### Steps toward Measles Eradication in Japan— A report from Okinawa Prefecture

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### Okinawa, a Measles-endemic Prefecture in Japan

In 1998–1999, Okinawa Prefecture recorded 2,304 cases of measles, including 8 infant deaths. In 2001, measles affected 1,565 persons and killed 1 infant, as shown in **Fig. 1**. This figure highlights the remarkably high occurrence of measles in Okinawa in comparison with the national average. During this period, there were many measles patients whose condition was severe enough to require admission to ICUs. There also were many cases of gestational and perinatal measles and infant measles.

More than 450 patients with measles were admitted to Okinawa Prefectural Chubu Hospital in this period. The data of patients admitted to its ICU and patients with perinatal measles are discussed below.

There were 13 patients with measles who were admitted to the ICU, 6 male and 7 female children. Of these, 5 patients were aged less than a year, 7 were aged 1, and 1 was aged 3. Two patients were extremely low-birth-weight infants (730g and 898g) who had been discharged from the neonatal ICU. The major complications of measles observed were pneumonia and ARDS (acute respiratory distress syndrome) in 9 cases, encephalitis in 4 cases, and hemophagocytic syndrome in 2 cases, with some overlap; 4 patients died.

The cases of gestational and perinatal measles are shown in **Table 1**.<sup>1</sup> Eight pregnant and 3 postpartum women contracted measles. Maternal complications were spontaneous abortion in 2 cases and pneumonia in 1 case. Four of the neonates developed measles (**Table 2**).<sup>2</sup> One neonate developed pneumonia and recovered. There were no deaths in either the mothers or the neonates. Gestational and perinatal measles is known to result in a higher mortality rate than measles in women in general. Starting from this period we have been conducting an educational campaign in Okinawa, emphasizing that measles is a disease that can affect everybody, from neonates to adults.

#### The Activities of the Okinawa Zero Measles Project

The three main factors responsible for the ignominious situation in Okinawa as the prefecture with the highest measles prevalence are: 1) the low vaccination coverage (60-70%), 2) the low awareness of people that measles is a severe infectious disease, and 3) the insufficient activity and lack of collaboration among government and medical institutions. The Okinawa Zero Measles Project was launched to change this situation. This project was organized by the Okinawa Prefectural Government, Okinawa Medical Association, Okinawa Society of Child Health, Okinawa Pediatric Society, and Okinawa Branch of the Japan Pediatric Society, and is supported by various entities, including municipalities and the mass media. The Okinawa Society of Child Health serves as the project's secretariat and plays a central role in providing funding for its activities and workforce.3,4

The Zero Measles Project prepared "Guidelines for Measles Outbreak Response" and conducted a prefecture-wide program for the

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complete reporting of all measles cases. Whenever measles was found, a network of relevant organizations, mainly Public Health and Welfare Centers and the Prefectural Institute of Health and Environment, worked promptly to prevent the outbreak of measles through a series of actions, such as serological and virological diagnosis, isolation of patients, and tracking of people

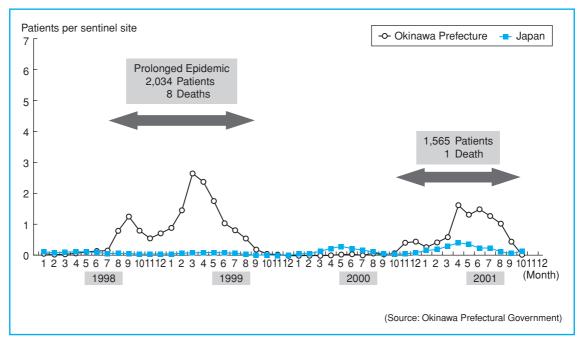


Fig. 1 Measles outbreaks in Okinawa Prefecture

Table 1	Gestational and	nerinatal	measles at	Okinawa	Prefectural	Chubu Hospital
	Gestational and	permatar	illeasies al	Okillawa	FIElectural	Chubu hospital

(1998-2001)

Case number	Age	Measles vaccination	Time of infection	Specific IgM	Specific IgG	Outcomes of the mother and child
1	22	Unknown	7 weeks gestation	13.4	19.7	Spontaneous abortion
2	30	No	7 weeks gestation	13.8	27.0	Spontaneous abortion, hepatic dysfunction
3	28	Unknown	9 weeks gestation	9.7	4.9	Spontaneous abortion, delivery (38 weeks)
4	37	Unknown	17 weeks gestation	16.7	90.6	Delivery (40 weeks)
5	22	Unknown	19 weeks gestation	13.7	12.9	Pneumonia, threatened abortion, delivery (38 weeks)
6	19	Yes	29 weeks gestation	6.5	12.0	Threatened abortion, delivery (40 weeks)
7	25	Yes	31 weeks gestation	13.3	25.0	Delivery (40 weeks)
8	18	No	38 weeks gestation			Delivery (38 weeks), neonatal measles
9	24	No	4 days postpartum			Neonatal measles
10	24	Unknown	8 days postpartum	13.0	8.7	Neonatal measles
11	27	Unknown	17 days postpartum			Neonatal measles

(Extracted from: Moriyasu Kohama. Perinatal Measles. In: Kaoru Ashimine, Masao Chinen, eds. The Day When Japan Becomes Measles-free. Tokyo: Nihon Shoni Iji Shuppansha; 2005:152–161.)

who were in contact with patients. IgM and PCR were used to confirm diagnosis, and genotyping was used to determine the source of infection. In 2005, Okinawa was successful in achieving no confirmed cases of measles. However, minor outbreaks still persist, including 18 cases in 2006, 22 in 2007, and 41 in 2008 (**Table 3**). Epidemiological studies and genotyping confirmed that many of these patients were tourists from outside the prefecture who had contracted the disease elsewhere, such as students on school trips and general travelers. However, the current vaccination coverage in the prefecture is insufficient to prevent outbreaks.

In Japan, currently the 2-dose measles vaccine is offered for four different age groups: 13–24 months (called Stage I), 5–6 years (preschool age) (Stage II), 12–13 years (Stage III), and 17–18 years (Stage IV). The third and fourth stages are being offered as part of a 5-year catch-up campaign to receive the second dose since 2008.<sup>5</sup> In Okinawa Prefecture, the measles vaccination coverage still remains low. As of the end of December 2008, the vaccination coverage was 68% for Stage II children (cf. the national average = 66.4%), 62.1% for Stage III (cf. 66.1%), and 51.1% for Stage IV (cf. 58.1%). With respect to Stages III and IV children, Okinawa is ranked among the lowest-performing prefectures. As seen in other prefectures, the low coverage of vaccination in urban areas is weighing down the performance of the prefecture as a whole. The vaccination coverage exceeds 90% on remote islands such as Miyako and Ishigaki.

Okinawa started its measles control efforts earlier than other prefectures in Japan in the form of the Zero Measles Project, which includes reporting of all cases, making prompt diagnosis, tracking people who have contacted with measles patients, and administering infant vaccination during outbreaks starting as young as 6 months of age. However, major outbreaks can still take place at any time in the future, considering the low vaccination coverage for Stages III and IV children.

The future challenge for us is to strengthen

Table 2 Reonatal measies at Oknawa Prefectural Onubu Hospital								
Case number	1	2	3	4				
Sex	Female	Male	Female	Male				
Days of diagnosis	3	9	14	14				
Fever	—	+	+	+				
Koplik Spots	—	-	+	+				
Rash	+	+	+	+				
Days of hospitalization	7	7	8	10				
Complication	_	_	_	pneumonia				

Table 3 Yearly trends in the number of reported and definitively diagnosed cases of measles in Okinawa

				(From J	anuary 1	to Dece	ember 31)
	2003	2004	2005	2006	2007	2008	Total
Reported cases	39	33	29	59	132	220	512
Number of serological tests performed (at medical institutions)	17	24	10	27	61	35	174
Number of virological tests performed	24	26	27	57	125	217	476
Confirmed cases of measles	19	16	0	18	22	41	116
Clinical diagnosis only	9	2	0	0	0	0	11
Clinical + laboratory tests	10	14	0	18	22	41	105

Zero measles occurrence was achieved in 2005.

collaboration among the Okinawa Medical Association, the Prefectural Government, and schools to improve the vaccination coverage among school-age children. Especially since the All-Japan Inter-High School Athletics Meeting will be held in Okinawa in 2010, the Okinawa Society of Child Health plans to strongly press the boards of education and administrative bodies to achieve the vaccination coverage of 100% by then. Gustafson and Brunell reported that measles outbreaks can occur in schools even when more than 99% of students have been vaccinated and more than 95% are immune.<sup>6</sup>

# Will the Day Come When Japan Is Measles-free?

Measles is endemic in Japan, and the country has repeatedly received WHO recommendations to improve measles control measures. Many countries, including those in the Americas, have already succeeded in eliminating measles. Our neighbor, the Republic of Korea, started a 2-dose vaccination program against measles in 1997, but a nationwide epidemic in 2000 that produced 49,000 patients and 7 deaths prompted the country to take more drastic measures to eliminate measles. In 2001, the measles-rubella (MR) vaccine was administered to more than 5 million students aged 8–16 nationwide, resulting in the Republic of Korea achieving zero measles occurrence in 2003.

In 2006, Japan finally started 2-dose measles vaccination, and a catch-up vaccination schedule for children aged 12–13 (Stage III) and 17–18 (Stage IV) was initiated in 2008.<sup>5</sup> Although individual vaccination is the norm, its coverage remain low. In contrast, mass vaccination is reported to achieve better coverage in many areas. While a few prefectures such as Fukui are achieving high vaccination coverage with individual vaccination, the national average for individual vaccination is alarmingly low, particularly in major urban areas.

The Ministry of Health, Labour and Welfare (MHLW) of Japan has announced a plan to eliminate measles from this country by 2012. Is it really possible to achieve this goal, considering the current circumstances in Japan? In my view, it is extremely difficult. I have been making proposals regarding the vaccination policies of Japan.<sup>7</sup> In the following, I recapitulate my opinion about what should be done.

The MHLW, in collaboration with the Ministry of Education, Culture, Sports, Science and Technology (MEXT), should express firm determination and take legal action to improve the vaccination coverage for Stages III and IV children. More specifically, MR vaccine administration should be made a mandatory condition for entrance into elementary school. Meanwhile, additional opportunities for immunization should be offered at high schools, universities, and other places. The expected objections should be refuted on the basis of social responsibility, citing the cases of countries that have succeeded in eliminating measles. Considering the convenience for students, mass vaccination should be promoted. This is likely to prove effective in urban areas. Although the MHLW and MEXT are formally advising local governments to encourage vaccination, they need to make firmer efforts to promote this 2-dose vaccination program as a national policy. In addition, vaccination coverage should be improved through more flexible implementation of the program, allowing students other than those in specific years of age to receive vaccination. It is rather unfair that students are exposed to the risk of infection because different school years receive vaccination at different times.

The National Institute of Infectious Diseases and the Japan Pediatric Society should use their influence on the MHLW and MEXT in the cause of protecting students from infection risks. They should not solely depend on the efforts made at the front line.

In the cause of protecting children's health, all citizens of Japan, including the mass media, should fulfill their responsibilities and seriously strive to achieve the 100% coverage of vaccination.

# Raising the Vaccination System in Japan to International Standards

Why is Japan so behind in measles control, despite its economic power in the world? Several factors have been pointed out as causes of the low vaccination coverage in Japan.<sup>8</sup> Many pediatricians consider that we might benefit from having an advisory system like the Advisory Committee on Immunization Practice (ACIP) that the Center for Disease Control and Prevention (CDC) in USA has.

It is important to have physicians control licensure and recommendations for vaccines. They also must be responsible for gathering basic epidemiological data and enforcing immunization policy. The longer we wait to correct problems in Japan, the more serious the consequences on children's health will be. To build a vaccination system that measures up to international stan-

dards, it is essential that not only national government organizations but also local governments, school personnel, and individual citizens improve awareness and take action.

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