Australian Government
Department of Health

ATAGI
Australian Technical Advisory Group on Immunisation

IFNAR1 Deficiency and Serious Adverse Events Following Immunisation

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Version 1

Summary

- Measles is an important vaccine preventable disease and, due to high vaccine coverage, is currently only seen in Australia in the setting of outbreaks and sporadic imported cases. The disease can be more severe in individuals that are immunocompromised.
- IFNAR1 deficiency is a rare inherited condition affecting some people in Australia of Western Polynesian heritage including Tongan, Samoan, and Niuean.[1]
- It is associated with severe illness and death from certain viral infections and also potentially from live-attenuated virus vaccines, mainly the measles, mumps, and rubella (MMR) vaccine.
- Currently, the diagnosis of IFNAR1 deficiency prior to vaccination is challenging.
- ATAGI recommends that all people in Australia, including people of Tongan, Samoan, and Niuean heritage, continue to receive the MMR vaccine given that illness from measles and mumps infections is more severe in unvaccinated individuals, including those with undiagnosed IFNAR1 deficiency. Ongoing work to assist in the early identification of individuals affected by this rare disorder is needed.

Overview

IFNAR1 deficiency is a newly described specific immune deficiency associated with severe adverse events and death following vaccination with some live-attenuated virus vaccines, including the measles, mumps, and rubella (MMR) vaccine, the yellow fever virus vaccine, and possibly the live varicella vaccine.[1] Although the condition is extremely rare worldwide, affecting very few people outside the Western Polynesian population, it appears more common in people who have two parents of Tongan, Samoan, or Niuean heritage. It is estimated to affect 1 in every 6450 people with parents of Samoan heritage.[1] At present, diagnosis prior to vaccination is difficult.

A recent study from New Zealand and Australia described 7 cases of children who were found to have this specific immune deficiency presenting for medical attention with a hyperinflammatory symptom complex of fever, rash, shock, and hepatosplenomegaly, or symptoms of encephalopathy within 1 week of MMR vaccination.[1] Although the role of MMR vaccine is not clear in all cases, 4 out of the 7 children in the study died and 3 had significant ongoing neurodevelopmental morbidity. An earlier report described complications following yellow fever virus vaccination in an adolescent with the condition.[2]

People known to have an IFNAR1 deficiency may have an increased risk of severe disease from certain viral infections, including measles, mumps, and SARS-CoV-2.[1] Advice on vaccination of children or adults who have been diagnosed with IFNAR1 or any other specific immune deficiency should be sought from their immunologist, noting that disease from wild-type measles and mumps is probably more severe than from the vaccine-strain viruses. People with IFNAR1 deficiency can safely receive the rotavirus vaccine and non-live vaccinations, including the influenza and COVID-19 vaccines.

Healthcare providers need to be aware that children of Western Polynesian heritage who present for medical attention and are very unwell in the 1-2 weeks following MMR vaccine may need further investigation by an immunologist to assess for an immune deficiency. Any suspected adverse event following immunisation

should be reported. Family members of individuals who have had a severe reaction to a live-attenuated virus vaccine, or are related to someone with known IFNAR1 deficiency, should be referred to an immunologist before consideration of the MMR vaccine. Children who have safely received a first dose of MMR vaccine (usually routinely administered at 1 year of age on the Australian National Immunisation Program), are highly unlikely to have IFNAR1 deficiency.[1]

While early diagnosis of IFNAR1 deficiency remains a challenge and the number of cases will be small in the Australian context, ATAGI believes the benefits of MMR vaccination continue to strongly outweigh the risks for all people in Australia, including those of Western Polynesian descent.

Recommendation

ATAGI recommends that all people in Australia, including people of Tongan, Samoan, and Niuean heritage, continue to receive the MMR vaccine given that illness from measles and mumps infections is more severe in unvaccinated individuals, including those with undiagnosed IFNAR1 deficiency. Ongoing work to assist in the early identification of individuals affected by this rare disorder is needed.

References

1. Bastard P, Hsiao KC, Zhang Q, et al. A loss-of-function *IFNAR1* allele in Polynesia underlies severe viral diseases in homozygotes. J Exp Med (2022) 219:e20220028. doi: 10.1084/jem.20220028. Epub 2022 Apr 20.

2. Hernandez N, Bucciol G, Moens L, et al. Inherited IFNAR1 deficiency in otherwise healthy patients with adverse reaction to measles and yellow fever live vaccines. J Exp Med (2019) 216:2057-2070.

Frequently Asked Questions (FAQs)

1. *What do I tell parents who may have concerns about IFNAR1 deficiency and the MMR vaccine?*

A paper has been published recently which reported on 7 cases of severe adverse events following MMR vaccine in NZ. To date, no similar cases have been reported in Australia.

You can reassure parents that the vaccine is still recommended for all children.

The illness from measles and mumps is more severe in unvaccinated individuals, including those with undiagnosed IFNAR1 deficiency. As such, given the rarity of IFNAR1 deficiency, the benefits of MMR vaccination continue to outweigh the risks for all people in Australia, including those of Western Polynesian descent.

Children who have safely received a first dose of MMR vaccine (usually routinely administered at 1-year of age on the Australian National Immunisation Program), are highly unlikely to have IFNAR1 deficiency and can proceed with the vaccines recommended on the National Immunisation Program.

2. *Can I still give the MMR vaccine to children with parents from Tonga, Samoa, and Niue?*

Yes, it is appropriate to still recommend the vaccine for these children. However, family members of individuals who have had a severe reaction to a live-attenuated viral vaccine, or are related to someone with a known immunodeficiency, including IFNAR1 deficiency, should be referred to an immunologist before consideration of the MMR or other live-attenuated vaccines.

3. *Do I need to consider the risk of other live-attenuated vaccines?*

The recently published paper on IFNAR1 deficiency highlighted the role of the MMR vaccine, with no cases presenting for healthcare following the oral Rotavirus vaccine. If there are any concerns of an underlying immunodeficiency, including IFNAR1 deficiency, then children should be referred to an immunologist before consideration of the varicella-zoster vaccine, the Bacillus Calmette–Guérin (BCG) vaccine, and travel vaccines such as the yellow fever virus and Japanese encephalitis virus vaccines.

4. *What do I need to look out for?*

The children in the study presented for medical attention within the 1-2 weeks following their MMR vaccine. They were very unwell at presentation and required hospitalisation with either a hyperinflammatory symptom complex of fever, rash, shock, and hepatosplenomegaly, or with encephalopathy. The presentations were very different to the more common and milder symptom complex of fever with or without rash seen in the 7-10 days following an MMR vaccine.

Healthcare providers need to be aware that children who are very unwell within the 1-2 weeks following MMR vaccine may need further investigations to assess for an immune deficiency. Referral to hospital or an immunologist is recommended. Any suspected adverse event following immunisation should be reported. For further information on reporting and managing adverse vaccination events see: www.health.gov.au/health-topics/immunisation/health-professionals/reporting-and-managing-adverse-vaccination-events