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Penicillin allergy

“I can’t have penicillin, I’m allergic to it. It makes me all queasy and I get diarrhoea.”

10% of the population reports that they are allergic to penicillin. However, studies suggest that fewer than 10% of those who say they are allergic genuinely are ([NICE 2014, CG183](#)). Labelling patients as penicillin allergic when they are not genuinely allergic increases the use of broad-spectrum antibiotics and the risk of antibiotic resistance ([Lancet 2025;1\(1\):100006](#)).

The DTB highlighted the issues of penicillin allergy and what it all means in practice ([DTB 2017;55\(3\):33](#)).

This article was updated in November 2025.

1. First, some pharmacology!

- Penicillins are a large group of antibacterials that have a beta-lactam ring in their molecular structure.
- From the beta-lactam ring comes varying side chains. These differ between the different antibiotics, and include cephalosporins, carbapenems (e.g. meropenem) and monobactams (e.g. aztreonam).
- Degradation products from the beta-lactam ring are the major trigger for most allergic reactions. The side chains contribute in a more minor way to allergic reactions.
- IgE-mediated immune reactions are normally rapid in onset (minutes to hours), and often involve symptoms including urticaria, pruritus, wheeze, cough, and, if severe, angioedema and anaphylaxis.
- Non-immune reactions usually occur more than an hour (often several days) after exposure, and, most commonly in the case of penicillins, include a maculopapular/morbilliform or urticarial rash.
- Rarely, antibiotics can cause severe non-IgE-mediated reactions such as Stevens–Johnson syndrome.

(For those who want a much more detailed explanation of the cellular immunology in different reactions, please see [Lancet 2019;393:183](#); for those who want to understand potential testing pathways in secondary care, please see [NEJM 2019;381:2338](#)).

What about cephalosporins?

- Cross-reactivity was initially reported to be about 10% with first-generation cephalosporins (e.g. cefalexin, cefadroxil, cefradine).
- With third-generation cephalosporins (e.g. cefotaxime, ceftazidime, ceftriaxone), the risk is thought to be lower, at 2–3%.

2. Risks for antibiotic allergy

- The risks seem to be exposure-related – **the more often you have a course of antibiotics, the more likely the risk of reaction.** This becomes a particular problem in those who need repeated courses of antibiotics, such as those with cystic fibrosis.
- Women and older people seem to be at increased risk, but this may, in part, be due to increased antibiotic use in these groups.
- Family history is often cited when you ask about allergy. For self-reported penicillin allergy, there is an association with family history, but the exact nature of the risk is not known.

3. Management, referral and investigation

- **Ensure patient notes are flagged clearly, that information is passed on to secondary care when referrals are made and that the allergy is visible to out-of-hours providers.**

Who to refer?

The [British Society of Allergy and Clinical Immunology](#) suggests that the following people are referred for investigation (whether their reaction was immune mediated or non-immune mediated).

- People with multiple drug ‘allergies’.
- A history of beta-lactam antibiotic hypersensitivity in those who require frequent antibiotics (e.g. people with cystic fibrosis, some diabetics) or who require a specific beta-lactam.

- A history of anaphylaxis during general anaesthetic when penicillins were used with a combination of other drugs (to work out whether the penicillin was the cause).

A referral should include the following information:

- Detailed clinical history, including timing between antibiotic use and the reaction, the nature of the reaction (photos of the rash are good!) and the time to resolution of symptoms.

Allergy services often offer email advice if you are not sure whether to refer!

Investigations in secondary care usually involve:

- Skin prick tests, then intradermal skin test if skin prick is negative.
- Oral provocation test if skin testing is negative.

What about direct antibiotic challenge?

Supervised oral antibiotic trials have been suggested as an alternative to skin testing (*rather than after skin testing, as recommended by BASCI*), offering a quicker and cheaper way to rule out suspected penicillin allergy ([DTB 2025;63:163](#)). Risk of allergic reactions is the greatest concern. For this reason, oral allergy challenge testing is carried out in secondary care clinics.

- A systematic review and meta-analysis of almost 10 000 patients reported in the DTB showed a low frequency of allergic response (3.5%). This is similar to that seen with initial skin testing.
- Risk of reaction was higher in children (6.6%) and in outpatient settings.
- There were 5 severe reactions reported, 4 of which were in children.

A study in the Lancet showed that primary care clinicians could successfully identify those labelled as penicillin allergic who were suitable for penicillin

challenge tests (direct oral challenge or skin testing) with the aid of a protocol. The intervention led to significant rates of de-labelling, with 96% of those testing negative in the intervention group being de-labelled. By contrast, of those in the 'usual care' group, <1% were de-labelled during the study period ([Lancet 2025;1\(1\):100006](#)).

Management

- In the case of suspected or confirmed previous anaphylactic reaction to penicillin, the patient should be given verbal and written information about the allergy and the drugs to be avoided.
- They should be advised to share this information with health professionals and carry it at all times, e.g. wear a MedicAlert bracelet ([DTB 2017;55\(3\):33](#)).
- Adrenaline auto-injectors are **NOT** usually given for drug allergy (you are unlikely to accidentally be exposed to penicillin in the way you might accidentally be exposed to nuts).

When to avoid penicillins

Scenario	Action
History of anaphylaxis, urticaria or rash <u>immediately</u> after penicillin OR Positive skin test OR Severe non-immune-mediated reactions (e.g. Stevens–Johnson syndrome)	• Avoid penicillins. • Avoid cephalosporins in primary care. Use only in secondary care if life-threatening infection and no alternative antibiotic is available. • Refer to allergy clinic if suspected anaphylaxis, positive skin test or severe non-immune-mediated reaction.

Minor rash (non-confluent, non-pruritic, restricted to a small area of the body) OR Rash more than 72h after penicillin administration OR Diarrhoea and vomiting without other features	• Probably not allergic to penicillin. • Penicillin should NOT be withheld during <u>serious</u> infection, but, if used, the risk of allergic reaction should be considered. <i>We think this would depend on whether there was a reasonable alternative, and how likely we thought the reaction was to be related to penicillin. If they had multiple drug allergies, as discussed previously, we would refer.</i> • Other beta-lactams (such as cephalosporins) can be used.
Suspected IgE-mediated reaction (rapid onset, often involves urticaria and pruritus; if severe, involves angioedema and anaphylaxis) AND Specific or regular treatment with penicillin needed (e.g. cystic fibrosis)	• Refer to allergy clinic. Avoid penicillins while awaiting referral. • Secondary care will investigate and advise avoidance if tests confirm penicillin allergy (this will include cephalosporin sensitivity testing) or consider desensitisation.
(DTB 2017;55(3):33, NICE 2014, CG183)	

4. Penicillin allergy and risk of MRSA and clostridium infections

In someone with a penicillin allergy, alternative, often broader-spectrum, antibiotics are used. Does this increase the risk of MRSA or clostridium? A

UK primary care-based population cohort study suggests that it does ([BMJ 2018;361:k2400](#)).

Those with a documented penicillin allergy were more likely to develop MRSA and clostridium infections. In penicillin-allergic people (compared with non-penicillin-allergic people), for every 100 000 person years, there were an extra:

- 49 clostridium infections.
- 27 MRSA infections.

The authors conclude that being careful to identify true allergy from other reactions is important to reduce the risk of these infections.

The DTB reminded us that when treating someone with a penicillin allergy, use the narrowest-spectrum non-penicillin drug you can to minimise the risks of MRSA and clostridium (and the other risks of unnecessarily broad-spectrum antibiotic use) ([DTB 2019;57:1:4](#)).

These articles made us think about how we document allergy.

Do we always make sure it is coded correctly as an allergy in the allergy section of the electronic records, or is it buried away on page 3 of the minor problem list, along with ear wax and the molluscum contagiosum they had when they were 10?!

When people have a code for 'Allergic to...' or we add such a code, consider adding in free text what the reaction was ('Allergic to penicillin: extensive urticaria, pruritus'). This might mean digging through the notes to see whether past reactions have been documented or simply asking what they remember. It is also a good opportunity to explain that getting thrush with antibiotics is an unpleasant side-effect, but it is not an allergy!



Penicillin allergy

- Greater risk with more courses of antibiotics.
Another reason not to prescribe any antibiotics for viruses or because it's Friday afternoon (we all know antibiotics work better on a Friday!).
- Refer people with:
 - Multiple drug 'allergies'.
 - A history of beta-lactam antibiotic hypersensitivity who require frequent antibiotics or who require a specific beta-lactam.
 - A history of anaphylaxis during general anaesthetic when penicillins were used in combination with other drugs (to work out whether the penicillin was the cause).
- Be clear about when cephalosporins can be used in people who might be allergic to penicillin.



Audit your patient database. Find everyone with the code 'Allergic to penicillins' (or 'allergic to *any drug*' if you are feeling brave and can cope with larger numbers!). Is this code correctly coded in the allergy section of your electronic records, or is it buried away on page 3 of the minor problem list?

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