Measles outbreak in the Republic of the Marshall Islands, 2003

Terri B Hyde,1,2* Gustavo H Dayan,1 Justina R Langidrik,3 Robin Nandy,4,5 Russell Edwards,2 Kennar Briand,3 Mailynn Konelios,3 Mona Marin,1,5 Huong Q Nguyen,1 Anthony P Khalifah,3 Michael J O’Leary,6 Nobia J Williams,2 William J Bellini,6 Daoling Bi,1 Cedric J Brown,1 Jane F Seward1 and Mark J Papania1

Accepted 29 September 2005

Background Measles is a highly contagious viral infection. Measles transmission can be prevented through high population immunity (≥95%) achieved by measles vaccination. In the Republic of the Marshall Islands (RMI), no measles cases were reported during 1989–2002; however, a large measles outbreak occurred in 2003. Reported 1-dose measles vaccine coverage among children aged 12–23 months varied widely (52–94%) between 1990 and 2000.

Methods RMI is a Pacific island nation (1999 population: 50 840). A measles case was defined as fever, rash, and cough, or coryza, or conjunctivitis, in an RMI resident between July 13 and November 7, 2003. A vaccination campaign was used for outbreak control.

Results Of the 826 reported measles cases, 766 (92%) occurred in the capital (Majuro). There were 186 (23%) cases in infants aged <1 year and 309 (37%) of cases in persons aged ≥15 years. The attack rate was highest among infants (Majuro atoll: 213 cases/1000 infants). Among cases aged 1–14 years, 281 (59%) reported no measles vaccination before July 2003. There were 100 hospitalizations and 3 deaths. The measles H1 genotype was identified. The vaccination campaign resulted in 93% coverage among persons aged 6 months to 40 years.

Interpretation Populations without endemic measles transmission can accumulate substantial susceptibility and be at risk for large outbreaks when measles virus is imported. ‘Islands’ of measles susceptibility may develop in infants, adults, and any groups with low vaccine coverage. To prevent outbreaks, high population immunity must be sustained by maintaining and documenting high vaccine coverage.

Keywords Measles, measles vaccine, MMR, vaccination campaign

Introduction Measles, a highly contagious acute viral illness, can be associated with complications such as diarrhoea, pneumonia, encephalitis, and death.1 Despite an effective vaccine, measles is the most frequent cause of vaccine-preventable childhood morbidity and mortality, particularly in developing countries.2 In 2000, ~39 million cases and 777 000 deaths due to measles occurred worldwide.3 Measles transmission patterns in island populations have provided important information concerning measles epidemiology. Endemic measles transmission requires populations >250 000 people.4,5 Island communities with smaller populations will not sustain endemic transmission and, owing to relative isolation, may not regularly be exposed to measles virus importation. Ongoing absence of measles transmission results
in lower levels of disease-acquired measles immunity compared with populations with endemic measles. Before vaccine availability, measles virus introduction into such communities often resulted in intense, rapidly spreading outbreaks involving all age groups born since the previous outbreak.

In the Republic of the Marshall Islands (RMI), measles epidemics occurred in 1968, 1978, and 1988 (CDC unpublished data) (Figure 1). Measles, mumps, and rubella (MMR) vaccine has been used since the early 1970s and was introduced into the routine childhood vaccination programme in 1982 (one dose administered at 9 months). In 1998, a 2-dose MMR vaccine schedule was implemented (administered at 12 and 13 months). During 1994–2002, three supplemental measles immunization activities were conducted: a campaign in response to a measles outbreak in the nearby state of Chuuk (Federated States of Micronesia) in 1994, a catch-up campaign targeting children aged 1–14 years in 1998, and a follow-up campaign targeting children aged 1–4 years in 2002. RMI reported no measles cases during 1989–2002. RMI national routine 1-dose MMR vaccination coverage reported to the World Health Organization (WHO) was 52% in 1990, 57% in 1995, 94% in 2000, and 80% in 2002 (Figure 2). Cluster surveys among children aged 2 years in 1998 and 2001 showed 93 and 80% vaccination coverage rates, respectively.

In July–November 2003, a measles outbreak occurred in RMI. We investigated the outbreak to describe its epidemiology, determine its cause, guide outbreak control efforts, and provide strategies to prevent future outbreaks.

Methods

Setting

RMI, a parliamentary democracy in free association with the US, consists of 29 coral atolls and five islands with an area of

---

Figure 1 Timeline of the measles vaccination programme, supplementary measles immunization activities, and history of measles outbreaks in the Republic of the Marshall Islands

Figure 2 Routine measles containing vaccine coverage among 12–23 month olds, Reported to WHO/Unicef, Republic of the Marshall Islands. Solid bars represent one dose measles vaccination coverage. Hatched bars represent second dose measles vaccination coverage.
~70 square miles widely scattered across the central Pacific Ocean. The total population in 1999 was 50,840. Two-thirds of the population live in two areas: 25,097 on Majuro atoll (6692 persons/square mile) and 11,556 on Ebeye Island (96,300 persons/square mile).11

Outbreak: case definition and data collection

A measles case was defined as reported fever, generalized rash, and at least one of three symptoms: cough, coryza, or conjunctivitis,12 occurring in an RMI resident between July 13 and November 7, 2003. Fever was based primarily on parental/patient report and was not commonly measured with thermometer. A laboratory-confirmed case was defined as a patient with serologic or virologic evidence of acute measles infection.

Cases were reported to the public health department daily from public and private medical staff in Majuro and Ebeye, and twice weekly via radio from all other islands. In Majuro, emergency room, outpatient, and hospitalization logs were reviewed daily for additional cases. The Ministry of Health coordinated radio and newspaper announcements to raise awareness of the outbreak. Community meetings were held at all embassies. Ill persons were asked to report to their local health clinic. Hospitals and health clinics updated staff at regular meetings.

All persons with a febrile rash illness were evaluated for measles. Demographic characteristics, vaccination history, clinical information, and information on complications, hospitalizations, and deaths were collected. Complications were self-reported by measles cases or parents/guardians and obtained from medical records. Vaccination history was obtained from parental/patient recall, personal and medical records, and immunization logs maintained by the local health department. Serum was collected from 197 patients for measles specific IgM and IgG and oropharyngeal swabs were collected for measles virus testing by reverse transcriptase-polymerase chain reaction (RT-PCR) and virus culture.13 All laboratory testing was performed at the Centers for Disease Control and Prevention in Atlanta, GA.

Outbreak: case management

Early in the outbreak, a separate evaluation area for suspect measles cases was established outside the Majuro hospital outpatient clinic and a measles ward was established to prevent nosocomial spread. All cases received vitamin A in age-appropriate doses, and were hospitalized for treatment of complications as medically indicated.

Outbreak control: limits on transportation, school closure and vaccination

Outbreak control strategies evolved as information became available regarding disease epidemiology and population vaccination coverage estimated from annual MMR coverage reported to WHO. In July and early August, the priority was to prevent measles transmission from spreading outside of Majuro, particularly to the Outer Islands (outside Majuro and Ebeye), which had limited public health infrastructure and were considered to have lower population immunity. Domestic travel was interrupted temporarily and all travellers (both domestic and international) leaving Majuro and Ebeye were required to show proof of measles vaccination before departure. Initial vaccine supply was provided from emergency loans from nearby states and territories. In mid-to-late August, outbreak control prioritized school-aged children. All students were required to show proof of measles vaccination for school entry.

From August through October, a mass vaccination campaign was conducted using vaccine provided from the US Vaccine Stockpile. Infants aged 6–11 months were vaccinated with MMR. Persons aged 12 months to 40 years were vaccinated with MMR unless they had written evidence of two MMR doses. Dates of previous routine and campaign MMR vaccinations were recorded in campaign logs and used to calculate vaccine coverage. A variety of campaign strategies were used, including fixed posts and door-to-door campaigns with revisits if needed to assure vaccination of all residents. Very late in the outbreak, immunoglobulin (IMIG) became available for contacts of cases with contraindications to vaccination including infants aged <6 months, pregnant women, and immunocompromised persons.

Data analysis

Data from case investigations and vaccination campaign were entered into Microsoft Excel and converted to SAS version 8 (SAS Institute Inc., Cary, NC) for analysis. Population estimates obtained from the 1999 census were adjusted for 1.5% population growth11 per year and used for calculating measles incidence and vaccination coverage.

Results

Outbreak: descriptive epidemiology

The first five reported measles cases, associated with an international church gathering in Majuro, had rash onset between July 13 and July 20, 2003. Three were housed in the same apartment complex. As the outbreak spread across Majuro, the number of cases reporting rash onset peaked approximately every 2 weeks (Figure 3). The first laboratory-confirmed case occurred on July 21 and the last occurred on October 31. The last reported case occurred on November 7, 2003.

During July 13 to November 7, 2003, 1122 rash illnesses were reported. Case investigations were completed for 1082 (96%) patients: 826 (77%) were classified as measles cases with 77 laboratory confirmed cases. Most of the cases were in Majuro (768, 92%). The remaining 58 cases were reported from Ebeye (28) and eight of the Outer Islands (30). Measles virus, genotype H1, was isolated in cell culture, and additional specimens were RT–PCR positive for measles genotype H1. No other measles genotypes were isolated.

Of the 821 reported cases with available age data, the median age was 10 years (range 2 weeks to 43 years). Most cases (76%) occurred in persons aged <20 years (Table 1), 23% were among infants aged <12 months and 35% were among persons aged 5–19 years. The highest age-specific incidence occurred among infants aged 6–11 months (RMI: 128 cases per 1000 infants; Majuro: 251 cases per 1000 infants) followed by infants aged 6 months, pregnant women, and immunocompromised persons.

Measles cases were reported among 425 males (52%) and 396 females (48%). The median number of persons living in households of measles cases was 11 (range, 3–29). Complications
were reported in 125 (15%) cases, with diarrhoea or acute gastroenteritis (8.7%) as the most common complication, followed by pneumonia (7.5%), dehydration (1%), and otitis media (0.5%). Hospitalization occurred in 100 (12%). The median age of hospitalized patients was 3 years (range 2 weeks to 39 years) and the median hospital stay was 4 days (range 1–9 days). Reported complications and hospitalizations were highest in pre-school aged children and adults (Table 1). Three persons with measles died (CFR: 4 deaths/1000 cases); a 39-year-old woman with shock and gastrointestinal bleeding, a 27-year-old woman with pneumonia, and a 15-month-old girl with pneumonia complicated by malnutrition and dehydration. No autopsies were performed.

Prior to the outbreak, 5 (2%) of the 186 cases aged <1 year were vaccinated against measles. Of the 635 measles cases aged ≥1 year, 475 (75%) had available vaccination status and 281 reported no MMR vaccine history prior to the outbreak (Table 2). Among cases 1–4 years whose vaccination status was known, 61% were unvaccinated (20% had received one MMR dose and 18% two MMR doses) compared with 30% unvaccinated among school-aged children 5–14 years 25% (1 MMR) and 45% (2 MMR). Of the 475 measles cases aged ≥1 year with
available vaccination status, 202 (42%) cases had received an MMR dose during the vaccination campaign: 93 (46%) within 6 days before rash and 83 (41%) 7–18 days before rash.

Only 48 (6%) cases reported recent travel outside of Majuro or Ebeye. Measles cases were imported into other countries from RMI; Guam (7 cases: 5 direct imports, 2 local spread), Palau (1 direct import), Hawaii (12 cases: 3 direct imports, 9 local spread), and Canada (1 direct import).

Outbreak control: limits on transportation, school closure and vaccination

Domestic air and sea travel was stopped from August 5 to August 15 while vaccination teams were dispatched to the Outer Islands. The start of the school year was postponed from August 17 to August 25. Vaccination posts were established at all schools for vaccination of school-aged children, and vaccination cards were required for school entry.

Initially, the campaign target population was age 6 months to 15 years based on the epidemiology of the initial cases. As the outbreak epidemiology changed with cases occurring in older age groups, the campaign target population was expanded to include all persons up to age 40 years.

Upon completion of the MMR vaccination campaign in November, 2003: 41,424 persons had been assessed (Table 3).

Of these 7,916 persons had previous documentation of complete measles vaccination and campaign doses of MMR were given to 33,508 persons representing 93% coverage nationally with at least one dose in the target population, and 95% coverage among those aged 6 months to 20 years. One dose MMR coverage in Majuro reached 90% on September 3 with 18,406 doses delivered (Figure 3). IMIG was administered to three pregnant women and three infants aged ≤6 months.

Discussion

With >800 cases, 100 hospitalizations, and 3 deaths, this was the largest reported measles outbreak to occur in a US associated Pacific island population in a decade and served as a reminder of the infectiousness and severity of measles. The outbreak disrupted routine healthcare services and impacted school, work, travel, and tourism. Rapid implementation of control and prevention efforts in the Outer Islands and Ebeye confined the outbreak primarily to Majuro, the most populous atoll. Spread to other countries was probably limited by the unprecedented requirement that departing international passengers show evidence of measles vaccination and by high population immunity in areas where importations occurred. Although the

### Table 2

<table>
<thead>
<tr>
<th>Age group</th>
<th>Unknown vaccination status</th>
<th>Known vaccination status</th>
<th>Before onset of measles outbreak</th>
<th>Vaccinated during vaccination campaign</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (% age group)</td>
<td>n (% of known)</td>
<td>0 MMR</td>
<td>1 MMR</td>
</tr>
<tr>
<td>&lt;6 months</td>
<td>15 (18)</td>
<td>67 (82)</td>
<td>67 (100)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>6–11 months</td>
<td>18 (17)</td>
<td>86 (83)</td>
<td>81 (94)</td>
<td>4 (5)</td>
</tr>
<tr>
<td>1–4 years</td>
<td>26 (18)</td>
<td>122 (82)</td>
<td>75 (61)</td>
<td>25 (20)</td>
</tr>
<tr>
<td>5–9 years</td>
<td>11 (13)</td>
<td>71 (87)</td>
<td>20 (28)</td>
<td>19 (27)</td>
</tr>
<tr>
<td>10–14 years</td>
<td>20 (21)</td>
<td>76 (79)</td>
<td>24 (31)</td>
<td>18 (24)</td>
</tr>
<tr>
<td>15–19 years</td>
<td>19 (18)</td>
<td>89 (82)</td>
<td>57 (64)</td>
<td>12 (13)</td>
</tr>
<tr>
<td>20–29 years</td>
<td>44 (35)</td>
<td>81 (65)</td>
<td>73 (90)</td>
<td>8 (10)</td>
</tr>
<tr>
<td>30–39 years</td>
<td>37 (56)</td>
<td>29 (44)</td>
<td>26 (90)</td>
<td>2 (7)</td>
</tr>
<tr>
<td>40–49 years</td>
<td>3 (30)</td>
<td>7 (70)</td>
<td>6 (86)</td>
<td>1 (14)</td>
</tr>
<tr>
<td>Total</td>
<td>193 (23)</td>
<td>628 (77)</td>
<td>429 (68)</td>
<td>89 (14)</td>
</tr>
</tbody>
</table>

**a** Age was not known for five individuals.

**b** MMR = measles, mumps, rubella vaccine.

### Table 3

<table>
<thead>
<tr>
<th>Location</th>
<th>Target age group population (6 months to 40 years)</th>
<th>Vaccination status assessed during campaign</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Documented ≥2 MMR before campaign (% target age group)</td>
<td>Received MMR vaccination during campaign (% target age group)</td>
</tr>
<tr>
<td>Majuro</td>
<td>20,639</td>
<td>4279 (21)</td>
</tr>
<tr>
<td>Ebeye</td>
<td>9685</td>
<td>1398 (14)</td>
</tr>
<tr>
<td>Outer Islands</td>
<td>14,378</td>
<td>2239 (16)</td>
</tr>
<tr>
<td>Nationwide</td>
<td>44,702</td>
<td>7916 (18)</td>
</tr>
</tbody>
</table>

**a** Coverage with ≥1 dose of MMR = (No. of persons with documented ≥ 2 MMR before campaign + persons who received MMR vaccine during the campaign)/ target age group population.

**b** Table does not represent MMR doses distributed to individuals outside the campaign target age range.
specific imported measles case that caused this outbreak was not found, the H1 measles virus identified has been documented to circulate in East Asia particularly China, Korea, and Japan. Factors contributing to this large outbreak were low population measles immunity due to inadequate vaccine coverage, absence of recent transmission of measles virus, and high susceptibility among infants. High population density facilitated rapid spread among susceptible individuals.

To prevent measles outbreaks, 95% population immunity is needed. In RMI, routine one dose MMR coverage >90% among children aged 2 years was only achieved three times during 1987–2002. Only one of three catch-up campaigns targeting young children reached >90% coverage. A routine second MMR dose was added to the vaccination schedule in 1998; however, reported coverage with two doses was low (40% in 2000). High vaccine coverage, including two doses for those aged 1–19 years, must be achieved and coverage must be assessed across a wide range of age cohorts to assure high population immunity. RMI reported no measles cases during 1988–2002, so very few people aged <15 years would have disease-acquired immunity. During this outbreak, 25% of cases occurred in adults, suggesting large pockets of adults without immunity to measles disease.

School entry immunization laws are very effective programmatic tools to assure high two dose MMR coverage in the US. School laws were implemented in the 1980s for single dose MMR and a two dose MMR requirement has been gradually phased in since 1989. By 2001, 98% of all states required two dose MMR coverage at school entry with 98% of elementary students in those states meeting the requirement. RMI had a school entry immunization law since 1981, but there was no system for its application or enforcement.

Because measles vaccine effectiveness is estimated to be 95% for one dose and 99% for two doses, in conditions of intense exposure, measles cases are expected to occur among vaccinated individuals. According to WHO routine coverage reports, 74% of children aged 1–19 years had one dose of MMR and 40% had two doses in 2000. In Majuro, assuming universal exposure to measles virus during the outbreak, at these coverage levels, we would expect 200 vaccine failures in one dose recipients and 33 in two doses recipients. We documented fewer one dose and more two dose vaccine failures than expected; this may partly be explained by vaccine documentation errors. A vaccine effectiveness study was conducted during this outbreak among household members of measles cases. The vaccine effectiveness for one dose of MMR vaccine was 92% (95% CI: 67–98%).

Previous studies in similar island populations indicate that although vaccine effectiveness was 85%, it was not a major contributor to previous measles outbreaks. Therefore, we conclude that decreased vaccine effectiveness did not contribute significantly to this outbreak.

Measles incidence was high, especially on Majuro atoll, when compared with other measles outbreaks in the region (Majuro: 30 cases per 1000, other outbreaks: 0.7–14.9 cases per 1000). In Majuro, the incidence among infants aged <1 year was 207 cases per 1000 infants. This was much higher than similar outbreaks in the Pacific (other outbreaks: 12–62 cases per 1000 infants). Consistent with previously described measles epidemiology, complications and hospitalizations were highest among very young infants and adult measles cases.

A contributing factor to the high measles incidence in infants aged <6 months is a result of low maternal antibody levels. Women who have vaccine-induced immunity develop lower antibody titers than women who have disease-induced immunity and women who have had neither disease nor vaccination do not have antibody to measles. Thus the high level of susceptibility seen in the adult population in Majuro was reflected in the infant population. During the US measles resurgence from 1988 to 1994, infants of mothers born in the post-vaccine era were at higher risk of developing measles owing to low or no maternal antibody compared with mothers with immunity from natural measles. The very high levels of susceptibility to measles among infants in the RMI should serve as caution to other countries without endemic measles transmission, where levels of measles antibody may be decreasing among women of child-bearing age. Currently, the best way to protect infants from exposure to measles is through very high levels of immunity to measles in the population aged ≥1 year.

High population density contributed to the size and rapid spread of the outbreak. Majuro has 6692 persons/square mile similar to Singapore with 6481 persons per square mile and Ebeye has a population density of 96 300 persons per square mile, one of the highest population densities in the world. RMI households are made up of large, extended families. It is common to have many (>5) preschool and school age children in a household, allowing opportunities for measles exposure among susceptible individuals.

There are limitations in interpreting the results derived from this outbreak. First, the case definition used was non-specific and some illnesses that were not measles may have been classified as measles. However, the 2 week illness intervals were characteristic of measles and we confirmed measles virus circulated throughout the period of the outbreak. Additionally, because some of the patients reporting measles illness were vaccinated during the 7–18 days before the rash onset, we could not clearly distinguish between vaccine reactions and wild-type virus infections. However, all cases met the case definition that included at least one respiratory symptom. Second, owing to limited follow-up of disease course, complications reported may be underestimated, though severe complications and deaths are probably captured. Third, assessing vaccine coverage was difficult owing to the non-uniform availability of vaccine records and limited availability of pre-outbreak population vaccination coverage, further complicated by a mass vaccination campaign implemented during the outbreak.

Measles elimination goals have been established in the US (by 2000; achieved 199728), the PAHO region (by 2005), the European region (by 2007), and the Western Pacific Region (date to be set). Many countries, including the US, have eliminated endemic measles transmission. Island patterns of measles epidemiology, illustrated by this outbreak, should be instructive for these countries as ‘islands of susceptibility’ may accumulate in various population groups. In infants this is due to low maternal antibody levels. Migration of susceptible adults into more densely populated areas may also create islands of susceptibility. Also, any sub-population where high vaccination coverage is not sustained may be at risk of an outbreak if measles virus is imported.

According to WHO, Pacific island countries had been free of indigenous measles since March 1998, although importations were reported in French Polynesia (1999) and Guam (2002) with
limited outbreaks. As long as measles remains endemic anywhere in the world, countries are at risk for measles re-introduction through importation. In populations where measles virus circulates, measles incidence serves as an indicator of population immunity and the effectiveness of immunization programmes. Absence of measles transmission may provide false confidence in vaccination programmes that may be inadequate. Countries should realize that while interruption of endemic transmission is a major milestone, measles elimination is not an endpoint but a status maintained by sustaining high measles vaccine coverage.

**Acknowledgements**

The authors would like to thank Jean-Paul Chaine, Richard Duncan, WHO Western Pacific Regional Office, the CDC measles outbreak response team, and the Republic of the Marshall Islands Ministry of Health, Public Health and Hospital staff for their dedicated work during this outbreak. We also thank Mary McCauley for reviewing and editing the manuscript. This investigation was funded through the Ministry of Health, Republic of the Marshall Islands, and the Centers for Disease Control and Prevention, Atlanta, GA, USA.

**KEY MESSAGES**

- Countries without endemic measles are still at risk for reintroduction of the measles virus through importation.
- Groups with low measles vaccine coverage can accumulate a large enough number of susceptible individuals who can sustain a measles outbreak.
- High population immunity through measles vaccination must be maintained to prevent future measles outbreaks.

**References**

