This update to the Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for the use of aminoglycosides in individuals with the *MT-RNR1* genotype was precipitated following contact from primary care physicians and pediatricians. These clinicians had asked whether patients with the m.1555A>G variant should avoid vaccines where aminoglycosides are used in the manufacture process. This update will be accompanied by a peer-reviewed commentary, the link for which will be posted here once available.

Aminoglycoside antibiotics are commonly used during the manufacture of vaccines to prevent bacterial contamination. Many of these agents are removed during the purification process, but some can remain as trace excipients. In January 2023, the CPIC *MT-RNR1* guideline writing group met to clarify how these guidelines might interact with the decision to provide routine vaccinations.

This writing group agreed that individuals with *MT-RNR1* variants associated with an increased risk of aminoglycoside-induced hearing loss (AIHL) should receive their vaccine schedule as normal. The rationale for this decision is threefold:

1. The antibiotic content in vaccines is extremely low and well below the therapeutic doses associated with AIHL.1-3 For example, an influenza vaccine contains no more than 0.00015mg per dose. Although prescribing regimens vary depending on the clinical context and local guidance, a typical dose of gentamicin in neonatal sepsis is 5mg/kg every 24-36 hours.4-7 Therefore, a 3kg newborn might receive a 15mg daily dose of gentamicin intravenously; a 100,000 order of magnitude greater quantity than found in the vaccine. As such, the possibility that such small quantities of aminoglycosides contained in vaccines could cause AIHL is extremely low and, at best, theoretical.
2. The CPIC guidelines for the use of aminoglycosides for individuals with the *MT-RNR1* genotype state that, in individuals with risk-conferring *MT-RNR1* variants, aminoglycoside antibiotics should be avoided unless the risk of AIHL is outweighed by the risk of not providing that antibiotic therapy, without safe or effective alternative therapies. In this clinical scenario, the guideline writing group agree that the extremely low theoretical risk of AIHL from vaccines is greatly outweighed by the benefits of vaccination.
3. The frequency of the most common risk-conferring *MT-RNR1* variant, m.1555A>G, is sufficiently high that is reasonably likely that if there was a signal to be observed, this would have been identified given the almost ubiquitous nature of this intervention.

In conclusion, the CPIC *MT-RNR1* writinggroup agree that presence of *MT-RNR1* variants associated with an increased risk of AIHL should not impact routine vaccination schedules.

**References**

1. Hayward RS, Harding J, Molloy R, et al. Adverse effects of a single dose of gentamicin in adults: a systematic review. British Journal of Clinical Pharmacology 2018;84(2):223–38.
2. Fjalstad JW, Laukli E, van den Anker JN, Klingenberg C. High-dose gentamicin in newborn infants: is it safe? Eur J Pediatr 2013;
3. Puia-Dumitrescu M, Bretzius OM, Brown N, et al. Evaluation of Gentamicin Exposure in the Neonatal Intensive Care Unit and Hearing Function at Discharge. J Pediatr 2018;203:131–6.
4. Cross CP, Liao S, Urdang ZD, Srikanth P, Garinis AC, Steyger PS. Effect of Sepsis and Systemic Inflammatory Response Syndrome on Neonatal Hearing Screening Outcomes following Gentamicin Exposure. Int J Pediatr Otorhinolaryngol 2015;79(11):1915–9.
5. Garinis AC, Liao S, Cross CP, et al. Effect of gentamicin and levels of ambient sound on hearing screening outcomes in the neonatal intensive care unit: A pilot study. Int J Pediatr Otorhinolaryngol 2017;97:42–50.
6. Children’s Hospital of Philadelphia. Vaccine Ingredients - Antibiotics [Internet]. 2014 [cited 2023 Feb 23];Available from: https://www.chop.edu/centers-programs/vaccine-education-center/vaccine-ingredients/antibiotics
7. National Institute for Health and Care Excellence. CG149. Neonatal infection (early onset): antibiotics for prevention and treatment. 2012.