

# Penicillin allergy delabelling of patients at risk of sexually transmitted infections in primary care

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In North America, a penicillin allergy is reported by about 10% of patients.<sup>1</sup> In relation to sexual health and sexually transmitted infections (STIs), this is especially important with the resurgence of syphilis (penicillin is the preferred treatment) and the rise of fluoroquinolone and macrolide-resistant gonococcal infections (cephalosporins are the recommended first-line therapy).<sup>2</sup> When properly assessed, 95% of reported allergic reactions are considered low risk for severe allergic reactions and can be successfully delabelled.<sup>3</sup> Although patients can be referred to an allergist for a drug allergy evaluation, this is often an impractical option as accessibility and appointment attendance tend to be poor, especially in patients who are young and may be navigating challenging sociodemographic circumstances.<sup>4</sup> An oral penicillin challenge is a simple alternative method to exclude penicillin allergy in patients at low risk for anaphylaxis. Although this has been shown to be effective in specialist outpatient clinics and hospital-based settings,<sup>5</sup> we are not aware of any reports of the use of an oral penicillin challenge in primary care community-based sexual health clinics.

## How did we perform an oral penicillin challenge and who was eligible?

From January 2019 to November 2020, we prospectively identified from our electronic medical records a list of patients who were considered at risk of STIs and had been identified with a history of allergy to penicillin. Patients were contacted by telephone and offered an in-person appointment to evaluate their history of allergic reaction in our local community health centre STI clinic in Montréal, Quebec.

We developed a risk-stratification algorithm based on Quebec provincial guidelines<sup>6</sup> to assess eligibility for an oral penicillin challenge (Figure 1). We first stratified patients as being at low or high risk of an allergic reaction based on their history. We defined low-risk reactions by an absence or lack of recall of severe symptoms (i.e., anaphylaxis, hypotension, respiratory difficulties, joint or hepatic involvement, serious cutaneous reactions, severe allergic syndromes or hospital admission) and that had occurred before the age of 16 years or more than

### Key points

- Most patients who report a penicillin allergy do not have a serious allergy.
- Penicillin allergy delabelling enables patients to receive penicillin and  $\beta$ -lactam antibiotics when indicated.
- A simple algorithm allows for stratification of allergy risk for patients.
- Patients at low risk of a serious allergic reaction can undergo an oral penicillin challenge in sexual health clinics and other primary care settings.

10 years previously. We offered patients with a history of a low-risk penicillin allergy an oral penicillin challenge supervised by a primary care physician, and referred high-risk patients to an allergist for further evaluation.

We performed an oral penicillin challenge in low-risk patients on the same day we administered the algorithm; standard equipment and medications to treat anaphylaxis were available. We administered amoxicillin (total dose of 1000 mg), an accessible penicillin antibiotic, to each patient. If the initial allergy history suggested a delayed reaction (more than 60 min after exposure to penicillin), we performed a 1-step challenge, with patients receiving 1 dose of 1000 mg of amoxicillin. We gave other patients a 2-step challenge (125 mg followed by 875 mg of amoxicillin with a 30-min interval between doses). The provocation test was followed by a 60-minute observation period. If no objective signs of an allergic reaction (i.e., urticaria, pruritus, angioedema or respiratory difficulties) were observed, the patient was no longer considered to have a serious penicillin allergy, and was discharged with instructions to contact the clinic if any adverse events occurred.

Among the 80 patients we identified with a penicillin allergy in our electronic medical records, 28 (32%) were enrolled and completed the risk stratification. Their characteristics were similar to the general patient population in our clinic; most patients were male (96%) and between the ages of 20 and 46 years (mean age 30.2 yr). Only 2 of the 28 patients were considered to be at high

risk and we referred them to an allergist. Among the 26 patients who we classified to be at low risk, 20 (77%) reported isolated cutaneous manifestations in the past and 6 (23%) did not recall their allergic reaction history. All but 1 patient received the

2-step oral penicillin challenge. There were no reactions during the immediate observation period in any patient who underwent a challenge, and no delayed symptoms or adverse events were reported afterwards.

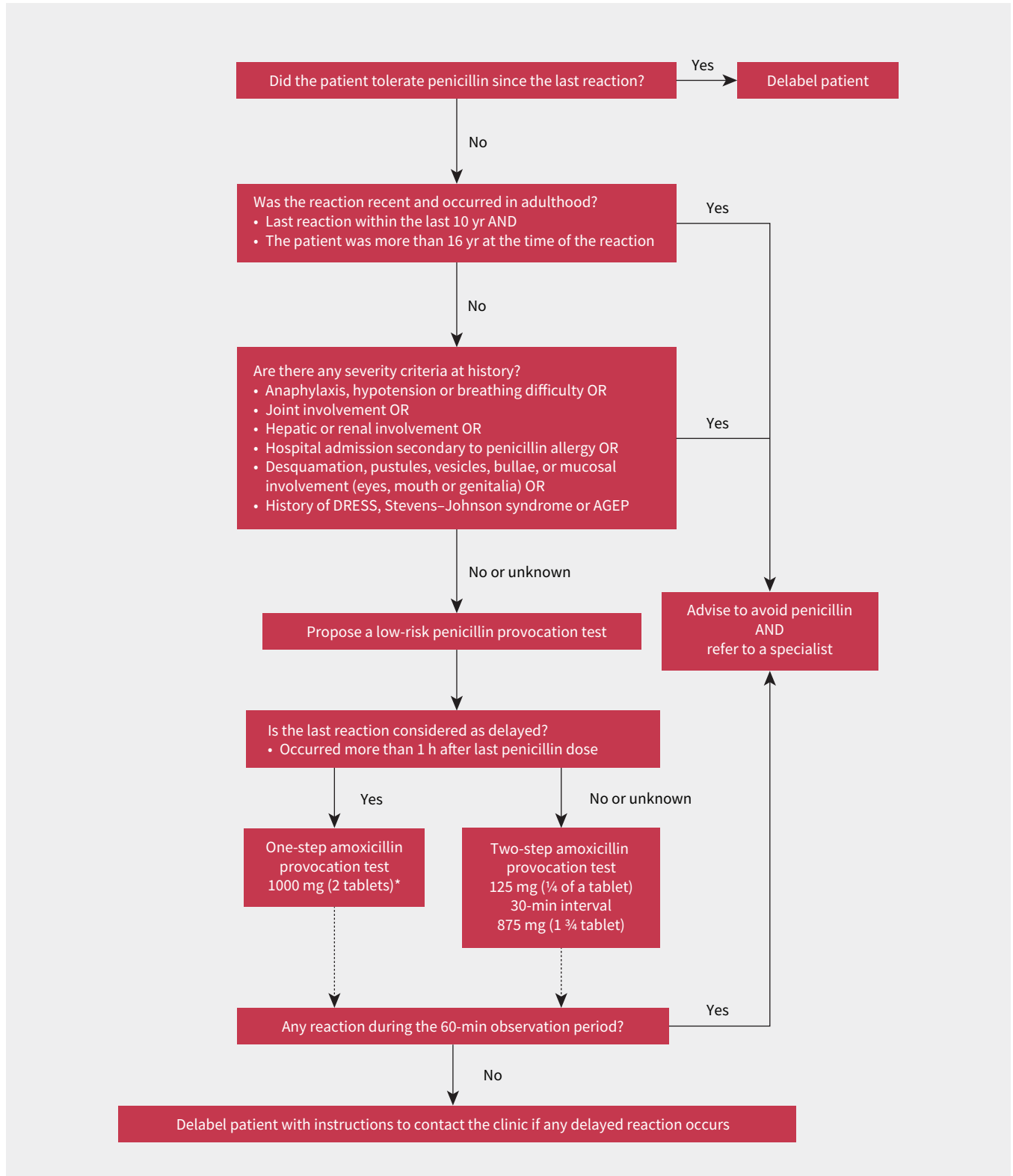


Figure 1: Risk stratification for penicillin allergy and provocation test algorithm for primary health care based on provincial guidelines.<sup>6</sup> Note: AGEP = acute generalized exanthematous pustulosis, DRESS = drug reaction with eosinophilia and systemic symptoms. \*One tablet is 500 mg.

## What is the evidence of benefit?

From our experience and based on experiences in other settings,<sup>5,7,8</sup> an oral penicillin challenge performed in patients with a history of low-risk penicillin allergy is a simple way to safely increase the appropriate use of penicillin and  $\beta$ -lactam antibiotics in a primary care setting. This has been shown in various hospital-based and outpatient settings, but not in STI treatment.<sup>9</sup> Practitioners in sexual health clinics are frequently faced with patients who have been labelled as allergic to penicillin and who are therefore prescribed second-line antibiotics. This may contribute to antimicrobial resistance and morbidity from STIs.

Our algorithm provides a step-by-step method to support primary care physicians in assessing patients who report a history of penicillin allergy, including patients with a poorly described allergic reaction, which differs from the protocol of a 2021 descriptive analysis done in a similar primary care setting.<sup>7</sup>

## What is the evidence of harm?

Previous studies have shown that an oral penicillin challenge is safe in patients at low risk, with most reactions consisting of subjective or minor symptoms and anaphylaxis occurring in less than 1 in 500 cases.<sup>1</sup> Fear of such reactions by practitioners and patients may still be a barrier to direct oral penicillin challenge in primary care, but they should be reminded that risk can be minimized if adequate stratification is performed.

## What are the resource implications?

Overall, few resources are needed to perform an oral penicillin challenge. Amoxicillin tablets are widely available and inexpensive. All nurses and physicians in the clinic must be familiar with the protocol for oral penicillin challenge; our training consisted of a 1-hour session with clinical scenarios where the evaluation algorithm (Figure 1) was applied. A physician certified in basic cardiac life support must be present on site for all oral penicillin challenges.

## What can be expected in the future?

Our experience supports the use of an oral penicillin challenge as a safe and accessible way to delabel patients at low risk of a penicillin or  $\beta$ -lactam allergy in community-based sexual health clinics. Since only 32% of patients we contacted agreed to a dedicated elective delabelling appointment, our algorithm has been implemented into routine practice at our clinic, and we can now delabel patients on the same day they require an antibiotic, if they agree.

Our patients were mostly young men without comorbidities; this must be considered when generalizing to other settings. However, with adequate risk stratification, an oral penicillin challenge without prior skin testing has been found to be safe in patients who were frail, those with comorbidities and children.<sup>8,10</sup>

Our findings and those from other studies<sup>5,7,8</sup> should encourage primary health care providers to establish local delabelling protocols and point-of-care assessments of patients who report

penicillin allergy. These protocols can be used in other areas of primary care where antibiotics are frequently prescribed with the hope of contributing to a bottom-up solution to the global public health problem of rising antimicrobial resistance.

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