**Student:** Silabhakta Livirya

**Title:** Direct oral amoxicillin challenge study of low risk general medical hospital inpatients

**Supervisor(s):** Dr Heather Isenman, Dr Alan Pithie, Dr Matt Doogue and Dr Ignatious Chua

**Sponsor:** Canterbury Medical Research Foundation

## Introduction

Penicillin is the most commonly reported drug allergy, found in up to 15% of patients, but on testing, fewer than 10% have immediate hypersensitivity reactions. A penicillin allergy label leads to prescription of alternative antibiotics, which may carry greater cost and increase adverse events leading to longer hospital stays.

Guidelines recommend skin testing (ST), followed by an oral challenge (OC) of penicillin if negative, to exclude an immediate reaction. ST requires specific reagents and training to execute, and as such is underutilised. Given the difficulties with executing ST, two recent studies assessed the safety of a direct penicillin OC on outpatients, showing only 1.5% experiencing a non-severe immediate reaction - suggesting that carefully selected patients can be challenged without prior ST.

## Aim

To determine whether a direct OC of low risk penicillin allergic patients is safe and feasible in hospital.

## Impact

If it is safe to use a direct OC on certain penicillin allergic patients, it would simplify penicillin allergy evaluation, leading to improved treatment options.

## Methods

Penicillin allergic general medical patients were identified daily from Christchurch Hospital. Patients were interviewed and categorised based on their allergy history. High risk patients were excluded from OC based on the following criteria: (1) history of a severe cutaneous drug reaction or a severe blistering rash; (2) interstitial nephritis, vasculitis or haemolytic anaemia; (3) angioedema or anaphylaxis. Patients who had cutaneous and/or respiratory symptoms occurring $\geq$ 6 months ago and $\leq$ 1 hour of drug administration, or had an exclusion criteria reaction that could have had other causes, were excluded but considered intermediate risk and referred to immunology for assessment. Those who had a limited cutaneous reaction occurring $\geq$ 6 months ago and $\geq$ 1 hour after drug administration, or unknown symptoms were deemed low risk. Those who had gastrointestinal (GI) symptoms alone were classed as low risk but non- allergic, and were simply relabelled. Patients who were at the end of life, frail, haemodynamically unstable, immunosuppressed, or pregnant were excluded regardless of their history.

Consenting low risk patients received 250mg of oral amoxicillin, with baseline, 30, and 60 minutes post dose blood pressure, heart rate, respiratory rate and oxygen saturation monitoring, and formal review at one hour. Their records were updated, and they were given a letter outlining the process. The study was approved by the Central Health and Disability Ethics Committee (HDEC) of New Zealand, study number 17/CEN/188.

## Results

Between November 20 2017 to 22 January 2018, 289 penicillin allergic patients were identified. 224 patients were screened. 37 high and 25 intermediate risk were excluded, leaving 162 low risk patients. The mean age of low risk patients was 74, (16-95 years). The mean time from the allergic event was 25 years, though 46 (28.4%) could not recall the date of the event. The culprit drug was unknown penicillin antibiotic in most (37.7%). Cutaneous symptoms were the commonest reaction in 61 patients (37.7%), followed by GI symptoms in 38 (23.5%), with 53 (32.7%) unknown reactions.

Of low risk patients, 12 low risk patients were excluded from OC – 10 (frailty), 2 (immunosuppressed), and 38 declined or were discharged. 56 (34.6%) had tolerated penicillin antibiotics since their reaction, and their penicillin allergy label was removed without a OC. 15 patients were relabelled without OC as their reaction was not allergic (GI symptoms alone). A total of 41 patients were OC without issue. Overall, 112 of the 224 screened patients had their allergy removed.

## Discussion

True IgE-mediated hypersensitivity to penicillin antibiotics, whilst rare, can be life threatening and thus a penicillin allergy label deters prescribers. The limitations of ST in excluding allergy highlight the need for an alternative approach. This study built on previous data demonstrating the safety of a direct OC in low risk patients, and employed this approach prospectively in a cohort of complex, older (median age 77 years) general medical inpatients successfully, with no adverse events.

We identified a prevalence of 16% penicillin allergic patients, similar to previous reports. The allergy description was poorly documented, with 80 (35.7%) of screened patients having a discrepancy between documentation and their recollection. In addition, despite tolerating penicillin subsequent to their reaction, 56 patients still had their allergy label. The majority of these would have been classified as low risk and challenged in our protocol, further supporting the safety of our criteria.

All OC patients either had a limited cutaneous reaction (n=24) or unknown symptoms (n=17). Patients with unknown symptoms were included with the assumption that a severe reaction would not be forgotten.

A limitation of the study was that 38 declined an OC or were discharged prior to one. This is related to our opportunistic study design, and may reflect patient reluctance to trial a clinically unnecessary treatment.

We have demonstrated a safe, resource-light method to safely exclude an immediate hypersensitivity in hospital patients. Bearing in mind the problems associated with carrying a penicillin allergy label and the obstacles in performing ST, we feel these criteria may now be used to generate a hospital pathway to address penicillin allergy.