International Importations of Measles Virus into the United States During the Postelimination Era, 2001–2016

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Background. Although measles was declared eliminated from the United States in 2000, measles cases and outbreaks continue to occur, resulting from importations of the disease from countries where it remains endemic.

Methods. We describe the epidemiology of international importations of measles virus into the United States during the postelimination era.

Results. From 2001 to 2016, 553 imported measles cases were reported to the Centers for Disease Control and Prevention. A median of 28 importations occurred each year (range: 18–80). The median age of imported case-patients was 18 years (range: 3 months–75 years); 87% were unvaccinated or had an unknown vaccination status. US residents (as opposed to foreign visitors) accounted for 62% of imported measles cases. Overall, 62% of all imported case-patients reported travel to countries in the Western Pacific and European Regions of the World Health Organization during their exposure periods. The number of measles importations from specific countries was related to the incidence of measles in and the volume of travel to and from the source country.

Conclusions. Our findings emphasize the importance of measles vaccination of US residents aged ≥6 months before international travel according to the Advisory Committee on Immunization Practices recommendations and supporting global measles elimination efforts.

Keywords. measles; measles elimination; international importation.
METHODS

Measles cases are categorized according to standard case definitions published by the Council of State and Territorial Epidemiologists [7]. All confirmed cases are reported to the Centers for Disease Control and Prevention through the National Notifiable Diseases Surveillance System and to the National Center for Immunization and Respiratory Diseases by telephone or e-mail [8]. Cases are classified as international importations if the case-patient reported international travel during at least some of the exposure period (7–21 days before rash onset), rash onset occurred within 21 days of entering the United States, and there were no known exposures to measles within the United States. All other cases are classified as US-acquired [8].

We analyzed the age, gender, clinical characteristics, residence and importation status, reporting US county and state, and the source country of internationally imported measles case-patients between 2001 and 2016. The residence status of imported measles case-patients was categorized as either foreign visitor (ie, international tourists and students, new international adoptees, recent immigrants, and cruise ship employees) or US resident, because ACIP vaccination recommendations only apply to US residents. Imported measles case-patients were considered underimmunized if they were US residents and were not vaccinated according to ACIP recommendations for international travelers (ie, documented receipt of 1 dose of MMR for infants aged 6–11 months and 2 doses of MMR for persons aged ≥12 months). Imported cases were considered preventable if they occurred in US residents aged ≥6 months who lacked presumptive evidence of immunity to measles (ie, laboratory evidence of immunity, laboratory confirmation of disease, age- and travel-appropriate vaccination, or birth before 1957). Imported cases were considered nonpreventable if they occurred in US residents aged <6 months or those aged ≥6 months who had presumptive evidence of immunity [2].

We compared demographic and clinical characteristics between internationally imported and US-acquired measles case-patients; we used Wilcoxon tests to assess differences in continuous variables and Mantel-Haenszel $\chi^2$ tests to assess differences in categorical variables. We evaluated changes in the proportion of importations that occurred in US residents compared with foreign visitors over the study years, using the Cochran-Armitage trend test. We calculated country- and region-specific rates of measles importations (per million travelers) by dividing the number of reported importations from each country and region each year, as reported by the United States Department of Commerce National Travel and Tourism Office [9–12]. When 2016 travel statistics were not available, 2015 data were used as the denominator. We calculated the reported annual median measles incidence (per million population) in source countries and regions by dividing the number of measles cases reported to WHO from those countries and regions [13] by the total population of each source country or region [14]. Data were analyzed in SAS 9.4 (SAS Institute Inc., Cary, NC).

RESULTS

During 2001–2016, 2098 confirmed measles cases were reported in the United States. Overall, 553 (26%) cases were internationally imported, and 1545 (74%) were US-acquired (Table 1). Half of all imported case-patients were male, and the median age of imported case-patients was 18 years (range: 3 months–75 years). Overall, 483 (87%) imported case-patients were unvaccinated or had an unknown vaccination status. The most commonly reported complications among imported

| Characteristic | Internationally Imported Cases | US-Acquired Cases | PValue |
|----------------|--------------------------------|------------------|--------|
| Male sex       | 277/553 (51)                  | 833/1538 (54)    | .18    |
| Age, y         | 18 (0–75)                     | 15 (0–89)        | .46    |
| Age group      |                                |                  |        |
| 0–5 mo         | 4/553 (1)                     | 32/1543 (2)      | .09    |
| 6–11 mo        | 81/553 (15)                   | 119/1543 (8)     |        |
| 12–15 mo       | 62/553 (11)                   | 71/1543 (5)      |        |
| 16 mo–4 y      | 46/553 (8)                    | 192/1543 (12)    |        |
| 5–17 y         | 79/553 (14)                   | 445/1543 (29)    |        |
| 18–29 y        | 133/553 (24)                  | 307/1543 (20)    |        |
| 30–49 y        | 119/553 (22)                  | 314/1543 (20)    |        |
| ≥50 y          | 29/553 (5)                    | 63/1543 (4)      |        |
| Birth before 1957 | 20/553 (4)                  | 26/1543 (2)      | .01    |
| Vaccination status |                                |                  |        |
| Unvaccinated   | 343 (62)                      | 1069 (69)        | .03    |
| Unknown        | 140 (25)                      | 289 (19)         |        |
| Vaccinated     | 70 (13)                       | 187 (12)         |        |
| Complications |                                |                  |        |
| Diarrhea, dehydration, and/or vomiting | 61 (11) | 90 (6) | <.0001 |
| Pneumonia      | 35 (6)                        | 39 (3)           | <.0001 |
| Otitis         | 19 (3)                        | 38 (2)           | .23    |
| Thrombocytopenia | 9 (2)                         | 12 (1)           | .13    |
| Encephalitis   | 3 (1)                         | 3 (0)            | .19    |
| Outcomes       |                                |                  |        |
| Hospitalized   | 207 (37)                      | 191 (12)         | <.0001 |
| Death          | 1 (0)                         | 2 (0)            | 1.00   |

aData are presented as median (range), No. (%), or no./No. (%).

bMissing values were excluded for bivariate analyses, and new totals are provided for each variable.

Differences in continuous variables were assessed using the Wilcoxon rank-sum test, and differences in categorical variables were assessed using the Mantel-Haenszel $\chi^2$ test; Fisher exact test was used for cell counts <15.

cDifferences in continuous variables were assessed using the Wilcoxon rank-sum test, and differences in categorical variables were assessed using the Mantel-Haenszel $\chi^2$ test; Fisher exact test was used for cell counts <15.

Included 1 US-acquired case-patient with pancytopenia.

fIncludes 1 US-acquired case-patient with pancytopenia.
case-patients were diarrhea, dehydration, and/or vomiting (11%), and pneumonia (6%); 37% were hospitalized (Table 1).

When compared with US-acquired case-patients, imported case-patients were more likely to be born before 1957; have an unknown vaccination status; have measles complicated by diarrhea, dehydration, and/or vomiting, or by pneumonia; and to be hospitalized (Table 1). One death was reported in an imported case-patient, and 2 deaths were reported in US-acquired case-patients during the study period.

The median annual number of importations was 28 (range: 18–80; Figure 1). Overall, 344 (62%) of 553 imported case-patients were US residents; 209 (38%) were foreign visitors. The annual proportion of imported case-patients that were US residents ranged between 37% in 2001 and 89% in 2014 and increased from 37% in 2001 to 67% in 2016 ($P < .0001$).

Imported measles case-patients who were US residents were older than those who were foreign visitors ($P = .04$; Table 2). The majority of US residents (84%) and foreign visitors (92%) were unvaccinated or had an unknown vaccination status; more foreign visitors had an unknown vaccination status. Among the 344 imported cases that occurred among US residents, 307 (89%) were considered preventable by vaccination; among 37 nonpreventable imported US resident case-patients, 1 was too young to be vaccinated, 16 were born before 1957, and 20 had received age- and travel-appropriate vaccination.

Imported case-patients reported travel to 76 different countries during their exposure period; 63% reported travel to countries in the Western Pacific and European WHO Regions (Table 3). India, China, and the Philippines were the top 3 source countries, both in terms of the number of importations and the rate of importations per million travelers (Table 4). The number of importations was closely related to the incidence of measles in, and the number of travelers to and from, the corresponding source country; for example, the number of importations was high from India and the Philippines primarily due to high measles incidence in those countries, and from the United Kingdom and Japan due to a high number of travelers to and from those countries. When assessing importation rates by world region, Africa had the lowest number of travelers to and from the United States during 2001–2016 but the highest median measles incidence and rate of importations per million travelers (Supplementary Table 1).

Importations were reported in 40 states, Washington DC, and New York City, and tended to cluster primarily in the West, Midwest, and Northeast regions of the country; 6 states (California, New York, Washington, Massachusetts, Florida, and Hawaii) accounted for over half (305 cases, 55%) of all imported cases (Figure 2). Over half of all importations (334 cases, 60%) occurred during the months January through May (Figure 3).

DISCUSSION

Over 25% of all reported measles cases during the postelimination era in the United States were internationally imported. This represents an increase in the proportion of reported cases that were internationally imported compared with the preelimination era (before 2000); 1.6% of cases from 1984–1992 were imported [15] and 17% of cases from 1993–2001 were imported [15]. This is not unanticipated; when there was sustained measles transmission in the United States, imported cases were expected to be a smaller fraction of all the cases [15]. The finding that, compared to the preelimination era, a larger fraction of all reported measles cases in the United States are internationally imported and fewer are US-acquired cases reflecting...
transmission after measles introductions, indicates improved measles control and is supportive of sustained interruption of endemic transmission of measles virus in the United States.

Despite similar numbers of US citizens traveling internationally and of nonresident arrivals to the United States (approximately 70–80 million travelers annually in recent years [9–12, 16]), 62% of imported measles case-patients were US residents; US residents returning from abroad accounted for an increasing proportion of importations during the study period. In contrast, the proportion of imported case-patients who were US residents decreased from 70% in 1986–1994 [17] to 37% in 1993–2001 [15], a finding attributed to improvements in measles vaccine coverage and measles immunity in the US population. Because the majority of US-imported case-patients were underimmunized and thus preventable, our findings emphasize the importance of age-appropriate vaccination of US residents before international travel [2]. Similarly, continued support of global efforts to ensure age-appropriate vaccination of all children, as recommended by WHO and local ministries of health, are needed [18]. While few complications were reported during our study period, internationally imported case-patients were more likely to be hospitalized than US-acquired case-patients. The reason for this difference is unclear, although it might be related to consideration by physicians of other more serious travel-related illnesses (eg, malaria, typhoid fever, dengue), or to less health seeking among travelers with milder measles presentations. Because hospitalized cases might be prone to transmit measles virus to persons at risk of severe disease (eg, immunocompromised persons) and health care workers, this finding further emphasizes the importance of improving vaccination coverage of international travelers to and from the United States.

Proof of immunity for entry of foreign visitors into the United States or for US travelers before departure is not required, and such a requirement would be challenging and difficult to implement [15, 17, 19]. Notably, a recent survey of adult US travelers presenting for a pretravel visit found that although 16% were eligible to receive MMR vaccine, only about half of these were vaccinated, highlighting missed opportunities for vaccination during pretravel consultations [20]. Thus, it is important to prioritize strategies such as improving travelers’ knowledge of, and educating health care providers about, the risk of measles exposure during international travel and about those conditions that constitute presumptive evidence of immunity in order to limit the number of measles importations into the United States.

Historically, the Americas, and in particular Mexico, had been the main source of measles importations to the United States, but this has not been the case since 1991, following improvements in measles control in the Western Hemisphere [17, 21]. The Western Pacific and European WHO Regions have been the source of over half of all importations into the United States since 1993 [15], a trend that has continued postelimination. As noted above, the number of measles importations into the United States from a particular country reflects both the measles incidence within the source country and the amount of travel between the United States and that country [15]. For example, more than 26 000 cases were reported in 36 of 53 European Region countries in 2011; a national outbreak in France accounted for approximately half of these cases [22]. In the same year, the United States experienced the highest

Table 2. Age and Vaccination Status of Internationally Imported Measles Case-Patients, by Residence Status—United States, 2001–2016

| Age, ya | Unvaccinated | Unknown | Vaccinateda | Total |
|---------|--------------|---------|-------------|-------|
| 0–5 mo  | 4 (0–68)     | 0 (0)   | 0 (0)       | 1 (0) |
| 6–11 mo | 50 (23)c     | 0 (0)   | 1 (2)d      | 51 (15) |
| 12–15 mo| 42 (19)      | 0 (0)   | 0 (0)       | 42 (12) |
| 16 mo–4 y| 22 (10)     | 0 (0)   | 6 (11)      | 28 (8)  |
| 5–17 y  | 30 (14)      | 1 (1)   | 9 (17)d     | 40 (12) |
| 18–29 y | 47 (21)      | 13 (18) | 15 (28)d    | 75 (22) |
| 30–49 y | 18 (8)       | 42 (59)e| 23 (43)d    | 83 (24) |
| ≥50 y   | 9 (4)e       | 15 (21)e| 0 (0)       | 24 (7)  |

*Data are presented as median (range) or No. (%).

**Vaccinated was defined as having received ≥1 dose of a measles-containing vaccine. Among 54 vaccinated US residents, 35 received 1 dose and 19 received 2 or more doses. Among 16 vaccinated foreign visitors, 11 received 1 dose and 5 received 2 or more doses.

*These case-patients were eligible for vaccination before international travel according to Advisory Committee on Immunization Practices (ACIP) recommendations.

*Of the 54 vaccinated US resident case-patients, 20 were appropriately vaccinated for age according to ACIP recommendations for international travelers and were considered to be nonpreventable.

*Sixteen of 66 cases occurred in persons born before 1957 and assumed to have presumptive evidence of measles immunity and thus were considered to be nonpreventable.

*Of 344 case-patients, 307 were underimmunized with no presumptive evidence of immunity, and were considered to be preventable.
Table 3. Sources of Internationally Imported Measles Cases, by World Health Organization (WHO) Regiona—United States, 2001–2016

| Year | Total Importations | WPR | EUR | SEAR | EMR | AFR | AMR |
|------|--------------------|-----|-----|------|-----|-----|-----|
| 2001 | 54                 | 43  | 7   | 0    | 3   | 1   | 0   |
| 2002 | 18                 | 6   | 3   | 3    | 3   | 2   | 0   |
| 2003 | 24                 | 12  | 6   | 4    | 1   | 1   | 0   |
| 2004 | 27                 | 15  | 2   | 8    | 1   | 1   | 0   |
| 2005 | 24                 | 7   | 7   | 4    | 2   | 3   |     |
| 2006 | 31                 | 8   | 10  | 7    | 3   | 3   | 0   |
| 2007 | 29                 | 11  | 7   | 10   | 0   | 1   | 0   |
| 2008 | 25                 | 3   | 17  | 3    | 1   | 0   | 0   |
| 2009 | 21                 | 5   | 9   | 6    | 0   | 1   | 0   |
| 2010 | 39                 | 3   | 16  | 6    | 2   | 10  | 2   |
| 2011 | 80                 | 15  | 33  | 20   | 3   | 4   | 3   |
| 2012 | 81                 | 1   | 2   | 5    | 5   | 6   | 5   |
| 2013 | 51                 | 9   | 23  | 8    | 8   | 2   | 1   |
| 2014 | 63                 | 37  | 6   | 15   | 2   | 1   | 3   |
| 2015 | 28                 | 8   | 8   | 8    | 5   | 0   | 0   |
| 2016 | 18                 | 10  | 1   | 6    | 7   | 3   | 2   |
| Total| 553                | 178 (32) | 165 (30) | 117 (21) | 45 (8) | 36 (7) | 12 (2) |

WHO region designations: WPR, Western Pacific Region; EUR, European Region; SEAR, South-East Asia Region; EMR, Eastern Mediterranean Region; AFR, African Region; AMR, Region of the Americas.

a N = 548. Four imported case-patients with travel to both WPR and SEAR and 1 case-patient with travel to both EMR and SEAR were counted twice; 5 case-patients were missing travel history. Data are presented as N (%).

number of international importations of the postelimination era (80 case-patients), with 33 of these case-patients reporting travel to the European Region, and 16 specifically reporting travel to France (Table 3, Supplementary Table 2). Similarly, the Philippines was a major source of importations in 2014 following a measles resurgence in that country [23]; an outbreak of 21,403 confirmed cases of measles was reported in the Philippines by WHO in 2014 [24], and led to 27 of the 63 importations of measles into the United States that year. On the other hand, some countries (eg, Japan and the United Kingdom) have been among the top source countries for measles importations into the United States despite relatively lower measles disease burden, because of the amount of travel to and from these countries [25].

The geographic distribution of internationally imported measles cases shows that most importations occur near major ports of entry into the United States. Internationally imported cases were also more likely to occur during the first 5 months of the year, with an additional increase in importations during the summer months. These peaks are likely caused by the seasonality of measles in endemic countries (ie, measles incidence increases during late winter and early spring in temperate climates, and after the rainy season in tropical climates [26]), and the timing of travel between the United States and the top source countries (ie, increased travel during US holidays and summer vacations; Supplementary Figure 1).

Our study was subject to several limitations. We were unable to calculate measles importation rates and measles incidence for all 76 source countries, as US travel data and measles case counts were not available for all countries. Differences in the vaccination status of internationally imported and US-acquired measles case-patients reflected importations occurring among foreign visitors who had an unknown vaccination status, highlighting the challenge of verifying immunity among foreign visitors. The “source country” might not have been the actual location where measles was acquired, because travelers might have visited several countries or might have acquired measles during transit (eg, in flight, in airports during layovers [27]). In these situations, sequence analysis of the measles virus might be helpful to identify a likely source country, distinguish between separate importations [28], and link or unlink contemporaneous cases [29]. Because of differences in case definitions of imported and US-acquired measles cases through the years, possible changes in surveillance sensitivity over time, and small number of importations and year-to-year variability, comparisons with previously published data and trends should be interpreted cautiously. Some underreporting of imported cases is expected, particularly of foreign visitors due to transitory stays or hesitance to seek medical care [15], although sustained surveillance adequacy has been documented [30].

Measles virus will continue to be imported into the United States as long as measles remains endemic around the world. While the global burden of measles has decreased significantly since the introduction of measles-containing vaccines, approximately 6,976,800 cases and 89,780 deaths were reported globally in 2016 [4], and international travel has increased in recent years [25]. Our findings emphasize the importance of maintaining a high level of measles immunity in the US population, measles vaccination of susceptible individuals aged 26 months before international travel according to ACIP recommendations, and supporting global measles elimination efforts.

Supplementary Data

Supplementary materials are available at The Journal of Infectious Diseases online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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Table 4. Measles Importations Per Million Travellers to and from the United States and Top Source Countries, 2001–2016

| Countries       | Number of Importations | Number of Travelers<sup>a</sup> | Rate per Million Travelers | Median Measles Incidence per Million Population (Range)<sup>b</sup> |
|-----------------|------------------------|---------------------------------|-----------------------------|---------------------------------------------------------------|
| India           | 81                     | 23,501,383                      | 3.45                        | 33.48 (2.62–55.24)                                           |
| China           | 59                     | 46,856,486                      | 1.26                        | 42.25 (4.55–98.67)                                           |
| Philippines     | 51                     | 10,329,663                      | 4.94                        | 22.79 (0.10–587.88)                                          |
| Japan           | 34                     | 75,364,533                      | 0.45                        | 3.85 (0.28–265.31)                                           |
| United Kingdom  | 33                     | 114,821,404                     | 0.29                        | 8.11 (1.23–32.84)                                            |
| Italy           | 27                     | 41,831,046                      | 0.65                        | 6.93 (2.33–191.61)                                           |
| Pakistan        | 26                     | NA                              | NA                          | 25.26 (2.04–48.64)                                           |
| France          | 25                     | 53,055,372                      | 0.47                        | 4.12 (0.57–228.78)                                           |
| Germany         | 21                     | 54,119,644                      | 0.39                        | 9.49 (1.47–73.15)                                            |
| Indonesia       | 15                     | NA                              | NA                          | 68.28 (1783–130.45)                                          |
| Thailand        | 15                     | NA                              | NA                          | 58.81 (2.24–160.99)                                          |

Top 10 source countries by number of importations

Source country was missing for 7 imported case-patients; case-patients with 2 travel destinations were counted twice.

Abbreviation: NA, data not available.

<sup>a</sup>Total number of inbound and outbound travelers from 2001–2016, according to the United States Department of Commerce [9–12]. When 2016 travel statistics were not available, 2015 data were used as the denominator. Complete travel data were unavailable for 51 of 76 source countries: Afghanistan, American Samoa, Armenia, Azerbaijan, Bangladesh, Belgium, Bulgaria, Cambodia, Cameroon, Cape Verde, Chile, Djibouti, Egypt, Ethiopia, Federated States of Micronesia, Ghana, Greece, Haiti, Hungary, Indonesia, Iran, Jordan, Kenya, Kuwait, Kyrgyzstan, Laos, Lebanon, Macedonia, Malawi, Malaysia, Marshall Islands, Mongolia, Morocco, Nigeria, Northern Mariana Islands, Pakistan, Panama, Qatar, Republic of Georgia, Romania, Saudi Arabia, Somalia, Sri Lanka, Sudan, Thailand, United Arab Emirates, Uganda, Ukraine, Vietnam, Yemen, and Zambia.

<sup>b</sup>Measles case counts were unavailable for Japan in 2005 and 2007; Italy in 2001, 2013, 2014, and 2016; France in 2001, 2003, and 2012; Thailand in 2014; Poland in 2008, 2011, 2014, and 2015; and Switzerland in 2002 and 2006. Case counts were obtained from WHO [13] and population data were obtained from the World Bank [14].

Figure 2. Geographic distribution of internationally imported measles case-patients by reporting state and county—United States, 2001–2016. The smallest dots represent 1 importation, and the largest dot represents 33 importations (N = 541; county data were unavailable for 12 case-patients).
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