 20% of drug related anaphylaxis in Europe.

Therefore, a thorough allergy history (and applying a new allergy label, if required) is essential for:

- Safe prescribing.
- Identifying patients who warrant a formal penicillin allergy assessment via a referral to the allergy service.

Step 1: Clinical assessment of penicillin allergy.

Obtain and document a detailed allergy history:

- What drug, dose, route, and indication? Were any other medicines or foods taken at the same time?
- Time between drug exposure and reaction onset?
- What exactly was the reaction and how was it managed? Is the reaction consistent with a type of drug hypersensitivity? See NICE CG183 on Drug Allergy for key features of types of drug allergy.
- How long ago did the reaction occur? Did it need emergency care and/or hospital admission?
- Has there been any subsequent exposure to the same drug or one that is closely related?

Some patients are at increased risk of penicillin allergy. Those who have:

- Received repeated courses of oral or IV penicillins.
- Medical conditions e.g. COPD, CF, which may have repeat exposure to antibacterials.
- Atopy does not predispose to penicillin allergy, but patients with other conditions, particularly asthma, can be more likely to have a severe reaction.

Step 2: Documentation of allergy status.

- If the patient has clearly had a **true allergic reaction** *(see symptoms below)*, document this in the patients records with as much detail as possible, including a read code for penicillin allergy.
- If the patient has not had a true allergic reaction record this as a drug sensitivity or side effect and NOT an allergy.

Step 3: Educate the patient on their allergy and provide safety netting on:

- How to recognise severe immediate reactions and to seek immediate medical attention if an anaphylactic or severe delayed onset reaction occurs.
- Provide clear advice on drugs or drug classes to avoid.
- Advising all healthcare professionals about their allergy prior to receiving prescriptions for antibiotics.
- Encourage patients to use various products on the market to alert others of their allergy.
- Reassure that in some cases distantly related antibiotic products related to penicillin's may be used without causing any problems, and there are also alternative unrelated antibiotics to penicillin available.

Step 4: Review and update allergy labels during routine patient reviews.

- Opportunistically review and update information on pre-existing allergy labels including removing a label if this has been applied in error.
- If an allergy label has been applied in error based solely on a history not suggestive of allergy *(see symptoms below),* this can be removed from the patient record (or re-classified, for example as a side effect) and the agent prescribed where indicated.[3]

Symptoms/signs NOT considered to be a penicillin allergy:

- Minor gastro-intestinal symptoms only: E.g. nausea and vomiting, abdominal pain, diarrhoea, bloating.
- Candidiasis (thrush).
- Minor symptoms unrelated to an allergic reaction: E.g. headache, arthralgia, strange taste in mouth.
- Family history of penicillin allergy without a personal history of penicillin allergy.

Reassure patients that these may be side-effects of the medication and not necessarily an allergic reaction. They could also be a result of the infection.

Symptoms/signs consistent with a penicillin allergy.[4,5]

'Red alert' symptoms and signs

1. Immediate onset reactions (usually within 60 minutes) Normally IgE mediated.

Anaphylaxis is likely when any one of the following two criteria are fulfilled:

1. Acute onset of an illness (minutes to several hours) with simultaneous involvement of the skin, mucosal tissue, or both (e.g., generalized hives, pruritus or flushing, swollen lips-tongue-uvula).

AND AT LEAST ONE OF THE FOLLOWING:

a. Respiratory compromise (e.g., dyspnoea, wheeze-bronchospasm, stridor, reduced PEF, hypoxemia).
b. Reduced BP or associated symptoms of end-organ dysfunction (e.g., hypotonia [collapse], syncope, incontinence).
c. Severe gastrointestinal symptoms (e.g., severe crampy abdominal pain, repetitive vomiting), especially after exposure to non-food allergens.

2. Acute onset of hypotension and/or bronchospasm or laryngeal involvement after exposure to a known or highly probable allergen for that patient (minutes to several hours), even in the absence of typical skin involvement.

Note: 'hives' or 'urticaria' is a rapid onset, nettle sting – like rash which typically resolves rapidly leaving normal skin appearances. See Primary Care Dermatology Society for further information and visual diagnostic aids: Drug rashes: mild to moderate, Drug rashes: severe.

2. Severe cutaneous adverse reactions (SCAR).

Non-immediate onset reactions with systemic involvement:

- Stephens Johnson Syndrome (SJS)
- Toxic Epidermic Necrolysis (TEN)
- DRESS syndrome (Drug Reaction with Eosinophilia and Systemic symptoms)
- Acute generalised exanthematous pustulosis (AGEP)

SCAR should be considered with one or more of the following symptoms: Systemic upset/prodromal illness with fever, mucosal involvement, blistering rash, pustular rash, or epidermal detachment.

Other non-immediate patterns of drug hypersensitivity.

- Maculopapular rash
- Morbilliform rash
- Delayed-onset urticarial rashes
- Fixed drug eruption

IgG or IgM mediated reactions can also develop though it is unlikely these will be encountered within primary care as are usually associated with prolonged courses of therapy.

Patients requiring a formal penicillin allergy assessment.

The NUH adult allergy service covers the whole of Nottingham and Nottinghamshire ICB.
Referrals to the adult drug allergy clinic for penicillin allergy testing will be accepted according to the British Society for Allergy and Clinical Immunology (BSACI) guidelines. Children and young people (<18 years of age) meeting these criteria can be referred to the paediatric allergy clinic.

Specific scenarios which are indications for investigation of patients with immediate or non-immediate reaction/s to penicillin and cephalosporins include:

- Patients with a label of multiple antibiotic allergy.
- Patients with a requirement for frequent antibiotics, for example patients with bronchiectasis, cystic fibrosis, diabetes, primary and secondary immunodeficiencies or those with asplenia/hyposplenism.

The full list can be found at Documents - Quick - eHealthscope, or seek advice and guidance from the adult allergy service via the NHS e-Referral Service (e-RS).

Useful links:

- NICE Drug allergy: Overview | Drug allergy: diagnosis and management | Guidance | NICE
- British Society for Allergy and Clinical Immunology (BSACI) penicillin allergy guideline: Management of allergy to penicillins and other beta‐lactams
- Patient information on drug allergies from Anaphylaxis UK: Drug Allergy | Anaphylaxis UK

References:

1. West et al. 'Warning: allergic to penicillin'. JAC. 2019 Jul 1;74(7):2075-2082. doi: 10.1093/jac/dkz127. PMID: 31225607
2. BMJ 2018;361:k2400
3. Savic L et al. BSACI guideline for the set-up of penicillin allergy de-labelling services by non-allergists working in a hospital setting. Clin Exp Allergy. 2022 Oct;52(10):1135-1141. doi: 10.1111/cea.14217. Epub 2022 Sep 21. PMID: 36128691
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5. Mirakian R et al. Standards of Care Committee of the British Society for Allergy and Clinical Immunology. Management of allergy to penicillins and other beta-lactams. Clin Exp Allergy. 2015 Feb;45(2):300-27. doi: 10.1111/cea.12468. PMID: 25623506.