

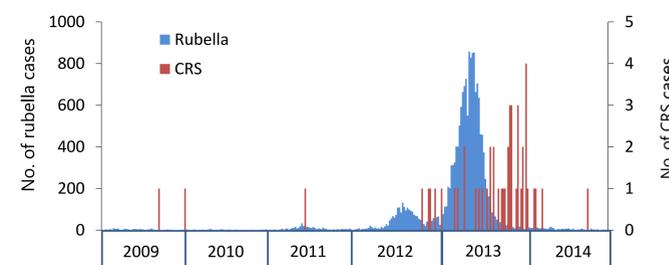
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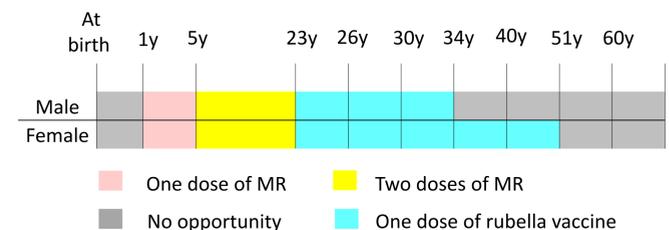
Introduction

- The public health importance of rubella is due to a potential risk to cause birth defects known as **congenital rubella syndrome (CRS)** if rubella infection occurred during the first 20 weeks of pregnancy ¹
- The main defects of CRS are known as classic triad; hearing impairment, congenital heart disease, and cataract ²
- In Japan, a large rubella outbreak occurred mainly among adults in their 20's to 40's in 2012-2013, and consequently CRS outbreak occurred in 2012-2014 ³

Epidemic curve of rubella and CRS in Japan, 2009-2016



Opportunities of receiving rubella-containing vaccine (RCV) by ages in 2013 through vaccination strategy to rubella and CRS in Japan



References

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- Bouthry E et al. Rubella and pregnancy: diagnosis, management and outcomes. Prenat Diagn. 34(13):1246-53. 2014
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Methods

- Conducted descriptive analysis of CRS cases notified to the national surveillance system between 2012 and 2014 (**Total 45 cases**)

Case definition of CRS

All cases are required to meet both clinical and laboratory criteria.

Clinical criteria

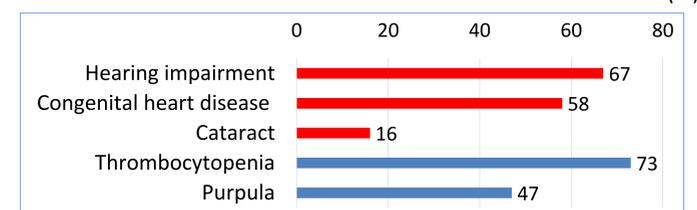
Fulfillment of at least one of the following conditions:
 cataract, congenital glaucoma, pigmentary retinopathy, hearing impairment, congenital heart disease, purpura, splenomegaly, microcephaly, mental retardation, meningoencephalitis, radiolucent bone disease, and jaundice within 24 hours after birth

Laboratory criteria

Fulfillment of at least one criterion below
 1) positive viral culture for rubella or detection of rubella virus by PCR from throat, saliva, or urine specimen
 2) positive blood test for rubella-specific IgM
 3) hemagglutination inhibition antibody levels sustained or higher than expected from passively transferred maternal antibody

- Collected epidemiological and clinical characteristics of CRS cases and their mothers by questionnaire to the physicians who diagnosed and notified CRS cases, and also interviews to several mothers of patient's association of CRS
- Ethics committee of NIID approved this study

Figure 1. Proportion of clinical manifestations of CRS cases at the time of diagnosis (N=45) (%)



- Only 7% of cases had all three manifestations of classic triad
- Other minor clinical manifestations are intracranial calcification (40%), followed by hepatomegaly (31%), splenomegaly (27%), and liver function abnormalities (22%)

Results

Table 1. Clinical characteristics of CRS cases (N=45)

	n (%)
Gender	
Male	25 (56)
Gestational age (weeks)	
Median (range)	38 (31-41)
Birth weight (g)	
Median (range)	2,262 (650-3290)
< 2500 g	30 (67)
Age at time of diagnosis	
0-3 months old	43 (96)
9 months old	1 (2)
13 months old	1 (2)
Outcome	
Dead	11 (24)

Table 3. Demographic and clinical characteristics of mothers (N=45) * Excluding one case of unknown status

	n (%)
Age (years)*	
Median (range)	25 (15-42)
Rubella symptoms during pregnancy	
Symptomatic	31 (69)
Asymptomatic	12 (27)
Unknown	2 (4)

Table 2. Clinical characteristics of fatal cases (N=11)

No.	Heart disease	Age at death (month)	Causes of death
1.	PDA, ASD, VSD, PS	0	Myocarditis suspect
2.	-	0	Severe neonatal asphyxia
3.	CoA	0	RDS, PPHN, CoA
4.	PDA	1	Unknown
5.	PDA	2	Portal hypertension
6.	PDA	3	Unknown
7.	PDA, PPS	3	Interstitial pneumonitis
8.	PDA	4	Interstitial pneumonitis
9.	PDA	5	Pneumocystis pneumonia
10.	PDA	6	Hemorrhage (Brain, Lung), Nephrotic syndrome
11.	PDA	15	RSV infection, Respiratory failure

ASD: Atrial septal defect, CoA: Coarctation of the aorta, PPHN: Persistent pulmonary hypertension of the newborn, PDA: Patent ductus arteriosus, PS: Pulmonary stenosis, PPS: Peripheral pulmonary stenosis, RSV: Respiratory syncytial virus, RDS: Neonatal respiratory distress syndrome, VSD: Ventricular septal defect

Figure 2. Vaccination history of rubella-containing vaccine (RCV) among mothers of CRS cases (N=45)



- No mother had history of two doses of RCV before pregnancy**

Summary

Total of 45 CRS cases were reported in 2012- 2014.

- Public health impact of CRS**
 - Case-fatality proportion was 24%
- Clinical characteristics of CRS**
 - Hearing impairment, congenital heart disease, thrombocytopenia, and low birth weight were most frequently reported
 - Majority of fatal cases were complicated by congenital heart diseases, and died before 6 months of age
 - Only 7 % of cases developed all three manifestations of classic triads
 - Two cases were diagnosed after 6 months of age due to late-onset manifestations
- Maternal characteristics of CRS cases**
 - None was born from mother with history of two doses of RCV before pregnancy

Conclusions

- Due to its high case-fatality proportion and possible lifelong physical or mental disabilities, CRS is of high public health impact in Japan
- Even if infant does not develop all manifestations of classic triad, suspecting CRS is important during rubella epidemic
- Providing two doses of RCV to all susceptible women before pregnancy is essential in preventing CRS

Acknowledgement

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