



Frequently Asked Questions to support use of the penicillin allergy de-labelling algorithm and oral challenge test

PRE-TEST CLINICIAN QUERIES

Why do the test?

Penicillin allergy label is associated with increased morbidity, greater healthcare costs, increased rates of methicillin resistant *Staphylococcus aureus* (MRSA), *Clostridioides difficile*, and vancomycin-resistant *Enterococcus* (VRE) infection, longer hospital stays, increased readmission rates, and more critical care admissions. This is most likely through the avoidance of 'best first-line' antimicrobial therapy with penicillins, and use of broad-spectrum alternatives. In surgical patients, there is evidence of increased risk of wound infections when penicillins are replaced with non-beta lactam alternatives, and of perioperative anaphylaxis from the alternatives used. Penicillin allergy de-labelling is a well-established process reported in peer reviewed journals and supported by several national and international allergy groups.

Can the test be used for patients with allergy to other beta-lactam antibiotics?

The β -lactam ring is a core part of the chemical structure of several antibiotic families, including penicillins, cephalosporins, monobactams and carbapenems. It can be this part of the drug that causes allergic reactions, so people allergic to penicillin may also be allergic to other antibiotics in different families, which share the beta lactam ring (cross-reactivity).

People with very severe allergic reactions / anaphylaxis to penicillin should generally avoid these other antibiotic families because of the risk of cross-reactivity.

The algorithm is only appropriate for people reporting allergy/intolerance to penicillin, and is not intended for use in patients reporting allergy/intolerance to other antibiotic classes including cephalosporins and carbapenems.

I'm seeking consent for the penicillin challenge test – what risks should I explain to the patient?

The main concern is for severe allergy / anaphylaxis. The risk is very low. A number of studies have been published looking at the use of oral penicillin challenge test using protocols similar to ours:

Leeds, pre-op assessment, patients likely to require penicillin for surgery. 56 patients were identified as low risk and eligible (of 219 screened), and were given sequential oral penicillin challenge tests. None had any immediate adverse reaction. One developed urticaria. Four had non-allergic symptoms during the prolonged course.

Penicillin allergy de-labelling ahead of elective surgery: feasibility and barriers, L. Savic, L. Gurr, V. Kaura, J. Toolan, J.A.T. Sandoe, P.M. Hopkins, S. Savic British Journal of Anaesthesia; Available online 19 October 2018

US Marine recruits. 328 recruits direct to amoxicillin challenge without skin testing, 5 (1.5%) had an acute objective challenge reaction – 4 were isolated cutaneous reactions, 1 included globus. None had anaphylaxis. All were treated with oral antihistamine and single dose IM adrenaline (to avoid reaction progression). None needed additional medication or transfer to higher level of care.

Tucker MH, Lomas CM, Ramchandrar N, Waldram JD. Amoxicillin challenge without penicillin skin testing in evaluation of penicillin allergy in a cohort of Marine recruits. The journal of allergy and clinical immunology. In practice. May - Jun 2017;5(3):813-815.

Australian cancer centre. Opportunistically identified patients. 195 identified, 98 with low risk. 46 underwent penicillin oral challenge. All patients (46/46, 100%) tolerated the oral challenge without adverse drug reactions (followed-up for 90days) and were subsequently de-labelled.

Jason A Trubiano, Olivia Smibert, Abby Douglas, Misha Devchand, Belinda Lambros, Natasha E Holmes, Kyra Y Chua, Elizabeth J Phillips, Monica A Slavin; *The safety and efficacy of an oral penicillin challenge program in cancer patients – A pilot multicentre study*, *Open Forum Infectious Diseases*, , ofy306, <https://doi.org/10.1093/ofid/ofy306>

“Is it safe for patients on antihypertensive agents such as beta-blockers and ACE inhibitors to have an oral penicillin challenge test?”

These antihypertensive drugs can impede management of anaphylaxis as the patient may have a more profound hypotensive episode and may require larger doses of adrenaline which makes recovery more problematic. However for those patients who have been assessed as low risk using the algorithm there is no evidence to suggest they should be excluded.

PRE-TEST PATIENT SCENARIOS

“I think I had a penicillin allergy as a child > 20 years ago but can’t remember any of the details”

If there were no features identified or remembered that suggest either a Type 4 hypersensitivity or a Type 1 hypersensitivity, and the reaction occurred more than 10 years ago, and it didn’t result in hospital admission, then the overall risk of immediate allergy is low, and so an oral challenge can be considered following senior review.

“I developed a rash after penicillin years ago but can’t remember when”

If there were no other features identified or remembered that suggest a Type 4 hypersensitivity or a Type 1 hypersensitivity, follow the “Uncertain” path on the algorithm and consider whether the reaction resulted in hospital admission and whether it happened more or less than ten years ago.

“My intolerance was really severe, e.g. terrible diarrhoea”

It may be that other factors were contributing to your symptoms, or you could be prone to significant side effects of penicillin. The oral challenge test is likely to be safe if you follow the algorithm.

“I think I had an allergic reaction to an antibiotic as a child but I don’t know if it was penicillin”

This test only assesses allergy towards penicillin and a negative result wouldn’t mean that all other antibiotics are safe to use. Checking penicillin allergy may still be very useful in this situation, though.

“I had a bad reaction (I think I collapsed) but I think it happened after more than one hour from administration”

Consider the context and other symptoms. Collapse could be a feature of a severe allergic reaction and would generally mean that an oral challenge test should not be performed.

DURING TEST CLINICIAN QUERIES

My patient’s heart rate climbed during the period of observation, does this mean they’re allergic?

Probably not. There’re lots of reasons the heart rate could have climbed, and if it was mild and isolated, this would not necessarily indicate allergy. The patient should be monitored closely and senior discussion should take place to consider the result of the test.

My patient reported an itch during observation, does this mean they’re allergic?

Probably not. If it was mild and isolated, and there was no rash, an itch would not indicate allergy.

POST TEST CLINICIAN QUERIES

My patient had a negative amoxicillin oral challenge. Does this mean that they are not allergic to other beta-lactams?

We have chosen amoxicillin for the oral challenge as this is the commonest penicillin antibiotic employed and would therefore allow the largest number of patients to be 'de-labelled' by this process. A negative challenge means, in general, that a patient with a negative oral challenge has the same risk of reaction to subsequent penicillin based antibiotics as a patient who has never had a label of penicillin allergy.

However it is also recognised that some patients have reactions to penicillin based antibiotics that are not covered by this approach, specifically side chain allergy e.g. flucloxacillin, rare reactions to clavulanic acid, and does not exclude allergy to excipients. If clarification is required around their ongoing risk to these antibiotics advice should be sought from local allergy specialists. Challenge with the incident antibiotic within this service can then be considered.

On rare occasions where a patient reports a history of allergy to a penicillin antibiotic that cannot be the subject of an oral challenge test, for example IV piperacillin/tazobactam (Tazocin), an amoxicillin challenge might still be helpful. Assuming the test is negative this would permit the administration of amoxicillin in the future but it would **not** allow the label of piperacillin/tazobactam allergy to be removed.

In such cases, on discharge you should inform the GP/community pharmacist that it is safe for the patient to take the tested drug (amoxicillin) but other beta-lactam should continue to be avoided if other allergies are suspected and have not been tested. The standard Negative test GP communication **cannot be used** in this circumstance and the test details along with its implications should be communicated within the Immediate Discharge Letter. Such cases represent a minority of patients as the majority will report a single beta-lactam allergy label.