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**IMMUNE STATUS AMONG JAPANESE DURING NATIONWIDE RUBELLA
OUTBREAK IN JAPAN 2012 – 2013**

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Dear Editors,

We recently described in this Journal¹ a nationwide outbreak of Rubella in Japan in 2012-2013. We have now assessed how many Japanese aged ≥ 15 years are susceptible to rubella. Disturbingly the fraction susceptible is greater in younger pregnant women and male adults. Therefore, implementation of a new strategy for vaccination targeting susceptible adult populations in addition to universal vaccination targeting children is urgently required to avoid another rubella outbreak in Japan.

In a previous outbreak that occurred in 2004, 10 infants contracted congenital rubella syndrome (CRS).¹ According to the Japanese Ministry of Health, Labour, and Welfare, the total number of rubella patients during the first 9 months of 2013 was 14,077 (108 per 1,000,000 population, 69% of cases were serologically confirmed).² Among 3,664 patients in this outbreak with known vaccinated status, 85.6% had not been vaccinated.² The majority of rubella cases occurred among adults aged 18 years or older: male and female adults aged 18 years or older accounted for 71.7% and 19.8% of all 14,077 cases, respectively.² Consequently, 20 infants (1.8 per 100,000 live births) were diagnosed with CRS during the 12-month period between October 2012 and September 2013 in Japan.²

We conducted retrospective and multicentre study to assess how many pregnant Japanese women were susceptible to rubella during the rubella outbreak that occurred in Japan in 2012 – 2013 after being approved by the Institutional Review Board of each of the six participating hospitals. Data on the rubella immunity determined by haemagglutination inhibition assay (HI test) were available in 20,363 pregnant women who gave birth during the 5-year period between January 2008 and December 2012 at

six hospitals located in Hokkaido, Toyama, Tochigi, Tokyo, and Kanagawa prefectures. The data on population immunity for rubella during the 5-year period from 2008 to 2012 were available from the official website of Japan National Institute of Infectious Diseases (JNIID).³ Women with HI titre $< 8\times$ were defined as having no immunity against rubella (susceptible to rubella) in this study.

Yearly changes in prevalence rate of seronegative (HI $< 8\times$) pregnant women, females, and males were not marked over the 5-year period between 2008 and 2012 (data not shown). Overall percentages of susceptible pregnant women decreased with advancing maternal age (Fig. 1): 19.8% [25/126], 12.6% [99/787], 7.0% [233/3,313], 3.6% [244/6,871], 3.8% [265/6,966] and 3.5% [81/2,300] for women aged ≤ 19 , 20 – 24, 25 – 29, 30 – 34, 35 – 39, and ≥ 40 years, respectively. Approximately 20% of male Japanese adults aged 30s and 40s were susceptible to rubella while susceptible fraction was relatively small among females who participated in the serosurvey conducted by the JNIID.³ In this situation, the rubella outbreak recurred in Japan in 2012 – 2013.

The current profile of seronegative rates according to age and gender may have reflected changes in Japanese strategy for rubella vaccination. In 1976, Japan introduced a rubella vaccine to the national immunization program, targeting girls in junior high school. Since 1987, the vaccine was targeted toward children 12 – 36 months of age as a standard program with several times of supplemental vaccination campaign targeting girls and boys in junior high school, and adolescent girls and boys in high school.

With low vaccination coverage, the immunization of boys and girls against rubella carries the theoretical risk of increasing the occurrence of CRS, which was confirmed in Greece in 1993.⁴ Even with a high coverage rate of 90% with universal vaccination policy targeting children, the paradoxical effect occurred: the illness shifts to other

target groups with a high seronegative rate, and CRS continues to occur.⁵ Thus, vaccination strategies focusing on women and children are associated with greater incidence of rubella in male adults leading to new outbreaks and CRS.⁵ With continuing circulation of rubella virus, there is persistent risk of infection in susceptible pregnant women, even when only 2% – 3% of pregnant women are non-immune.⁶ The principal rationale for an accelerated vaccination strategy is to reduce the time needed to interrupt rubella virus circulation and to prevent CRS. Eradication of only one manifestation (such as CRS) of a prevalent rubella infection is not a realistic goal.

As demographic characteristics of participants in the serosurvey were not published,³ the reasons for a large dissociation in the fraction size susceptible to rubella between younger pregnant women and younger female participants in the serosurvey are unknown. We speculated that participants in the serosurvey conducted by the JNIID had a greater interest in healthcare than in the general population. In contrast, teenage pregnant Japanese women may have constituted a group at risk for rubella and not representative of women of similar age. This speculation was based on the findings that the risk of no antenatal care was high among women with teenage pregnancies in Japan,⁷ suggesting that women becoming pregnant as teenagers may have been less likely to receive social support from the community. The actual percentage of women susceptible to rubella may have fallen to a figure intermediate between those of pregnant women and female participants in the serosurvey.

As of October 2010, the WHO Region of the Americas and European Regions established rubella elimination goals for the years 2010 and 2015, respectively. Programs to eliminate rubella have indeed been successful in the USA⁸ and appear to have been successful in some European countries⁹ and the Americas.⁵ It will be

necessary to revise the strategy for rubella vaccination in Japan. The combined vaccination strategy with a universal approach, two doses in children 1 – 6 years of age and one dose in susceptible adult populations (both men and women) through a speed-up campaign, may have contributed to rubella elimination in a short time in some countries in the Americas.⁵ Treatment of CRS is costly and rubella vaccination programs are highly cost-effective.¹⁰

References

1. Minakami H, Kubo T, Unno N. Causes of a nationwide rubella outbreak in Japan, 2012 – 2013. J Infect (2013), [http:// dx.doi.org/10.1016/j.jinf.2013.09.002](http://dx.doi.org/10.1016/j.jinf.2013.09.002)
2. Japanese Ministry of Health, Labour, and Welfare. Rubella. Cited in 28 October 2013 from URL:
http://www.mhlw.go.jp/seisakunitsuite/bunya/kenkou_iryou/kenkou/kekkaku-kansenshou/rubella/
3. National Institute of Infectious Diseases (Japan); Rubella immunity status according to ages in 2012, 2011, 2010, 2009, and 2008.
Cited in 3 October 2013 from URL:
<http://www.nih.go.jp/niid/images/idsc/disease/rubella/RubellaHI-EIAtiter.pdf>,
<http://www.nih.go.jp/niid/ja/y-graphs/1911-rubella-yosoku-serum2011.html>,
<http://www.nih.go.jp/niid/ja/y-graphs/1912-rubella-yosoku-serum2010.html>,
<http://www.nih.go.jp/niid/ja/y-graphs/1914-rubella-yosoku-serum2009.html>, and
<http://www.nih.go.jp/niid/ja/y-graphs/1915-rubella-yosoku-serum2008.html>,
respectively.
4. Panagiotopoulos T, Antoniadou I, Valassi-Adam E. Increase in congenital rubella

occurrence after immunization in Greece: retrospective survey and systematic review.

BMJ 1999; 319: 1462–1467

5. Mongua-Rodriguez N, Díaz-Ortega J L, García-García L, Pina-Pozas M,

Ferreira-Guerrero E, Delgado-Sánchez G, et al. A systematic review of rubella

vaccination strategies implemented in the Americas: impact on the incidence and

seroprevalence rates of rubella and congenital rubella syndrome. Vaccine 2013; 31:

2145–2151

6. Galazka A. Rubella in Europe. Epidemiol Infect 1991; 107: 43–54

7. Yamada T, Cho K, Endo T, Hanatani K, Minakami H. Pregnancy outcome in women

with no antenatal care in Hokkaido, Japan 2008. Journal of Japan Society of Perinatal

and Neonatal Medicine 2009; 45: 1448–1455

8. Centers for Disease Control and Prevention. Elimination of rubella and congenital

rubella syndrome—United States, 1969-2004. MMWR 2005; 54 (11): 279–282

9. Muscat M, Zimmerman L, Bacci S, Bang H, Glismann S, Mølbak K, et al., and the

EUVAC.NET group. Toward rubella elimination in Europe: An epidemiological

assessment. Vaccine 2012; 30: 1999–2007

10. Babigumira J B, Morgan I, Levin A. Health economics of rubella: a systematic

review to assess the value of rubella vaccination. BMC Public Health 2013; 13:

406–417

Figure legends

Fig. 1: Prevalence rate of subjects susceptible to rubella during the 5-year period from 2008 to 2012

Numbers of pregnant women were 3,369, 4,268, 4,412, 4,056, and 4,258 for 2008, 2009, 2010, 2011, and 2012, respectively. Figures for female and male participants in the serosurvey were obtained from official websites of Japanese National Institute of Infectious Diseases.³ Totals of 1,274, 1,135, 1,297, 1,354 and 1,212 males participated in the serosurvey in 2008, 2009, 2010, 2011 and 2012, respectively.³ Totals of 1,596, 1,473, 1,806, 1,903 and 1,832 females participated in the serosurvey in 2008, 2009, 2010, 2011 and 2012, respectively.³

Figure 1

