

# Aotearoa New Zealand clinicians respond to the 2022 American Heart Association Presidential Advisory Statement regarding penicillin reactions in people with severe rheumatic heart disease

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In 2022, the American Heart Association (AHA) published a Presidential Advisory Statement highlighting sudden cardiac deaths in 10 individuals with severe symptomatic rheumatic heart disease (RHD), shortly after they received intramuscular benzathine penicillin G (BPG).<sup>1,2</sup> The Advisory Statement authors concluded that BPG should no longer be recommended for individuals with most subtypes of severe RHD, on the basis that such events may undermine public confidence in the safety of secondary penicillin prophylaxis programmes in high-prevalence RHD populations. They concluded that oral penicillin is the preferred form of secondary prophylaxis for this group of patients.

BPG secondary prophylaxis has been the cornerstone of RHD control globally for decades, and it is well established that BPG is superior to oral penicillin in preventing acute rheumatic fever (ARF) recurrences.<sup>3,4</sup>

We sought to consider the implications of the AHA recommendations for Aotearoa New Zealand. A group of ARF/RHD clinicians reviewed the AHA statement and local safety data. Additional consultation occurred with Medsafe (the national pharmacovigilance centre) and with colleagues working across the sector. Differences in clinical profiles and management between the AHA Advisory cases and the Aotearoa New Zealand context were evaluated.

In Aotearoa New Zealand, BPG has been administered via register-based programmes in community settings since the 1980s. Injections are given by nurses in homes, schools and primary

care clinics. Pfizer brand pre-formulated Bicillin® L-A is used exclusively, in contrast to most other RHD-endemic populations where cheaper reconstituted lyophilized dry powder formulation is used.<sup>5</sup> In Aotearoa New Zealand, BPG injections are given at the ventrogluteal site, deemed to be safer than the dorsogluteal site due to its greater distance from neurovascular structures.<sup>6</sup> Community nurses undergo competency-based training in BPG administration. Analgesia and non-pharmacologic measures to reduce injection-related pain are routinely used,<sup>7</sup> and adrenaline and basic resuscitation equipment are carried by community nurses.

The high level of confidence in the safety of the BPG programme is backed up by reassuring pharmacovigilance data. A December 2022 review undertaken by Medsafe found only seven reports of adverse reactions in the last 10 years, most on the hypersensitivity spectrum, and no deaths (2023 May, email, Nevin Zhong, Medsafe NZ).

Aotearoa New Zealand is different to many other regions with high prevalence of RHD. Unlike other endemic settings, where problems with BPG quality and stock-outs are frequently encountered,<sup>5</sup> in Aotearoa New Zealand there is a secure supply of high-quality preformulated BPG. With well-established register-based delivery of preformulated BPG and extremely low ARF recurrence rates (around 6% overall, less in children),<sup>8</sup> the benefit of BPG secondary prophylaxis is clear. Recurrence prevention minimises damage to affected valves, prevents damage to healthy valves and may delay or avert the need

for cardiac surgery. This is particularly important in growing children and teenagers. Publicly funded healthcare, including cardiac surgery, is available to all Aotearoa New Zealand residents with severe RHD.

The 10 AHA Advisory cases had symptomatic decompensated advanced RHD. Very little clinical information was provided to accurately stratify risk among the very small group of individuals with severe RHD. While the vasovagal pathogenesis postulated by the AHA authors is a consideration, vasovagal syncope is generally associated with a benign prognosis. Despite hundreds of people with severe RHD in Aotearoa New Zealand receiving BPG, no cases of cardiovascular collapse associated with BPG have been recorded. As published on the AHA website, we have postulated that a more likely mechanism for the episodes reported is severe decompensated RHD with co-existing advanced pulmonary hypertension.<sup>9</sup> Any such patients in Aotearoa New Zealand would be under cardiology specialist monitoring and consideration for cardiac surgery.

No sudden cardiac events have been observed in Aotearoa New Zealand following administration of Bicillin® L-A, and therefore we do not favour adopting the AHA recommendations in Aotearoa New Zealand at this time. Currently, our position is that adopting the AHA Advisory recommendations in Aotearoa New Zealand could result in excess harm due to ARF recurrences and loss of trust in national secondary prophylaxis programmes.

### Recommendations:

- All persons with ARF/RHD should be offered BPG prophylaxis as first line, according to New Zealand Heart Foundation Guidelines.<sup>10</sup>
- It is strongly recommended that BPG

injections are administered by trained nurses working in regional register-based programmes.

- Adverse reactions should continue to be notified through the usual reporting systems to Medsafe. Any person with a suspected adverse reaction should be reviewed by a specialist paediatrician or physician to determine the most appropriate antibiotic choice for secondary prophylaxis.
- We agree with the AHA Advisory recommendation that it is prudent to ensure that fluids and food have been consumed in the hours before the injection to avoid hypovolaemia and syncope.
- Best practice guidelines to reduce injection-related pain (including the use of lignocaine and Buzzy® device) should be followed.
- For individuals with severe RHD who may be anxious about the safety of IM BPG, prophylaxis recommendations can be discussed on an individual basis with a paediatrician, physician or cardiologist experienced in RHD management.
- Ongoing safety monitoring should continue via existing mechanisms, including the Centre for Adverse Reactions Monitoring (CARM) and register programmes. The new National Care Coordination System should assist with this.

The above position has been considered in light of circumstances in Aotearoa New Zealand, where there is access to high-quality preformulated Bicillin® L-A, excellent adherence and safety monitoring, and where end-stage cardiac disease is uncommon. These views may not apply in other ARF/RHD endemic countries where circumstances may be very different.

**COMPETING INTERESTS**

Nil.

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