# Antibiotic allergy de-labelling in children:
## a practical guide for primary care

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Antibiotic allergy is the most commonly reported drug allergy in children, with approximately 5% of children in the US carrying a penicillin allergy label.[1] However, a 2023 international systematic review found that 95% of those labelled are not truly allergic.[2] In the UK, reliable prevalence data for children are lacking.[1] Most labels in children are acquired before the age of 3 years — typically when an incidental viral rash is misattributed to a concurrent antibiotic — and persist unchallenged for life.[3–5]

Carrying an inaccurate antibiotic allergy label has measurable consequences: affected children receive broader-spectrum, less effective antibiotics for future infections, with increased risks of treatment failure, *Clostridium difficile* (*C. difficile*), and methicillin-resistant *Staphylococcus aureus* (MRSA) infection, longer hospital admissions, and higher healthcare costs.[6,7] Labels acquired in childhood impose these harms over a lifetime and represent a direct threat to antimicrobial stewardship.

A structured allergy-focused history alone, taken in primary care, is sufficient to de-label many children without drug challenge testing. Formal specialist referral is only required in the presence of red-flag features. Where the history suggests allergy symptoms without red flags, prescribing a single dose of the antibiotic to be taken at home, with a 1-week follow-up, provides a simple and evidence-supported route to de-labelling.

## How labels arise and why they persist

Most paediatric drug allergy labels originate when a child develops a rash during a course of antibiotic from a coincidental viral exanthem. Symptoms such as headache, fever, arthralgia, and rashes associated with Epstein–Barr virus (EBV) infection are often miscoded as allergy. Penicillin mislabelling predominates in children (>90%), although spurious cephalosporin and other antibiotic 'allergies' may also be inappropriately coded. True allergy is confirmed in only 7%–20% of children who undergo formal assessment after a suspected antibiotic reaction.[4]

Labels may persist when reaction details are limited or historical records are incomplete. In one large US primary care study, half of paediatric allergy entries were recorded as 'unable to classify', with insufficient reaction detail documented.[5] Family history can also propagate labels: UK data show 61% of paediatric clinicians would avoid penicillin if a family member reported an allergy, even without any confirmed reaction in the child.[8]

### Key messages

- Up to 95% of children labelled as antibiotic-allergic are not truly allergic; most labels arise from viral rashes in early childhood, but incorrectly attributed to antibiotics, particularly amoxicillin.
- Inaccurate labels drive use of broader-spectrum antibiotics, increasing the risk of antimicrobial resistance, *Clostridium difficile* infection, and treatment failure.
- A structured allergy history can be safely used to 'de-label' patients in primary care. If the history reveals no allergy symptoms, the label can be removed in primary care without further investigation or referral.
- If red-flag features are present — anaphylaxis (shortness of breath, wheeze, throat tightness, dizziness, or collapse) or severe delayed reactions such as Stevens–Johnson syndrome, toxic epidermal necrolysis, or drug reaction with eosinophilia and systemic symptoms — refer to paediatric allergy or immunology services.
- If allergy symptoms are present but without red flags, prescribe a single therapeutic dose of the antibiotic to be taken at home. Contact the family after 1 week to confirm no reaction — then de-label.

## A structured, history-based approach

Given the lifelong consequences of being incorrectly coded as having an antibiotic allergy, it is important that incorrect labels are removed and coding corrected. Most children can be reviewed and, where appropriate, de-labelled safely in general practice. This can be done by taking a careful allergy-focused history using a structured approach.

The British Society for Allergy and Clinical Immunology guideline for antibiotic allergy de-labelling by non-allergists provides a UK framework supporting this history-based approach.[9] The ALABAMA randomised trial in UK primary care demonstrated that a GP-initiated assessment pathway safely increases penicillin prescribing and improves antibiotic stewardship.[10] A systematic review confirmed that history-based de-labelling is safe and effective in reducing inappropriate antibiotic use.[2]

In using this approach, the following need to be established: 1) the antibiotic involved and its class; 2) the nature and timing of the reaction (from immediate to within 1 hour suggesting possible IgE-mediated allergy), or delayed (more likely viral or non-immune); 3) whether the child was unwell with a concurrent viral illness; 4) the severity of the reaction; 5) whether treatment was required; 6) any subsequent tolerance of the same antibiotic without adverse effect; and 7) whether the label derives from a witnessed reaction in the child or from a family member's history. These are highlighted in Box 1.

## De-labelling on history, and when to refer

Where the history reveals no allergy symptoms, the GP can de-label directly, updating the allergy record and associated coding while documenting the clinical rationale. This does not dismiss the original reaction; rather, it applies current evidence to correct a record that is likely inaccurate and causing ongoing

## Box 1. The structured allergy history

The allergy-focused history is the foundation of all decisions. It should establish the:

- antibiotic involved — amoxicillin, penicillin V, flucloxacillin, co-amoxiclav, another beta-lactam, or another antibiotic class.
- nature and timing of the reaction — immediate (within 1 hour, suggesting possible IgE-mediated allergy) or delayed (hours or days later, more likely viral or non-immune).
- context — was the child clearly unwell with a concurrent viral illness?
- severity — did the reaction require antihistamines, steroids, or emergency treatment?
- subsequent tolerance — has the child received the same or a similar antibiotic since without adverse effect? Tolerance on re-exposure strongly argues against true allergy.
- source of label — witnessed reaction in the child, or a family member's reported allergy?

harm. Written confirmation to the family, noting that the antibiotic may be prescribed in future when clinically indicated, helps manage anxiety and informs other healthcare providers. In practice, this discussion can take place during the consultation itself, with the outcome documented as free text in the notes and the allergy record updated accordingly.

Children with red-flag features such as anaphylaxis (urticaria/angioedema accompanied by shortness of breath, throat tightness, wheeze, dizziness, or collapse), severe cutaneous adverse reactions, or severe systemic reaction should be referred to paediatric allergy or immunology for formal assessment. Some NHS regions have streamlined direct-referral pathways for antibiotic allergy de-labelling; local antimicrobial stewardship teams can advise on what is available.

Where the history reveals allergy symptoms without red flags, prescribing a single therapeutic dose of the antibiotic to be taken at home, followed by a telephone or eConsult follow-up at 1 week, is a practical and well-evidenced approach. If no reaction is reported, the label can be removed. If the child develops a rash or other reaction, further review or referral to paediatric allergy is appropriate. A UK cohort study from Sheffield delivered direct oral provocation challenges in children aged 2–16 years from four primary care centres and a paediatric emergency department, demonstrating safety and feasibility in the community setting.[11] In an Irish study of 162 children, 93% of challenges were negative; the three immediate reactions were mild urticaria occurring within 1 hour and resolving with a second-generation antihistamine, further supporting the safety of this approach.[12] GPs adopting this approach should document their clinical rationale and ensure that the patient has an antihistamine available. A positive result is classified as one producing objective symptoms such as urticaria, angioedema, new rash, respiratory symptoms, or cardiovascular compromise. Parents/carers should be told to stop the antibiotic and seek urgent medical attention (call 999 or attend the emergency department) if the child develops any signs of anaphylaxis (for example, shortness of breath, throat swelling, wheeze, dizziness, or collapse). If the child develops hives or skin swelling, a dose of second-generation

## Box 2. A history-based approach to antibiotic allergy de-labelling in children[9–12]

| Pathway | History features | GP action |
|---|---|---|
| **No allergy symptoms** | Symptoms not consistent with allergic reaction:<br>• minor gastrointestinal symptoms only (nausea, abdominal pain, and/or diarrhoea) — these are adverse effects, not allergy;<br>• headache, arthralgia, and/or strange taste in the mouth;<br>• child has since tolerated the same antibiotic without reaction; and<br>• label based on a family member's reaction, with no adverse event in the child themselves. | **De-label on history alone**.<br>Update the allergy record, document the clinical rationale, and provide written confirmation to the family |
| **Allergy symptoms, no red flags** | Rash that may represent a drug reaction, but without red-flag features, for example:<br>• delayed maculopapular (flat, blotchy, measles-like) rash, onset >1 hour after dose;<br>• urticaria/angioedema without respiratory or circulatory symptoms; and<br>• child was well-appearing. | **Prescribe a single therapeutic dose of the antibiotic to be taken at home**.<br>Ring the family 1 week later to confirm no reaction then de-label. In the unlikely event of a rash or other reaction, review further or refer to paediatric allergy |
| **Red-flag features** | Any of the following:<br>• anaphylaxis — difficulty breathing, tightness of the chest, wheeze, dizziness, collapse, or cardiovascular compromise;<br>• severe cutaneous adverse reactions: Stevens–Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia, and systemic symptoms;<br>• severe or prolonged rash with systemic features (mucosal or multisystem involvement); or<br>• severe or poorly controlled asthma. | **Refer to paediatric allergy or immunology**.<br>Do not attempt de-labelling or home challenge. Some NHS regions have direct-referral pathways; local integrated care board antimicrobial stewardship teams can advise |

antihistamine should usually be sufficient. If a rash develops after 24 hours, parents should take photographs to share with the healthcare professional (HCP). An HCP (nurse, pharmacist, or GP) should contact the family 1 week later and, if there are no objective symptoms, the drug allergy label can be removed.

## Preventing labels and proactive review

Before recording an antibiotic allergy at the point of prescribing, clinicians should consider whether the reaction represents true allergy or more likely a viral rash, drug side effect, or EBV interaction. Documenting the full reaction details at the time including the nature, timing, severity, and clinical context is essential for future de-labelling decisions. Where parents telephone in or send a request for an alternative antibiotic following 'allergy', further information should be sought.

Proactive label review is a straightforward quality improvement intervention. A practice-level search can identify all children with a coded antibiotic allergy; those labelled in early childhood or >5 years ago can be invited for a brief allergy review consultation. Electronic health record prompts have been shown to significantly increase de-labelling rates in paediatric primary care settings.[13]

## Conclusion

Most children labelled as antibiotic-allergic are not truly allergic, and the label causes real, avoidable harm. De-labelling can often be safely undertaken in primary care through a structured allergy history (Box 2), without the need for specialist involvement. For those with allergy symptoms but no red flags, prescribing a single dose of the antibiotic at home with a 1-week follow-up is simple, safe, and supported by paediatric primary care evidence including a UK study. A confident conversation with the family, a careful allergy-focused history, and a low threshold for proactive review can resolve inaccurate antibiotic allergy labels in the surgery — with appropriate referral for those with red-flag features.

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