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## Measles in our time: the US experience

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Measles; measles vaccine; outbreak; philosphical exemptions

For a viral illness first described a thousand years ago, vaccine-preventable for 50 years, and eliminated from the USA in 2000, the interest associated with measles in 2015 is notable [1–4]. Most virologists only dream of a solution as successful as live-attenuated measles vaccine, with 97% two-dose efficacy and literally billions 'served.' Success can breed complacency, skepticism or even attack. All these reactions play a role in the current US experience with measles. The dynamics involved with recent US measles outbreaks may have more to do with cultural attitudes and consumer behavior than with  $R_0$  and airborne transmission.

From 4 January to 10 April 2015, 159 people were reported to have measles in the USA [1]. Seventy percent of cases are part of an outbreak associated with Disney amusement parks in Southern California. Eighteen states and the District of Columbia have identified measles cases so far this year, with multiple genotypes (B3, D4, D8, D9 and H1) detected. Based on available information, 45% of the reported cases occurred in people who were never vaccinated (68 of 155 US residents), while more than a third (60 or 38%) had unknown vaccination status. Of those who had not been vaccinated, 29 (43%) were unvaccinated because of personal, philosophical or parental beliefs, while 26 (35%) were too young to receive the vaccine. Cases with links back to the Disney parks occurred in seven states, Mexico and Canada. In 2015, smaller outbreaks unrelated to the amusement parks have involved a childcare center in Illinois, extended family in Washington State, and community exposures in Nevada.

In order to declare that measles was eliminated in the USA in 2000, authorities determined that indigenous circulation of the virus for more than 12 months had been interrupted [5]. Cases detected since 2000 have been directly or indirectly linked to importation of the virus from endemic areas, and transmission from such importations has not resulted in sustained chains of transmission. In the first decade of the elimination era in the USA, a median of 60 measles cases were reported annually (range: 37–220) and an average of 33 annual importations occurred. Outbreaks were relatively small (3–34 cases), but each still required

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extensive public health responses. Since 2011, about twice as many importations occurred most years (range: 21–80), with a median of 205 annual cases. Some larger outbreaks (58–383 cases) occurred, affecting a variety of religious congregations characterized by very low immunization rates [6,7]. Although the period from 2000 through 2014 was associated with substantial reductions in measles-related deaths around the world, particularly in Africa [8], Americans traveling abroad still could easily encounter the virus, especially during travel in Europe and Asia. When the virus is imported to the USA, clustering of underimmunized individuals provides fertile ground for extensive spread and represents a threat to sustaining elimination within the USA [9].

Importations to the USA can be evaluated based on travel history, molecular epidemiology (i.e., genotyping) or both. The frequency of importations from particular regions reflects the volume of travelers and state of measles immunization in particular destinations. The majority of measles importations occur after Americans travel abroad, rather than from international visitors to the USA. Importations from Latin America have virtually ceased since countries within the Pan American Health Organization Region first interrupted transmission in 2004. Recently, large measles outbreaks in France (2010–2011) and the Philippines (2013–2014) accounted for numerous importations. The California Disney-associated outbreak is caused by genotype B3, which has been circulating in 14 different countries within the past 6 months, and the source of the outbreak has not been determined.

Vaccinating one's children continues to be a social norm in the USA. Less than 1% of 19-35-month olds have received no vaccines, and 92% of toddlers have received at least one dose of MMR [10]. Two-dose coverage with MMR among the nation's kindergarten students is also high (median: 94.7%, range: 81.7% in Colorado to 99.7% in Mississippi) [11]. However, high MMR coverage at the national and state level can mask much lower coverage in specific communities, schools or within social networks [12]. Recent analysis of immunization patterns in California revealed geographic clusters where underimmunization with MMR and vaccine refusal were more common [9]). Analysis of measles cases in the past several years suggests a pattern – many of those who were not vaccinated had exempted due to personal beliefs, some had delayed receipt of the vaccine and an important portion were <12 months of age, i.e., too young to be vaccinated routinely [1,13–14]. Refusal or delay in vaccination may result from a variety of concerns, including parents' desire to reduce the number of shots a child receives on a particular visit, reluctance to accept vaccinations if mild illness is present, concern about risk of adverse events and belief that vaccine-preventable disease is not a risk to one's child. Although surveys of parents reveal relatively stable confidence in vaccines and vaccine safety, a persistent, sizable portion of the general population still believes that vaccines may cause autism, even though there have been numerous studies finding no such association, the original article proposing this link has been retracted and exhaustive reviews by the Institute of Medicine and others have found no association [15].

Infants are at particular risk of measles and its complications. MMR vaccination in the USA targets children at 12–15 months and 4–6 years of age for routine immunization. The presence of maternal antibody to measles in the first several months of life blunts the response to vaccination. Vaccination between 6 and 11 months can provide short-term

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protection, and is recommended for infants who are traveling internationally where measles is endemic, but two additional doses beginning at 12 months of age are still needed to assure long-term protection. Protection of infants and others who cannot themselves be vaccinated (e.g., persons with immunosuppressive conditions for whom live viral vaccines are contraindicated) depends on very high population immunity to measles. The introduction of measles virus into communities where unimmunized people cluster, as through a returning traveler, can lead to outbreaks among those susceptible. One outbreak in 2015 occurred at a child care center in Illinois, where nearly all of the unimmunized infants less than 1 year of age in the classroom developed measles. Thus far, high immunization rates in the USA have provided the herd immunity that has sustained elimination of measles.

One factor contributing to pockets of underimmunization is the clustering of children who have exempted from school requirements for MMR vaccine. An outbreak of measles in San Diego in 2008 revealed that some schools had more than 20% of children exempting from MMR vaccination [12]. Several studies have found that the higher the proportion of school children with exemptions, the higher the risk of disease and/or outbreaks due to measles or pertussis [16–18]. Other studies have linked policies where exemptions are easily obtained with higher proportions of children with exemptions, and some data suggest that increasing the rigor required for exemptions can lead to a reduction in people obtaining exemptions [19]. States vary in the approach for administrative implementation of exemption policies. State requirements are being reexamined by several legislatures in the wake of the 2015 Disney outbreak [20].

What then can be done to be sure that measles does not reestablish a foothold in the USA? Continued commitment from clinicians seeing young children is vital, as healthcare professionals hold the greatest influence on parents' vaccination decisions. Reinforcement of system checks (e.g., verifying vaccine history for child care, kindergarten and middle school entry) is also critical. Better use of Immunization Information Systems (IIS), especially to make sure that adults have documentation of vaccines received across the lifespan, can improve understanding of the evolving epidemiology of measles in the postelimination era. A national survey of serologic evidence of immunity demonstrated that more than 90% of adults have immunity against measles [21]. Continued efforts at global control of vaccine preventable diseases, including achieving regional targets for measles elimination, will reduce importation risk and ultimately achieve a world without unnecessary deaths from measles.

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