

# Prevalence of Serum Antibodies Against Vaccine-Preventable Diseases in Students of A Japanese University of Health and Welfare and its Advisory Standard of Vaccination for Clinical Training

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## ABSTRACT

The incidence of vaccine preventable diseases has increased in the adult Japanese population. The purpose of this study was to determine the need for vaccinations in students of co-medical field. Status of the students attending to International University of health and welfare, Japan-were surveyed in 2008 to 2011 academic year for vaccination and past medical history by self-administered questionnaire and the serum antibody prevalence for enrollment concerning measles, rubella, varicella and mumps. Majority of the students in all years had immunity for measles, rubella and varicella but not for mumps by EIA assay. Although positive rates of measles antibody had risen since 2009, which of rubella was extremely low in the year of 2011. Serum antibody titers of rubella were lower than those of measles in all years. Freshman of 2008 showed highest antibody titers against measles and rubella. These results suggest that the forth stage of measles and rubella mixed regular vaccination targeted since 2008 in Japan was effective. Also determined what should be done the encouraging vaccination based on specific past medical history, vaccination histories (including dates and times) about encouraging vaccination, appropriate for the individual.

**Key Words:** Measles, rubella, varicella, mumps, vaccine

**Japonyadaki Sağlık ve Refah Üniversitesi Öğrencilerinde Aşı ile Önlenebilir Hastalıklara Karşı Serum Antikorlarının Prevalansı ve Klinik Eğitimleri İçin Aşılama Standart Tavsiyeler**

## ÖZET

Aşı ile önlenebilir hastalıkların insidansı yetişkin Japon nüfusunda artmıştır. Bu çalışmanın amacı, tıp alanındaki öğrencilerin aşı ihtiyacını belirlemektir. 2008 - 2011 yılları arasında, "International University of Health and Welfare, Japan" a devam eden öğrencilerin, aşılama durumları ve geçmişteki tıbbi hikâyeleri, anketle ve serum antikor prevalansı ile (kızamık, kızamıkçık, suçiçeği ve kabakulak) incelendi. EIA ölçümlerinde, öğrencilerin çoğunda tüm yıllarda kızamık, kızamıkçık ve suçiçeği için bağışıklık vardı, fakat kabakulak için yoktu. Kızamık antikorlarının pozitiflik oranları 2009 yılından bu yana artmış olmasına rağmen,

*kızamıkçık 2011 yılında son derece düşük idi. Kızamıkçık serum antikor titreleri tüm yıllardaki kızamıktan daha düşüktü. 2008'in birinci sınıfı, kızamık ve kızamıkçığa karşı en yüksek antikor titreleri gösterdi. Bu sonuçlar, Japonya'da 2008 yılından bu yana hedeflenen düzenli kızamık ve kızamıkçık karma aşılmasının ileri evrelerinin etkili olduğunu göstermektedir. Keza, özel tıbbi geçmişe, aşı hikâyesine dayanan (tarih ve zamanını da içeren) aşılamanın, bireysel uygun aşılamaı teşvik edici olduğu kanaatine varılmıştır.*

**Anahtar Kelimeler:** Kızamık, kızamıkçık, suçiçeği, kabakulak, aşı

## INTRODUCTION

Although measles, mumps, rubella, and varicella (MMRV) are vaccine-preventable diseases (VPD) common in childhood, the incidence of these viral infections has increased in the adult Japanese population (1). The risk for death from measles or its complications is greater for infants, young children (2). The most common causes of death are pneumonia and encephalitis. Since measles vaccine became available, professional and voluntary medical and public health organizations have collaborated in vaccination programs that have reduced the reported incidence of measles by greater than 99% (1). Even countries that measles had been eradicated still have the high risk of importation from countries that have not yet eliminated the disease (3). For prevention against MMRV infection in medical facilities, it is important to assess the immunity against these viruses and to achieve immunocompetence by vaccination.

In 2009, the Regional Committee of the Western Pacific Region Office (WPRO) of WHO formally declared a regional measles elimination target date of 2012 (3,4). Reported cases of measles in Japan which was 11,015 in 2008 decreased to 434 in 2011. This fact was estimated due to the effect of third and fourth routine vaccination opportunity for measles and rubella (MR) started in the year of 2006 by the Japanese Ministry of Health and Labor. The two dose of immunization program with combined measles and rubella (MR) vaccine has been started since April 2006. But not yet reached the number of patients achieving measles elimination required. The third and fourth routine vaccination rates also have been too low. As VPD are important in the health and welfare of infection control perspective, positive control serum antibody or vaccine and its effects have been reported.

In this study for the establishment of immediate infection

control system for future construction, we made analysis of serum prevalence of antibodies of students and with a history of disease and vaccination history. The purpose of this study was to determine the need for MMRV vaccinations in students by means of a seroprevalence survey for these viral infectious diseases and to recommend vaccination.

## MATERIALS AND METHODS

Serum samples for all students in the International University do Health and Welfare (IUHW), Tochigi, Japan were examined by the serum antibody titers at the time of admission to the university. One hundred and seventy one students in the year of 2008, 256 students in 2009, 265 students in 2010 and 300 in 2011 were analyzed about vaccination and past medical history of each disease. Self-administered questionnaire survey, antibodies and related factors were analyzed. Serum was separated from other blood components and kept refrigerated at 4 °C until testing. All study procedures were approved by the research ethics committee of IUHW.

Serum antibodies to measles, varicella and mumps were determined by enzyme immunoassay (EIA) and those to rubella were determined by hemagglutination inhibition (HI) assay. Until the year of 2009 antibodies to varicella and mumps had been determined by complement-fixation (CF) test and by HI assay. EIA index more than 4.0, HI titers more than 1:16 and CF titers more than 1:4 were considered for positive. Recommendation for vaccination was sent in writing to all subjects with negative antibody titers. Statistical data analyses were conducted using SPSS® software. Continuous parameters with normal distribution were analyzed by Student's t-test. Binary variables were analyzed by the chi-square and Fisher exact tests. A two-tailed test was used for all statistical analyses. In all cases,  $p = 0.05$  was considered as the threshold.

## RESULTS

Measles antibody-positive rates of 2008-2009, 2010 and 2011 were 93.6%, 99.2%, 98.9 % and 98.7% respectively. The prevalence rate for measles antibody was higher in all years; however, difference was not statistically significant. Those to rubella were 89.5%, 91.8%, 94.0% and 80.0%, to chickenpox were 39.2% (by CF), 40.8% (by CF), 93.2% and 92.0% (by EIA) and to mumps were 11.1% (by

**Table 1.** Seropositivities of serum antibodies to measles, rubella, varicella and mumps of each year.

	2008		2009		2010		2011	
	Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative
Measles	93.6	6.4	99.2	0.8	98.9	1.1	98.7	1.3
Rubella	89.5	10.5	91.8	8.2	94.0	6.0	80.0	20.0
Varicella	39.2	60.8	40.8	59.2	93.2	6.8	92.0	8.0
Mumps	11.1	88.9	11.7	88.3	71.7	28.3	72.7	27.3

HI), 11.7% (by HI), 71.7% and 72.7 % (by EIA) (Table 1). Measles and rubella antibody positive rates rose in 2009 and 2010. The prevalence rate for the rubella antibody was significantly lower in subjects of 2011 ( $p = 0.005$ ). A high prevalence rate for the varicella antibody by EIA was observed in subjects of 2010 and 2011. The prevalence rate for the mumps antibody by EIA was lower in subjects of 2010 and 2011. The seropositivity for varicella by CF and that for mumps by HI in the year of 2008 and 2009 was considered to be not reliable.

Average antibody titers to measles of 2008, 2009, 2010 and 2011 were 24.8, 23.4, 21.8 and 21.9 EIA index respectively. Those to rubella by HI assay of 2008, 2009, 2010 and 2011 were 1:80.5, 1:59.1, 1:48.3 and 1:54.9 respectively. (Table 2) (Figure 1, 2, 3, 4) Significantly higher distribution of average measles and rubella antibody titers were found in 2008 ( $p = 0.005$ ).

## DISCUSSION

Although vaccination produces lower antibody levels than natural disease, both serologic and epidemiologic evidence indicate that the vaccine induces lifelong immunity in most persons (5). Findings of some studies indicate that immunity can wane after successful vaccination (secondary vaccine failure), but this phenomenon appears to occur rarely and to have little effect on measles transmission and the occurrence of outbreaks (5-7). There is no clinically-useful rapid diagnosis for measles over the world (8,9). Measles was estimated to infect 20 million people per year worldwide, and to result in

242,000 deaths (1,2).

Since monovalent vaccines containing measles, rubella, and mumps vaccine viruses and subsequently combined measles-mumps-rubella (MMR) vaccine were licensed, the numbers of reported cases of measles, mumps, rubella, and congenital rubella syndrome (CRS) have decreased by more than 99% in the United States. The anomalies most commonly associated with CRS are sensorineural deafness, congenital cataracts and heart anomalies. In addition, infants with CRS frequently exhibit both intrauterine and postnatal growth retardation. The primary objective of the rubella immunization program is the prevention of CRS.

Although Japanese regular measles and rubella immunization has been changed to two-dose schedule, introducing live attenuated MR combined vaccine since April 2006, the first immunization (12-24 months after birth) and the second one (5-6 years, less than 1 year before primary school entrance), there are still estimated 5 to 10 hundreds measles cases and several measles death annually in Japan. This epidemic of combined MR vaccine was a just when the inoculation was started 2 times next year that had predicted a pandemic outbreak. The decrease in measles cases owes much to the raising up in the measles vaccination rate among 1-2 year children by success of countermeasures taken by the whole country, academic societies, local governments, and medical associations since 2001. Also missing a kit for lack of vaccination or measles antibody measurement and social disruption occurs.

**Table 2.** Average antibody titers to measles, rubella, varicella and mumps of each year.

	2008	2009	2010	2011
Measles (EIA index)	24.8	23.4	21.8	21.9
Rubella (HI)	1:80.5	1:59.1	1:48.3	1:54.9
Varicella	1:4.4 (CF)	1:2.7 (CF)	20.3 (EIA index)	22.0 (EIA index)
Mumps	1:6.4 (HI)	1:5.4 (HI)	7.4 (EIA index)	7.3 (EIA index)

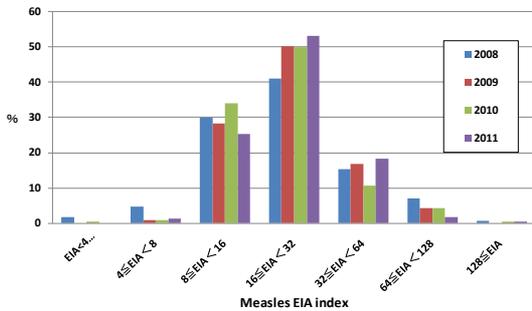


Figure 1. Prevalence of serum antibodies to measles.

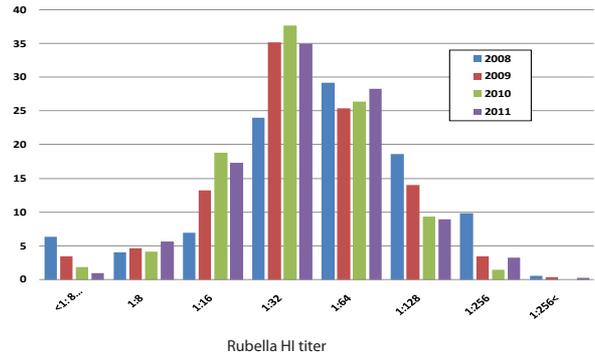


Figure 2. Prevalence of serum antibodies to rubella.

The third and fourth periodic inoculation of MR combined vaccine has been induced since 2008. Be under 23 years old, school-aged population vaccination 2 opportunities for measles and rubella vaccine given supplementary vaccination 2013 onwards. Vaccinations in Japan are not enforced and like the United States for final vaccination activities entrusted to guardians and personal perceptions and judgment, limits in encouraging vaccination for legal status. Environment surrounding the vaccination in Japan in 2012, measles elimination goals are in jeopardy began to move forward at last in recent years an increasing as any approval of a new vaccine. But is not enough vaccines to the public concerning information transmission, are important issues for the future. Most serious complications of mumps are more common among adults than among children (10,11). Although orchitis may occur among up to 38% of postpubertal men in whom mumps develops, sterility is thought to occur only rarely. Aseptic meningitis affects 4%-6% of persons with clinical cases of mumps and typically is mild. In the prevaccine

era, mumps was a major cause of sensorineural deafness among children. Deafness may be sudden in onset, bilateral, and permanent.

Infection defense can be antibody prevalence of measles, rubella, and varicella is results of this study, population immunity has had inadequate in and about mumps. Low vaccination rates are a chickenpox comes high natural incidence rates are estimated factors. Effect of phase 4 measles / rubella vaccination routine suggested as its influence, in measles and rubella antibody prevalence rises observed in year of 2009 and 2010. Due to changes in inspection methods considered difference between antibody prevalence of varicella, mumps grade, determined to assay system for fiscal 2010 better suited antibody screening in terms of sensitivity, specificity. However, the detection level of antibodies to defend is not clearly EIA laws but not necessarily. Therefore considered thorough inoculation with immune acquisition rate is higher that 2 doses are effective in infection prevention practices.

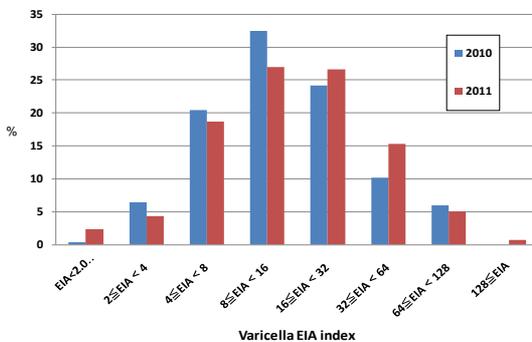


Figure 3. Prevalence of serum antibodies to varicella.

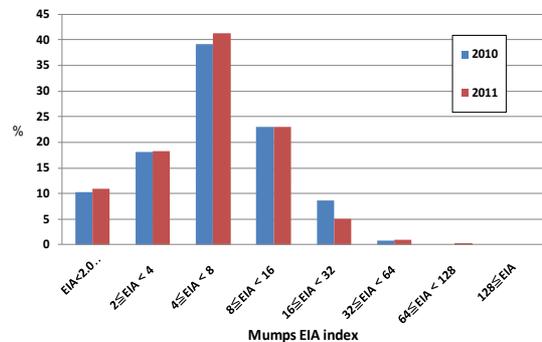


Figure 4. Prevalence of serum antibodies to mumps.

But for integrated College's standards are not necessarily equipped with advanced data analysis also untested on infection prevention measures inadequate conditions during clinical practice. A confirmation of antibody acquisition and inoculation encouragement manages the accurate information about the history of the student unless the possibility of an appropriate individual. Future vaccination rates improved and common understanding for more students to investigate the trends of the University as a whole, public should have the flexibility.

The criteria for acceptable evidence of immunity to measles, rubella, and mumps provide presumptive rather than absolute evidence of immunity (12,13). In the past, the most commonly used laboratory test for assessing immunity to measles was the HI test but more sensitive assays such as EIA are now used in most laboratories. Serologic screening for measles, rubella, or mumps immunity generally is neither necessary nor recommended if a person has other acceptable evidence of immunity to the disease. Serologic screening is appropriate only when persons identified as susceptible are subsequently vaccinated in a timely manner. Screening is most applicable when the return and vaccination of those tested can be ensured. If these conditions are not met, serologic screening is inappropriate (14). Likewise, during an outbreak of measles, rubella, or mumps, serologic screening before vaccination generally is not recommended because waiting for results, contacting, and then vaccinating persons identified as susceptible can impede the rapid vaccination needed to curb the outbreak.

Colleges, universities, technical and vocational schools, and other institutions for post-high school education should require that all undergraduate and graduate students have received two doses of MMR vaccine or have other acceptable evidence of measles, rubella, and mumps immunity before enrollment. Regular inoculation effect was found for measles and rubella chickenpox, mumps vaccine inoculation of desired 2 times. Suggested vaccine immunocompromised persons regardless of the number of inoculations in the meantime, cannot win the antibody presence suggests the antibodies after vaccination review during clinical practice and matter management. To encouraging vaccination shall be is determined to what should be done the encouraging vaccination based on specific past medical history, vaccination histories (including dates and times), appropriate for the individual. State requirements for pre-enrollment vaccination ensure the best protection against widespread

measles transmission among students at college campuses and other post-high school educational institutions. Students who do not have documentation of live measles, rubella, chickenpox or mumps vaccination or other acceptable evidence of immunity at the time of enrollment should be admitted to classes only after receiving the first dose of MMRV vaccine.

### Conflict of Interest

No conflict of interest associated with this work.

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