# The changing epidemiology of mumps in a high vaccination era

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The introduction of measles, mumps, and rubella (MMR) vaccine programmes has led to a dramatic reduction in all three infectious diseases globally. However, whereas measles and rubella remain under control wherever coverage is high, mumps outbreaks continue to flare up. Before universal vaccination, mumps was primarily a disease acquired during childhood and was characterised by fever and parotitis with potential complications including orchitis or oophoritis, encephalitis, meningitis, and hearing loss.[1] In countries with mumps immunisation programmes, the incidence of mumps has decreased from 100–1000 cases per 10 000 to less than one case per 100 000.[2] However, following implementation of MMR vaccination programmes the incidence of mumps has begun to increase in older adolescents and young adults, in which the disease might be more severe and complications more frequent.[3]

Recent outbreaks of mumps in the USA, Europe, and Australia as reported in the study by Darren Westphal and colleagues[4] have mostly occurred in older adolescents and young adults.[4-7] Westphal and colleagues[4] report a second protracted mumps outbreak in Western Australia despite high vaccine coverage between March, 2015, and December, 2016, with a peak notification rate in 15–19 year olds.[4] Of 893 cases notified, 798 (89%) were in Aboriginal people and 40 (4%) people were admitted to hospital. 371 (89%) of 419 people aged 1–19 years were fully vaccinated and 29 (7%) were partly vaccinated. In Australia a two-dose vaccination schedule is provided, previously administered at 12 months and 4 years of age, with a change in 2013 to the second dose being administered at 18 months of age.[2] Westphal and colleagues[4] report an outbreak of genotype G mumps disease in a highly vaccinated community of mainly Aboriginal people in northern Western Australia, where an outbreak of genotype J disease had occurred in 2007–08. This protracted second outbreak commenced in the same community, but involved different individuals and spread more widely.

There are several explanations for outbreaks occurring in highly vaccinated populations. Waning immunity is probably the most important contributing factor and is plausible because antibody responses to mumps vaccine in general are less long-lived than those induced by natural immunity.[8] By contrast with childhood immunisation, mumps infection is more efficient at inducing persistent polyclonal CD8 memory T cells. [9] In their meta-analysis, Lewnard and colleagues[10] found that although immunity following mumps vaccination persists an average of 27·4 years (95% CI 16·7–51·1 years), 25% of vaccinated individuals might lose protection within 7·9 years (4·7–14·7). Additionally, vaccine escape or mismatch between the vaccine and wild-type virus has been postulated to contribute to recent outbreaks, which have been due to genotypes G, H, and K, whereas the vaccine virus is either genotype A (Jeryl Lynn) or B (Urabe).[11] Genotype-specific antibodies are more efficient at inactivating the corresponding wild-type mumps genotypes.[11] The absence of boosting due to decreased natural exposure to the disease might also play a role.[12]

Circumstances that increase transmission, such as crowded households and increased contact through social behaviours, contribute to the spread of mumps virus; adolescents and young adults in particular are more likely to engage in behaviours which involve close contact. In the Australian cohort reported by Westphal and colleagues,[4] high population mobility as seen in many Indigenous populations was considered a factor involved in the outbreak. Aboriginal people often need to travel long distances in remote Australia to visit family members and attend funeral ceremonies, which are held over several days or weeks and involve the whole community as part of their culture and traditions.

The incidence of orchitis in the mumps outbreak reported by Westphal and colleagues[4] was lower than expected; this finding is consistent with vaccination protecting against severe disease and complications in highly vaccinated populations.[4,5]

A third MMR vaccine dose was used to successfully contain the outbreak and the authors suggest that a third dose might be warranted in high-risk populations. However, in a study assessing the immunogenicity of a third MMR vaccine dose, 12 months after vaccination antibody levels were similar to those before vaccination, despite initially increasing after the third dose.[13] A recommendation for early third-dose vaccination in an outbreak might be more feasible and cost-effective. Alternatively, a third dose administered to high-risk

groups later in life when disease is more likely to be severe might be warranted in highly vaccinated populations such as those in universities, although often vaccine uptake in young adults is low. Those who are unvaccinated because of contraindication or who are not vaccinated as children might be at increased risk of more severe disease and complications later in life.[14] In Australia and other countries which administer a second dose of mumps as a tetravalent vaccine at 18 months of age, continued surveillance of mumps disease is essential for early detection of disease outbreaks.

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# Mumps outbreaks in ethnic subpopulations: what can we learn?

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Mumps outbreaks are being reported with increasing frequency, particularly among teenagers and young adults.[1,2] Outbreaks in ethnic subpopulations are also increasing. In *The Lancet Infectious Diseases*, Virgie S Fields and colleagues[3] report a mumps outbreak in a highly vaccinated Marshallese community in Arkansas, USA. This mumps outbreak is the second largest in the USA since the two-dose measles, mumps, and rubella (MMR) vaccine was introduced in 1989.[2] High two-dose MMR coverage among cases (92% of patients aged 5–17 years) was not sufficient to prevent this outbreak. Other features associated with disease transmission were observed, including poverty, household overcrowding, high social connectivity, and mistrust of medical services. What can we learn from outbreaks in communities such as this one? In the era of vaccine-induced immunity to mumps, other strategies beyond two-dose MMR might be needed.

To our knowledge, only six studies have reported mumps outbreaks among moderately to highly vaccinated ethnic subpopulations. These include the study by Fields and colleagues[3] and reports on the 2009–10 outbreak among Chuukese and Pohnpeian residents in Guam,[4] the 2009–10 outbreak in Orthodox Jewish communities in New York (NY, USA),[5] the 2007–08 and 2015–16 outbreaks among Aboriginal Australians in Western Australia,[6,7] and the 2017–18 outbreak among Native Hawaiian and other Pacific Islanders in Alaska.[8] The commonality of all six outbreaks was that patients belonged to small subpopulations, without considerable transmission into the wider community; hence, household overcrowding or other intense exposure settings have been postulated to sustain transmission. Secondary vaccine failure (waning immunity) increases susceptibility to mumps.[2,9] However, waning immunity is not the only explanation for the outbreak in the Marshallese population in Arkansas because there was no apparent increase in patient numbers with time since two-dose