September 2025

– TE WHATA KURA (ADULT AND CHILD) –

Use of cephalosporins in patients with penicillin allergy (adult and child)

"…for those rare patients with a history of anaphylaxis to penicillin, a non-cross-reactive cephalosporin (e.g. cefazolin) can be administered routinely…"

AMERICAN ACADEMY OF ALLERGY, ASTHMA & IMMUNOLOGY (2022)[1]

- About 10% of adults report penicillin allergy, but most do not have a true immune-mediated allergy.
- Penicillin allergy labels often lead to avoidance of beta-lactam antibiotics, causing use of less effective alternatives and harms such as surgical site infections, longer hospital stays and increased mortality.[2,3]
- Clinicians can help improve patient care and reduce harms by:
  - verifying the reported reaction and removing inaccurate penicillin allergy labels (see here), and
  - ensuring patients with confirmed penicillin allergy receive the best alternative antibiotic.
- Most patients with confirmed penicillin allergy (including anaphylaxis) can safely receive structurally dissimilar cephalosporins (and carbapenems).
- This details the evidence-based approach used for handling cross-reactivity in *Te Whata Kura*.

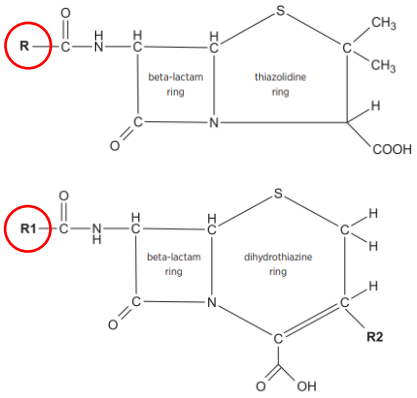
Historical context

- Studies from the 1960s and 1970s greatly overestimated cross-reactivity (up to 50%) due to contamination of cephalosporin formulations with penicillin and also to methodological flaws.[4]
- These misconceptions have driven decades of inappropriate antibiotic prescribing, which must now be corrected to prevent avoidable patient harm.
- Cross-reactivity is now known to mainly depend on similarities in the R1 side chain rather than the beta-lactam ring itself (Figure 1).
- The actual rate of penicillin-cephalosporin cross reactivity is < 2%, rising to 16% when the side chains are very similar or identical as seen with amoxicillin (an aminopenicillin) and the aminocephalosporins, cefalexin and cefaclor.[5]
- Penicillin-carbapenem cross-reactivity is < 1%.

Approach used in *Te Whata Kura* (Table 1)

- For **immediate penicillin allergies including anaphylaxis**, *Te Whata Kura* recommends a cephalosporin with a structurally dissimilar side chain (e.g. cefazolin, cefuroxime or ceftriaxone) if this is the best treatment. Cefalexin and cefaclor are not recommended due to higher cross-reactivity with the most common penicillin, amoxicillin.
- For **severe delayed reactions** (e.g. Stevens-Johnson syndrome), less is known about the safety of structurally dissimilar beta-lactams, thus all beta-lactams are avoided and early discussion with Infectious Diseases/Clinical Microbiology advised.

Figure 1: Structure of penicillins and cephalosporins:[6]



Watch for co-reactivity

- Patients with true allergy to one antibiotic have a higher likelihood of reacting to any new antibiotic, whether structurally related or not – this is co-reactivity, not cross-reactivity.

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"For decades, it has been taken as fact that cephalosporins should be avoided in the setting of a penicillin allergy, with no valid data supporting the theory that this prohibition improves overall patient safety or global outcomes. Decisions made to improve perceived safety in the short term can have severe, unintended, adverse long-term outcomes. The warning not to use cephalosporins, when they are the antibiotic of choice, in the setting of a penicillin allergy is a classic example of penny-wise and pound-foolish."

ERIC MACY (2021)[4]

TABLE 1: *TE WHATA KURA* 'RULES' FOR BETA-LACTAM RECOMMENDATIONS IN ADULT AND CHILD PATIENTS WITH PENICILLIN ALLERGY

- *Culprit penicillin is assumed to be amoxicillin, an aminopenicillin and the most used penicillin in Aotearoa.*
- *The 'rules' below are consistent for adult and child patients, except in non-severe delayed reactions. For these, different states of practice mean a penicillin will be recommended for children (but not for adults) with minor rashes without urticaria or mucosal involvement where it is the optimal treatment.*

TYPE OF PENICILLIN 'ALLERGY' HISTORY		TRANSLATION INTO TE WHATA KURA		
		PENICILLINS	CEPHALOSPORINS	CARBAPENEMS
NON-IMMUNE-MEDIATED ADVERSE EFFECT, e.g. nausea, vomiting, diarrhoea, mild headache, thrush		GIVE	GIVE	GIVE
IMMEDIATE *IgE mediated* *Usually occurs within 1 hour*	**NON-SEVERE**, e.g. immediate rash and no systemic symptoms	AVOID	AVOID: cefaclor, cefalexin CAN GIVE: cefazolin, cefuroxime, ceftriaxone, cefepime	GIVE
	SEVERE, e.g. • compromised airway • angioedema • hypotension or collapse • anaphylaxis *Hospitalisation or treatment with adrenaline, corticosteroids and antihistamines may have been required*	AVOID	AVOID: cefaclor, cefalexin GIVE: cefazolin, cefuroxime, ceftriaxone, cefepime	GIVE
DELAYED *T-cell mediated* *Usually occurs within days, but can occur more rapidly on rechallenge*	**NON-SEVERE**, e.g. mild childhood or maculopapular rash *No renal or hepatic injury, mucosal involvement, skin blistering or exfoliation*	AVOID – ADULT GIVE – CHILD	GIVE	GIVE
	SEVERE, e.g. severe cutaneous adverse reactions (SCARs) such as • drug reaction with eosinophilia and systemic symptoms (DRESS) • Stevens-Johnson syndrome (SJS) • toxic epidermal necrolysis (TEN) *Red flags include mucosal ulceration (mouth, eyes and/or genitals), desquamating skin lesions, and renal or hepatic injury*	AVOID	AVOID	AVOID

References:

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