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### Seroprevalence of measles, mumps and rubella among children in American Samoa, 2011, and progress towards West Pacific Region goals of elimination ★

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#### Abstract

**Introduction:** In line with the global goals for measles elimination, countries in the West Pacific Region (WPR) have set a goal to eliminate measles by 2012. Due to its contagiousness, high population immunity is needed for achieving and documenting measles elimination. We assessed population immunity to measles, mumps and rubella among first grade children in American Samoa (AS) through a seroprevalance study.

**Methods:** Using commercial indirect enzyme-linked immunosorbant IgG assays (Wampole Laboratories, Cranbury, NJ) we determined IgG antibodies against the measles, mumps, and rubella (MMR) viruses in sera collected from first grade students in AS in April–May 2011. Vaccination status was retrieved from the immunization cards. Factors associated with seropositivity of measles, mumps, and rubella were analyzed separately.

**Result:** Among 509 first grade students, measles, mumps, and rubella seroprevalence were 92%, 90%, and 93%, respectively. The proportions of first grade students with documented one or two

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doses of MMR vaccine were 93% and 84%, respectively. The vaccination status of 6% of the first graders was unknown and 1% was unvaccinated. Receiving two-doses of MMR vaccines was associated with high measles and mumps seropositivity (p < 0.01).

**Conclusion:** The high measles seroprevalence among children shows the progress by American Samoa towards measles elimination. Achieving and maintaining high two-dose MMR vaccine coverage in all age groups will aid in attaining the measles elimination status and prevent transmission of measles from potential imported measles cases from other countries.

#### Keywords

Seroprevalence; Measles; Mumps; Rubella; American Samoa

#### 1. Introduction

The World Health Organization (WHO) has set elimination goals for measles and rubella to reduce measles-related deaths and rubella-related disabilities [1]. Elimination is defined as the absence of endemic measles or rubella cases in a defined geographical area for a period of at least 12 months or more, in the presence of high-quality surveillance [2]. Although effective and inexpensive vaccines have been available, measles and rubella continue to result in morbidity and mortality among children in different regions of the world including the Western Pacific Region (WPR) [1,3]. Prior to the introduction of measles vaccine in the Pacific Islands, measles resulted in large outbreaks associated with high morbidity and mortality: in Hawaii (1848), Aneityum, Vanuatu (1861), and Rotuma, Fiji (1911) when the isolated indigenous populations were exposed to the measles virus for the first time [4-6]. The measles vaccine was introduced in 1982 in most island countries in the WPR, however the region continued to experience measles outbreaks on an average of four outbreaks every year until the late 1990s [6]. To interrupt measles transmission and achieve measles elimination in the region, the WHO WPR office, embarked on a Pacific-wide coordinated mass measles vaccination campaigns among children and adolescents during 1996–2002 (periods of measles accelerated control) and 2003–2008 (elimination) [7].

In 2005, the 37 countries and areas of the WHO WPR established a goal to eliminate measles in the region by 2012 [8]. WHO established several operational criteria to measure the elimination status, including reporting measles incidence of less than one confirmed case per million population per year and achieving high (>95%) two-dose measles vaccine coverage [9]. Furthermore, age-group specific susceptibility targets estimated from vaccine coverage data or seroprevalence studies could be used to assess progress [10]; for example, the percentage of children aged 5–9 years (the age group in our study) who are measles seronegative should be 10% [11]. In addition to measles elimination goals, countries of the region also implemented an accelerated rubella control and prevention of congenital rubella syndrome (CRS) program to decrease the annual rubella incidence to <10 cases per million population by 2015 [12].

Serosurveys are routinely used to complement disease surveillance. The serosurveys aid in the determination of a population's antibody level, identify the sub-populations at risk, assess accuracy of the vaccine coverage; these factors assist in the evaluation of

the achievement of elimination [13,14]. To aid the American Samoa (AS) surveillance in attaining the goals for measles, mumps and rubella (MMR) control and elimination, we conducted a cross-sectional serosurvey among first grade students and assessed the MMR vaccine coverage among these children.

#### 2. Methods

#### 2.1. Study location

American Samoa (AS), an unincorporated territory of the United States, consists of six islands located between Hawaii and New Zealand in the South Pacific Ocean [3]. In 2010, the population of American Samoa was 55.519 with 95% residing in the main island of Tutuila [15]. Tutuila is divided into Eastern and Western districts, which are subdivided into counties and villages. In our study, we grouped villages into broad geographical areas of Central, East, Midwest, and West, using the AS Department of Education (ASDOE) list of schools location. The American Samoa Department of Health (ASDOH) provides all the recommended vaccines by the United States Advisory Committee on Immunization Practices (ACIP), with the exception of Varicella and Human Papillomavirus vaccines [16], through a network of public health clinics that maintain written immunization records and a centralized immunization database. The MMR vaccine has been in use in American Samoa since 1973. The first dose of MMR vaccine is administered at 12–15 months of age and the second dose at 4–6 years of age. Two doses of MMR vaccine are required to start kindergarten or first grade.

#### 2.2. Study participants

The ASDOH in collaboration with ASDOE invited principals of all 36 elementary schools (private and public) in the main island of Tutuila to allow their schools to participate in a cross-sectional serosurvey study among first-grade students to assess the seroprevalence of five vaccine-preventable diseases [measles, mumps, rubella, hepatitis B and varicella]. All the elementary schools in Tutuila agreed to participate in the study and distributed invitation letters and questionnaires, written in English and Samoan, to all parents/guardians of first-grade students. The questionnaire collected information on demographics including age, sex, and place of birth. Parents returned the completed questionnaires with student's immunization card, also known as "yellow shot card" a family-held vaccination records. Information on the date and doses of vaccination was retrieved only from immunization card was not cross-checked with immunization registry or medical records. Written informed consent was obtained from participating parents of elementary students as well as assents from the children themselves. The serosurvey was conducted from April to May, 2011.

This study was reviewed and approved by the Institutional Review Boards (IRB) in American Samoa. Since the serosurvey was considered part of the immunization program evaluation, this study was designated as non-research by Centers for Disease Control and Prevention (CDC) IRB. This report presents the seroprevalence of measles, mumps, and rubella among first-grade students.

#### 2.3. Laboratory testing

The blood samples were centrifuged to separate the serum and stored at -20 °C at Lyndon B. Johnson Tropical Medical Center in American Samoa. Serum was then transported on dry ice to CDC, Atlanta, Georgia, to be tested for the presence of MMR immunoglobulin (IgG) antibodies. Three commercially available indirect enzyme-linked immunosorbent IgG assays (Measles (Rubeola) IgG ELISA II, Mumps IgG ELISA II, Rubella IgG ELISA II; Wampole Laboratories (Cranbury, NJ) were used for the detection and qualitative determination of IgG antibodies to measles, mumps, and rubella virus in serum specimens. Positive, equivocal, and negative status of sera was determined using the cut-offs specified by the manufacturer based on index standard ratio (ISR) values. Seronegativity was defined for all the viruses as a serum ISR value of 0.90; sera with ISR values of 0.91–1.09 were considered equivocal and sera with ISR values of 1.10 were defined seropositive. All negative and equivocal serum specimens were retested along with an equal number of positive specimens. A 10% random-sample repeat of the entire specimens was done for quality assurance and quality control purposes. All samples were tested by laboratory personnel blinded to the subject's vaccination status.

#### 2.4. Statistical analysis

Children who completed the survey but did not provide serum specimens were excluded from the analysis. Data were analyzed using SAS (Version 9.3; Cary, NC). Pearson chi-square or Fisher exact test was used to compare categorical variables; *p*-values <0.05 were considered significant. Assuming a binomial distribution, the exact 95% confidence intervals were determined by the Mid-P Exact method using OpenEpi Version 2.3.1 [17].

MMR vaccine coverage was calculated by dividing number of students with documented vaccine administration dates by the total number of students included in the study. Students were classified as two-dose recipients if two doses of MMR vaccine, separated by at least 28 days, were recorded on the immunization cards; single-dose recipients if only one dose of MMR vaccine was recorded on the immunization cards. If the immunization cards were missing, vaccination status was classified as unknown. Finally, if there was no record of receiving the MMR vaccine on the immunization card, vaccination status was classified as unvaccinated.

#### 3. Results

Of the 1310 first-grade students in the 27 schools that participated and where study questionnaires were distributed, 800 (61%) completed the questionnaires. Of these, consent for the serosurvey was obtained for 566 (71%); 509 (90%) sera were tested for IgG antibodies to the MMR viruses. There were no significant differences between participants and non-participants in relation to age, sex, vaccination coverage, and residence (Table 1). There were significant differences in terms of place of birth (p < 0.01); 460 (90.4%) of the study participants were born in American Samoa while 151 (64.5%) of the non-participants were born in American Samoa. However, 81 (34.6%) of the non-participants tested for MMR IgG antibodies was 7 years (range: 5–9 years) and 257 (51%) were female (Table 1).

Page 5

Among the 509 participants, vaccine coverage was 84% (n = 429) for two-doses of MMR vaccine and 93% (n = 475) for one-dose MMR vaccine; 93% (475) received at least one dose of MMR vaccine, 28 children (6%) had unknown vaccination status, and 6 (1%) were unvaccinated. Among the 6 unvaccinated children, five were born in American Samoa and one in Tonga (Table 1). Three of the 6 unvaccinated students tested negative for measles and mumps IgG antibodies. One of the 6 unvaccinated students tested negative for rubella IgG antibodies and only one student tested negative for all the antibodies. Among the 28 students with unknown vaccine status, one student tested negative for measles IgG antibodies, another student tested negative for mumps IgG antibodies, two students were equivocal for mumps IgG antibodies, none of the student tested negative for all the IgG antibodies.

#### 3.1. Measles

The overall measles seropositivity for first-grade students included in our analysis was 91.9% (95% CI 89.3–94.1%) (Table 2); 3.5% and 4.5% of the serum specimens were equivocal and negative for measles IgG antibodies, respectively. Measles seropositivity did not significantly differ by age group, sex, and place of birth, residence, age at receiving first dose MMR vaccine, and age at receiving second dose MMR vaccine (Table 2). Seropositivity was significantly associated with MMR vaccination status; it was highest among two-dose MMR vaccine recipients and lowest among unvaccinated [93.2% (95% CI 90.6–95.3%) versus 50.0% (955 CI 14.7–85.3%); p = 0.005] (Table 2). Among MMR vaccinees, 444 (92.6%) were seropositive for measles IgG antibodies.

#### 3.2. Rubella

The overall rubella seropositivity was 92.9% (95% CI 90.5–94.9%) (Table 2); 3.1% and 3.9% of the serum specimens were equivocal and negative for rubella IgG antibodies, respectively. Rubella seropositivity was not significantly different by sex, place of birth, residence, MMR vaccination status, age at receiving first dose MMR vaccine, and age at receiving second dose MMR vaccine. Children less than 6 years of age had a higher seroprevalence: 94.7% (95% CI 91.8–96.9) versus those older, 90.2% (95% CI 85.6–93.8) (p > 0.05) (Table 2). Among the MMR vaccinees, 444 (93.5%) were seropositive for rubella IgG antibodies.

#### 3.3. Mumps

The overall mumps seropositivity among the first-grade student included in our analysis was 90.0% (95% CI 87.1–92.4%) (Table 2); 4.3% and 5.7% of the serum specimens were equivocal and negative for mumps IgG antibodies, respectively. Mumps seropositivity was not significantly different by age group, sex, place of birth, age at receiving first dose MMR vaccine, and age at receiving second dose MMR vaccine (Table 2). Statistical differences were observed in mumps seropositivity between regions (p = 0.01); the East region had the highest mumps seropositivity of 98.5% (95% CI 93.0–99.9%) and lowest in Midwest region 87.0% (95% CI 82.3–90.8). Mumps seropositivity was associated with MMR vaccination status; it was lowest among unvaccinated [50.0% (95% CI 14.7–85.3%)] versus 2-dose MMR vaccine recipients [91.4% (95% CI 88.4–93.8%)] (p = 0.004) (Table 2). Among MMR vaccinees, 429 (90.3%) were seropositive for mumps IgG antibodies.

#### 4. Discussion

To the best of our knowledge this is the first serosurvey to assess measles, mumps, and rubella seroprevalence in American Samoa, estimated to be 92%, 90%, 93%, respectively, among first-grade students. The high seroprevalence is consistent with the high MMR vaccine coverage of 93% for at least one-dose and 84% for two-doses among first grade students. First grade students with no documented MMR vaccination had significantly lower prevalence of measles and mumps IgG antibodies. Previous vaccination surveys in American Samoa have also found a high MMR immunization coverage; based on their report to the National Immunization Program by the states and US territories, the vaccination coverage survey for children at kindergarten entry in the school year 2003–2004 found MMR vaccine coverage among kindergarten students to be 98.2% [18]. A household vaccination coverage survey conducted in 2008–2009 among children aged 6 years found one or more dose MMR vaccine coverage to be 91% among 6 year-old children [19].

The proportion of measles seronegative children among the school-age children in our study was 8%, below the WHO susceptibility target of 10% for 5–9-year-olds. This low proportion of seronegative children confirms the WHO WPR assessment that American Samoa is on the goal towards measles elimination status [20]. In our study, 3 of the 6 unvaccinated students tested positive for measles antibody raising the question of whether there were undetected or unreported vaccine-preventable disease (VPD) cases or whether receipt of vaccines were not documented on the immunization card. However, most illnesses arising from VPDs, except varicella, are notifiable in American Samoa. Surveillance is thought to be sensitive; initial cases of mumps in an outbreak in 2007–2008 were detected by surveillance (*ASDOH, unpublished data*). It is possible that some of the students may have received the MMR vaccine without documenting the receipt in the immunization card and that some students may not have responded immunologically to one or more of the antigens in the MMR vaccine [21].

As American Samoa lies geographically in a region where measles is not yet eliminated, the risk of measles importations from the regional countries or globally and subsequent outbreaks exist [20]. The estimated two-dose MMR vaccine coverage of 84% in our study is consistent with a household vaccination coverage survey conducted in 2008–2009 among children aged 6 years [19], below the required 95% vaccine coverage, which may lead to outbreaks. Low levels of two-dose measles vaccination coverage in some of the Pacific Islands have resulted in measles outbreaks in the neighboring island countries. An outbreak of measles in Republic of Marshall Islands in 2003 [22] and Fiji in 2006 [23] led to 826 and 132 measles cases respectively. Tourists from measles endemic countries coupled with high mobility of the local people within the pacific islands poses a threat to the islands that have achieved elimination status [22,23]. Measles is currently eliminated or nearly eliminated in 24 of the 37 countries in the WPR [20]. Therefore, strengthening regional surveillance, attaining high levels of immunization, and genotyping is of paramount importance to all the countries in the region. Furthermore, ensuring two-dose coverage of >95% among school age-children and other age groups will accelerate the path towards measles elimination in American Samoa and other countries in the region [1].

Mahamud et al.

Elimination of rubella is now considered feasible with the introduction of rubella-containing vaccine. In 2003, the WHO WPR implemented an accelerated rubella control and prevention of CRS program that dramatically reduced rubella incidence in the region [24] with the goal to decrease the annual rubella incidence to <10 cases per million population by 2015. The seroprevalence of rubella in our study is consistent with other seroprevalence studies in the West Pacific countries with rubella-containing vaccination programs; a study in Australia found rubella seroprevalence to be 91% among first grade students [25]. Studies have indicated that the estimated threshold for interruption of virus transmission is 87.5% [26]. The combination of high vaccination coverage, and high rubella seroprevalence (>87.5%, among first-grade students), indicates that American Samoa is on the road to rubella elimination [26]. Nonetheless, if the vaccination coverage and the seroprevalence were to be lowered, rubella could easily be established in American Samoa. Neighboring islands have experienced outbreaks of rubella; most recently in 2002–2003 in Tonga, Samoa, and Tokelau. The rubella outbreak in Samoa was associated with a relatively high number of cases of encephalitis and high mortality rate [6].

Mumps vaccine has been implemented in the vaccination program in American Samoa since it was recommended in the United States in 1977 [27]. With implementation of the MMR vaccination program American Samoa has achieved an adequate mumps control with few sporadic cases of mumps reported in 1994 and 2001, until 2007–2008 when a laboratory confirmed mumps outbreak of 75 cases was reported among school aged-children (*ASDOH, unpublished data*).

There are several limitations to this study. First, our findings are not generalizable to the general population. Second, we may have underestimated the vaccination coverage since we relied on household-retained vaccination cards. A household immunization coverage survey in American Samoa found that household-retained vaccination cards had lower coverage compared to medical records cards [19]. A similar study in one of the US-associated Pacific islands found vaccination card-estimated coverage to be 35–50% points lower than coverage based on medical records [28]. Third, we did not capture the disease history of measles, mumps, and rubella, because of errors in the questionnaire translation. Lastly, the children included in our study may not be representative of all the children in that age group in American Samoa. However, American Samoa is a small island, and therefore we believe that the MMR seroepidemiology is reflective of the specific age group we included since we did not find significant demographic differences between study participants and non-participants apart from place of birth.

The measles, mumps, and rubella seroprevalence in our study reflects the relatively high vaccination coverage achieved in American Samoa. Despite the limitations, our finding of the high measles seroprevalence shows the progress of American Samoa towards measles elimination goal. Achieving and maintaining high two-dose MMR vaccine coverage in all age groups will aid in the elimination and would prevent transmission of potential imported measles from other countries.

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#### Abbreviations:

AS	American Samoa
ASDOE	Department of Education
ASDOH	American Samoa Department of Health
ACIP	Advisory Committee for Immunization Practices
CDC	Centers for Disease Control and Prevention
MMR vaccine	measles-mumps-rubella vaccine

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Mahamud et al.

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## Table 1

Demographic characteristics of measles, mumps, and rubella serosurvey participants and non-participants, American Samoa, April–May, 2011 (*n* = 787).

Mahamud et al.

Variable	Participa	ats $n = 509$	Non-par	ticipants n	= 278	<i>p</i> Value
	u	%	u	%		
Age group						0.3
<6 years	304	59.7		86	55.7	
6 years	205	40.3	ţ.	78	44.3	
Sex						0.4
Female	257	51.1	~	33	46.9	
Male	246	48.9		94	53.1	
Place of birth						<0.01
In A. Samoa	460	90.4	15	51	64.5	
Outside A. Samoa	21	4.1		2	0.9	
Unknown	28	5.5	~	81	34.6	
Residence						0.2
Central	90	17.7	~	81	34.6	
East	68	13.4	7	43	18.2	
Midwest	246	48.3		22	9.3	
West	105	20.6	1	32	55.9	

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# Table 2

Seroprevalence of measles, mumps, and rubella antibodies among first graders by selected variables, American Samoa, April–May 2011 (n = 509).

Variable	u	Measles seroprevalence	Mumps seroprevalence	Rubella seroprevalence
Overall	509	91.9 (89.3–94.1)	90.0 (87.1–92.4)	92.9 (90.5–94.9)
Age group				
<6 years	304	92.8 (89.4–95.3)	90.5 (86.8–93.4)	94.7 (91.8–96.9)
6 years	205	90.7 (86.2–94.2)	89.3 (84.5–93.0)	90.2 (85.6–93.8)
Sex				
Female	257	92.6 (88.9–95.4)	89.9 (85.7–93.1)	94.9 (91.7–97.2)
Male	246	92.3 (88.4–95.2)	90.2 (86.0–93.5)	91.5 (87.5–94.5)
Place of birth				
In AS	460	92.0 (89.2–94.2)	90 (87.0–92.5)	93 (90.4–95.1)
Outside AS	21	95.2 (78.7–99.8)	85.7 (65.9–96.2)	$100 \ (86.7 - 100.0)$
Unknown	28	89.3 (73.6–97.2)	92.9 (78.4–98.8)	85.7 (69.1–95.3)
Residence				0.2
Central	90	92.2 (85.2–96.5)	87.8 (79.8–93.4)	95.6 (89.6–98.6)
East	68	94.1 (86.4–98.1)	98.5 (93.0–99.9)	92.7 (84.5–97.3)
Midwest	246	90.2 (86.0–93.5)	87.0 (82.3–90.8)	91.9 (87.9–94.8)
West	105	94.3 (88.5–97.7)	93.3 (87.3–97.0)	93.3 (87.3–97.0)
Vaccine status		*	*	
Two-dose	429	93.2 (90.6–95.3)	91.4 (88.4–93.8)	93.9 (91.4–95.9)
Single-dose	46	87.0 (74.8–94.5)	80.4 (67.1–90.0)	89.1 (77.5–95.9)
Unvaccinated	9	50.0 (14.7-85.3)	50.0 (14.7–85.3)	83.3 (40.9–99.2)
Unknown	28	89.3 (73.6–97.2)	92.9 (78.4–98.8)	85.7 (69.1–95.3)
Age at first MMR vaccination				
<12 months	5	$100.0\ (54.9 - 100.0)$	100.0 (54.9–100.0)	100.0(54.9 - 100.0)
12 months	469	92.5 (89.1–94.7)	90.2 (87.3–92.6)	93.4 (90.9–95.4)
Age at second MMR				
<4 years	18	94.4 (75.5–99.7)	94.4 (75.5–99.7)	100 (84.7–100.0)
4 years	411	93.2 (90.4–95.3)	91.2 (88.2–93.7)	93.7 (91.0–95.7)
Years since last MMR2				

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Variable	u	Measles seroprevalence	Mumps seroprevalence	Rubella seroprevalence
<2 years	76	94.7 (87.8–98.3)	92.1 (84.3–97.7)	93.4 (86.0–97.6)
2–3years	268	92.9 (89.4–95.6)	91.4 (87.6–94.4)	94.8 (91.6–97.0)
>3 years	85	92.9 (85.9–97.1)	90.6 (82.9–95.5)	91.8 (84.4–96.3)

*Note:* CI, confidence interval; AS, American Samoa; MMR, measles, mumps, and rubella. \* p < 0.01.