Research Title

Measuring and strengthening waning immunity to measles in fully immunised young adults

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Summary

Measles is an extremely contagious disease which even in high resource settings like Aotearoa New Zealand (ANZ) can be lethal. Since 2019, outbreaks have been reported from several high-income measles-eliminated settings, including ANZ. A large proportion of these cases are occurring in young adults previously vaccinated with two doses of measles, mumps, and rubella (MMR) vaccine in childhood. During the 2019 measles outbreak in ANZ, about 14% of measles-infected young people aged 20-29 years had previously received ≥1 dose of MMR. This measles susceptibility is particularly important among tertiary students enrolling in healthcare programs as they are at increased risk of exposure to measles cases. Therefore, to better understand measles immunity in young adults, this research project aimed to investigate the prevalence of measles seronegativity, diagnostic accuracy of tests measuring measles immunity, and whether alternative routes of 3rd dose of MMR (MMR3) administration could strengthen measles immunity in tertiary students enrolling in healthcare programs.

The 1st research component investigating the measles immunity status among students joining health-related courses at the University of Otago, found that about 20% of students with evidence of previous receipt of 2 MMR doses tested between 2015-20 were seronegative (non-immune) by the commercial assay used then (Trinity). The predictors of measles antibody levels in the seronegative range were overseas birth and being seronegative to either mumps or rubella.

The 2nd research component evaluated the diagnostic accuracy of a commercially available test (DiaSorin (LIAISON®)), commonly used to screen measles immunity in several measles-eliminated settings, including University of Otago. The assay had inferior sensitivity and specificity in identifying measles immune and non-immune individuals when compared to the gold-standard test (plaque-reduction neutralization test (PRNT)). An alternative bead-based Luminex assay (bead-based multiplex immunoassay (MIA)) was better correlated to PRNT in the identification of true seropositives but performed similarly to DiaSorin with respect to false positives. MIA and PRNT testing were done overseas, at National Institute for Public Health and the Environment, the Netherlands, due to their unavailability in ANZ.

The 3rd research component aimed to understand the short-term antibody responses to intramuscular MMR3. Post-MMR3, the antibody to measles, mumps, and rubella were greatest in those whose pre-MMR antibody levels were in the lowest tertile. Following MMR3, all subjects were measles seropositive, as defined by an antibody level ≥0.12 IU/ml to measles by MIA and PRNT.

The final research component compares the measles antibody responses to MMR administration by intramuscular, intradermal, and aerosol routes in a randomized controlled trial (RCT) conducted among subjects who were seronegative or equivocal for measles and/or mumps antibody as measured by the DiaSorin assay. The initial findings from this study suggest that the measles antibody responses (post- to pre-MMR antibody ratios) were highest for aerosol, followed by intramuscular and intradermal delivery at about 28 days after receiving MMR (more in the lowest pre-MMR tertile). When measured by MIA, as there were substantial number of participants who were not eligible for the RCT based on their DiaSorin level but by MIA assay were in the lower range of pre-MMR antibody, we added MIA antibody data from non-RCT participants (challenge study, bloods only and 2021 cohort) to RCT participants who received MMR via intramuscular and aerosol routes (intradermal participants were only recruited into the RCT). The increased sample size in this analysis confirmed significantly higher antibody responses to aerosolized MMR in those in the lowest tertile of pre-MMR antibody when compared to the reference route (intramuscular delivery).

Safety is an important consideration for the potential use of alternative MMR delivery routes. The most common side effects reported for all routes of administration were headache and fatigue, with sore throat and cough also frequently reported with aerosol delivery. Post-MMR symptoms were transient, and reported as interrupting normal daily activities by only 4 participants – 2 in each of aerosol and intramuscular and intradermal. Findings reported here are based on the initial data available from this study.

Funding

Te Niwha, the Infectious Diseases Research Platform – co-hosted by PHF Science and the University of Otago and provisioned by the Ministry of Business, Innovation and Employment, New Zealand funded this project. The clinical studies on which this research is based were primarily funded by Human Research Council (HRC) and Otago Medical Research Foundation (OMRF).

This research project addresses the Te Niwha aims by identifying the need to build domestic research capabilities in ANZ to bring more sensitive assays (e.g., MIA) that could produce more accurate measles immunity assessments in population-level serosurveys. Furthermore, for populations at increased risk of acquiring measles during outbreaks (e.g., Māori and Pacific people), the adoption of non-invasive and potentially more immunogenic aerosolised MMR delivery methods might help reduce immunity gaps. Finally, this research is closely linked to the international context of waning immunity and the emerging need for additional MMR doses - issues that are also concerns in other countries in the World Health Organization (WHO) Western Pacific Region (WPR) region (e.g., South Korea, Japan) and in the WHO South-East Asia Region (SEAR) (e.g., Thailand).

Achievements:

Publications

1. Saha, S., Millier, M., Samaranayaka, A., Edmonds, L., Best, E., Ussher, J., Anglemyer, A., Lee, J., Tatley, M., Cutts, F., van Binnendijk, R., & McIntyre, P. (2025). Immunogenicity and safety of measles-mumps-rubella vaccine delivered by the aerosol, intradermal and intramuscular routes in previously vaccinated young adults: a randomized controlled trial protocol. PLOS ONE, 20(3), e0318893-e0318893. https://doi.org/10.1371/journal.pone.0318893.
2. Saha, S., van Binnendijk, R., Ussher, J., ten Hulscher, H., Millier, M., & McIntyre, P. (2025). Limitations of serological screening for measles immunity in young health care workers in New Zealand. Vaccine, 68, 127931. https://doi.org/https://doi.org/10.1016/j.vaccine.2025.127931

Conference presentations

3. Saha S, Millier M, Ussher J, ten Hulscher-van Overbeek H, van Binnendijk R, McIntyre P. Accuracy of measles serology and post MMR measles antibody responses via alternate vaccine delivery routes. Oral presentation at Aotearoa New Zealand, Infectious Diseases and Pandemic Preparedness Summit 2025, Hamilton New Zealand.
4. Saha S, Millier M, Ussher J, ten Hulscher-van Overbeek H, van Binnendijk R, McIntyre P. Low accuracy of routine measles serology in New Zealand and Me antibody responses post MMR given intradermally or by aerosol vs intramuscular route. Oral presentation at Aotearoa New Zealand Immunisation Conference 2025, Hamilton New Zealand.
5. Saha, S., Millier, M., Ussher, J., van Binnendijk, R., & McIntyre, P. (2025). Post-MMR3 measles, mumps, and rubella antibody level changes in seronegative young adults. Oral presentation at Communicable Diseases and Immunisation Conference (CDIC), Australia.
6. Saha, S., Davie, G., de Graaf, B., Miller, M., Ussher, J., van Binnendijk, R., & McIntyre, P. (2024). Measles antibody responses in tertiary students to third dose of measles-mumps-rubella vaccine. Oral presentation at Communicable Diseases and Immunisation Conference (CDIC), Australia.
7. Saha, S., Davie, G., de Graaf, B., Miller, M., Ussher, J., van Binnendijk, R., & McIntyre, P. (2024). Accuracy of thresholds for measles seroprotection in immunized young adults. Oral presentation at Communicable Diseases and Immunisation Conference (CDIC), Australia.
8. Saha, S., Davie, G., de Graaf, B., Miller, M., Ussher, J., van Binnendijk, R., & McIntyre, P. (2024). Limitations of serological screening for low measles immunity in health-science students fully vaccinated in childhood. Oral presentation at Aotearoa New Zealand Infectious Diseases and Pandemic Preparedness Summit 2024, Wellington, New Zealand
9. Accuracy of thresholds for measles seroprotection in immunized young adults – Poster presentation at Research Leaders & Emerging Researchers Forums, Wellington, New Zealand (June 2025)
10. Saha, S., Philip, M., & McIntyre, P. (2025). Patterns of measles seronegativity in health professional students at University of Otago. Oral presentation at Communicable Diseases and Immunisation Conference (CDIC), Australia.