

# Current Incident Status of Vaccine-Preventable Bacterial and Viral Infectious Diseases in Japan

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## Abstract

An important step to evaluate infection control measures of a country is to understand its current disease epidemiology status. Accurate understanding of the current disease status allow us identify the area that needs to be improved, evaluate vaccine effectiveness, and reveal the needs to introduce new vaccines for public relief. This paper discusses the occurrence of vaccine-preventable bacterial and viral infectious diseases in Japan, referring to the surveillance results conducted by Infectious Disease Surveillance Center of National Institute of Infectious Diseases and other sources.

The current surveillance data for the diseases under the routine vaccination program shows that measles and rubella are controlled well, while the tendency of increase in pertussis in young adults calls for the improvement of vaccination strategies. The data for the diseases under voluntary vaccination revealed a lack of preventive effect in the overall population as a result of low vaccination coverage.

In order to rectify this situation, it is important to take measures such as revising the routine vaccination program to include currently voluntary vaccines, approving vaccines that have not been approved in Japan, and promoting the use of newly approved vaccines. It is also necessary to expand the response system including enriching the surveillance of vaccine-preventable diseases.

**Key words** Vaccination, Vaccine-preventable disease, Surveillance, Epidemiology

## Introduction

An important step to assess infection control measures of a nation is the correct grasping of present status. Accurate understanding helps us identify the merits and problems of the present system, evaluate vaccines, and consider the need to introduce new vaccines.

**Table 1** shows the situation of vaccine-preventable diseases in Japan from 2000 to 2008. The data for some diseases are based on all reported cases, while some are based on the reports provided by the physician and medical facilities designated as sentinel sites for surveillance. This article reviews the occurrence of two groups of vaccine-preventable diseases; the diseases covered under routine (compulsory)

vaccination program, and the others that are covered under voluntary vaccination as well as by vaccines that are used in overseas but not in Japan.

## Diseases under the Routine Vaccination Program

The Preventative Vaccination Law (also known as the Preventative Vaccination Act) of Japan specifies routine vaccination against eight Class-1 diseases (polio, diphtheria, tetanus, pertussis, measles, rubella, Japanese encephalitis, and tuberculosis) and one Class-2 disease, influenza. Of those, current epidemiology of the diseases covered by the routine vaccination program (except tuberculosis and influenza) is discussed in this section.

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**Table 1 The cumulative numbers of reported cases for diseases under total surveillance of all cases and those under surveillance at sentinel sites based on the infectious diseases surveillance study in Japan (as of March 4, 2009)**

Category	Disease	Method	2000	2001	2002	2003	2004	2005	2006	2007	2008
Under routine vaccination (class-1 & -2 diseases)	Diphtheria	T	0	0	0	0	0	0	0	0	0
	Tetanus	T	91	80	106	73	101	115	117	89	123
	Pertussis	P	3,804	1,760	1,458	1,544	2,189	1,358	1,504	2,932	6,753
	Polio	T	1 <sup>†</sup>	0	0	0	0	0	0	0	2 <sup>†</sup>
	Measles* (excluding adult measles)	P/T	2,552	33,812	12,473	8,285	1,547	537	516	3,133	4,446
	Adult measles*	B/T	426	931	440	462	59	7	39	975	6,561
	Rubella*	P/T	3,123	2,561	2,971	2,795	4,239	895	509	463	303
	Congenital rubella syndrome	T	1	1	1	1	10	2	0	0	0
	Japanese encephalitis	T	7	5	8	1	5	7	7	10	3
	Influenza	I	769,964	305,441	747,010	1,162,290	770,063	1,563,662	900,181	1,212,042	621,447
Under voluntary vaccination	Varicella	P	275,036	271,409	263,308	250,561	245,941	242,296	265,453	245,880	224,835
	Epidemic parotitis	P	132,877	254,711	180,827	84,734	127,592	187,837	200,639	67,803	65,361
	Hepatitis A	T	381	491	502	303	139	170	320	157	170
	Hepatitis B	T	425	330	332	245	241	209	228	198	179
Diseases preventable by non-approved vaccines	Bacterial meningitis	B	256	278	300	298	379	309	350	383	410
	Penicillin-resistant pneumococcal infection	B	4,321	5,254	6,132	6,447	6,692	6,233	5,294	4,840	5,257
	Infectious gastroenteritis	P	886,174	874,241	889,927	906,803	952,681	941,922	1,148,962	989,647	1,056,747

[Method] T: total surveillance, P: pediatric facilities designated as sentinel sites (approx. 3,000 in Japan), I: basic sentinel sites (hospitals practicing internal medicine and pediatrics accommodating 300 or more patients, approx. 500), B: sentinel sites for influenza (approx. 5,000 in internal medicine + 3,000 in pediatrics).

\* An adult measles patient is defined as the measles patient aged 18 years or older until April 2006. From April of 2006, it was redefined as 15 years or older. Additionally, the monitoring method for measles and rubella was changed to total reporting of all cases on January 1, 2008.

† Cases caused by vaccine strains.

Notes 1) The reports of the diseases under total surveillance are provided by all the physicians and medical institutions that made the diagnosis. Those diseases under surveillance at sentinel sites only are provided by pediatric sentinel sites, basic sentinel sites, and sentinel sites for influenza, which cover roughly 10% of all patients.

2) Although tuberculosis is also listed as a Class-1 disease under Preventive Vaccination Law in Japan, it is not shown in this table. Please refer to the website of the Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association <http://jata.or.jp/rit/ekigaku/> for the trend of tuberculosis occurrence.

[Source: NIID, IDSC. Infectious Diseases Surveillance Study. Cumulative Number of Reported Cases (Diseases under Surveillance at Sentinel Sites) <http://idsc.nih.go.jp/vaccine/freport.html>, extracted and modified.]

**Polio (acute poliomyelitis):** Physicians in Japan are required to report all polio cases to the authority. With high vaccination coverage, no cases of wild strain polio have been reported in Japan since 1980. On the other hand, 21 cases of post-vaccination paralysis (vaccine-associated paralytic poliomyelitis, VAPP) has been reported as virologically confirmed cases from 1981 to 2007 (data obtained from Japan Polio Eradication Committee). The countries that have achieved polio control are increasingly introducing the use of inactivated polio vaccine (IVP) to avoid the risk of VAPP, and a clinical study for the approval of this vaccine is in progress in Japan.

**Diphtheria/pertussis/tetanus:** DPT vaccine is a combination vaccine against these three diseases. Last reported case of diphtheria was in 1999 for one case.<sup>1</sup>

Tetanus is reported to occur about 100 cases every year. After the routine DPT vaccination began in 1968, the numbers of patients and deaths decreased dramatically. Recent reported cases include very few patients in the generations that received routine vaccination. Thus, the vaccine appears to have achieved good control of tetanus.

Pertussis is the only disease occurring in large numbers among the target diseases of the DPT vaccine. Apart from the number of patients, a notable trend is the shift in the age distribution of patients, from children to adolescents and adults. This trend, also observed in the U.S.A. and other countries with well-developed vaccination systems, has been attributed to the gradual decrease in antibodies acquired through pertussis vaccination as well as the growing awareness of elderly pertussis patients in physicians.<sup>2</sup> As a counter-measure, the U.S. government has included a combination vaccine against three diseases including pertussis designed for adults (Tdap) as a part of the routine vaccination program since 2005. Japan should also consider the relevance of additional vaccination to cover pertussis in adolescents and adults without delay.

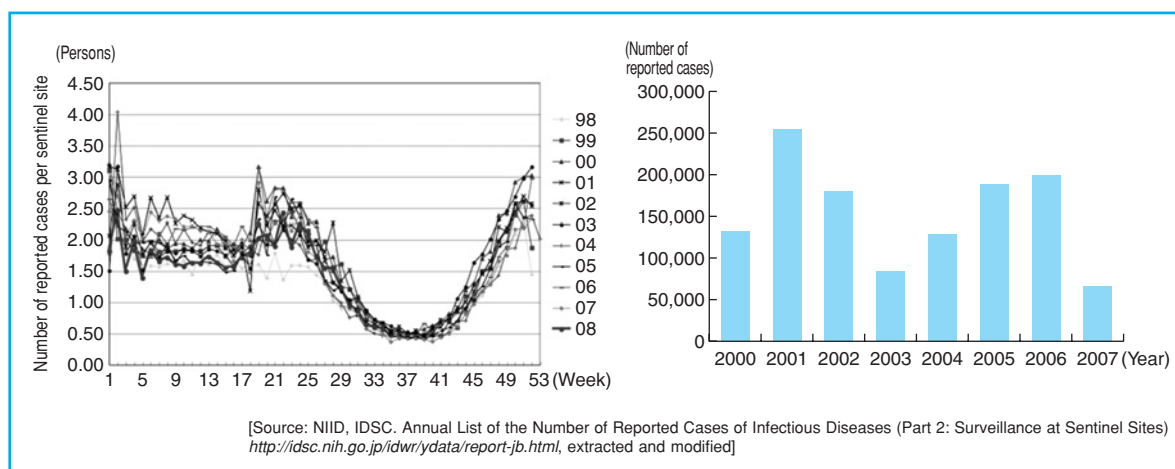
**Measles:** Previously, the measles vaccine as part of the routine vaccination program in Japan was 1-dose immunization at 12–90 months after birth. The combination vaccine against measles and rubella (MR vaccine) was introduced in April 2006, and a 2-dose immunization program using MR vaccines started in June 2006.<sup>3</sup> Under this new system, the first dose is to be given at age 1 (Stage I), and the second dose at ages 5–6 (Stage

II). However, in response to the measles outbreak that mainly affected the age group of 10–29 in 2007,<sup>4</sup> a 5-year interim measure was put in place for schoolchildren from 2008 to 2012, providing two additional vaccination opportunities of the second dose to be given at either Stage III (for ages 12–13, corresponding to the first year in junior high school in Japan) or Stage IV (ages 17–18, corresponding to the third year in high school). Furthermore, the surveillance method was changed in January 2008 from sentinel sites' reports only to all-case reporting. This change is expected to help grasping the measles occurrence correctly and improve the ability to take counteractions in the future.

Under the initiative of World Health Organization, the world is moving toward the elimination of measles. Eradicating measles from Japan is important both as a developed country fulfilling its responsibility and as the measure to protect infants aged less than 1 year who are still too young to be vaccinated. It is therefore highly desirable to further improve measles vaccination coverage in Japan.

**Rubella:** As was in measles, rubella has been monitored based on the reporting of all cases since January 2008, allowing us to expect further improvement of disease control in the future. The main problem associated with rubella is the frequent development of congenital rubella syndrome (CRS), in which the primary infection of a mother during her first half of pregnancy further infects the fetus and results in various symptoms including congenital defects. Just as measles, CRS should be eliminated by sufficient vaccination in women of childbearing age and younger.

**Japanese encephalitis:** While over 100 people contracted Japanese encephalitis every year in the first half of the 1970s, the annual number of patients has been less than 10 in recent years. The improvement of pig breeding practice (the pig is the host of the Japanese encephalitis virus), the decrease in exposure to the mosquitoes carrying the pathogen, and the changes in people's living environment—all those contributed to this drastic decrease, but the main factor is believed to be the promotion of vaccination.<sup>5</sup> However, evidence still shows the frequent occurrence of pigs that are positive for the antibodies against the Japanese encephalitis virus, especially in the western parts of Japan. The inferred presence



**Fig. 1** Number of varicella patients reported per sentinel site in Japan showing weekly trends in each year (1998–2008) (left), and the annual trends in the cumulative number of mumps cases reported from sentinel sites (2000–2007) (right)

Both varicella and mumps show no changes in the epidemic cycles in Japan, indicating the lack of effectiveness of vaccination in terms of disease control.

of the Japanese encephalitis virus in Japan calls for continuing vigilance. On February 23, 2009, a freeze-dried, cell culture-derived Japanese encephalitis vaccine was approved under the Pharmaceutical Affairs Law. Even with this new vaccine, it is nevertheless important to make efforts for successive prevention.

### Diseases Not Covered by the Routine Vaccination Program in Japan

**Varicella:** In Japan, the majority of reported varicella cases are infants and young school-age children. The number of reported cases increases in winter and spring (Fig. 1, left). Many people are infected by varicella virus by the age of 10, and as many as 90–95% of adults are positive for the varicella antibody. The high infectivity of varicella ranks next to that of measles ( $R_0$  [basic reproduction number] 7–11). The likelihood of transmission within a household is 80–90%, and asymptomatic infection is rare (See Table 1 for the cumulative number of cases at sentinel sites).

**Mumps:** Epidemics of mumps are reported every year in Japan, increasing and decreasing in cycles of 3 to 4 years (Fig. 1, right). The age distribution of patients shows that there are few patients aged less than 1 year. But the number increases as the age goes up, and approximately 60% of all patients are 3 to 6 years of age.<sup>6</sup> (See Table 1 for

the cumulative of number of cases reported from sentinel sites).

Unfortunately, the vaccination coverage of varicella and mumps in Japan are both low, at about 30%. The epidemic cycles of these diseases are therefore following their natural courses, and the effectiveness of vaccination in terms of disease control is virtually absent. The introduction of MMR (measles-mumps-rubella) vaccine in 1991 temporarily lowered the prevalence of mumps in Japan to the lowest level since the surveillance of this disease started. In the U.S.A., where the varicella vaccine is included in the routine vaccination program, the vaccination coverage in the children aged 19–35 months increased to 85% by 2002, resulting in substantial decreases in varicella outbreaks and the number of hospitalized patients.<sup>7</sup> Considering the fact that varicella vaccine was developed in Japan by the pioneering work of Dr. Michiaki Takahashi, professor emeritus at Osaka University, Japan should strive to improve the vaccination coverage and disease control by including varicella vaccine into the routine vaccination program and through other efforts.

**Bacterial meningitis:** Children less than 5 years of age represent about one-half of the cases of bacterial meningitis in Japan, followed by the elderly. The most common causative agents are *Haemophilus influenzae* followed by *Streptococcus*

*pneumoniae*. The vaccine against *H. influenzae* type b (Hib) was approved under the Pharmaceutical Affairs Law of Japan on January 26, 2007. In the U.S.A., this vaccine was incorporated into the routine vaccination program in the latter half of the 1980s and achieved very high vaccination coverage, which contributed to the 99% drop in the number of patients.<sup>8</sup> The vaccine against *Streptococcus pneumoniae* was licensed in Japan in December 2009. This vaccine has dramatically reduced the number of meningitis induced by pneumococcal infection in the U.S.A., already. To observe similar successes in Japan with these two vaccines, we need to accomplish very high vaccination coverage.

## Discussion

In Japan, a disease which vaccine fee is covered by the routine vaccination program under the Preventive Vaccination Law has high vaccination coverage and is relatively well controlled. For example, a remarkable decrease has been seen in the occurrence of measles with the catch-up campaign since 2007. On the other hand, the number of pertussis cases is increasing among adolescents and adults in spite of the high vaccination coverage of the DPT vaccine. It is important to consider actions against pertussis for the

future, including the possibility of administering additional vaccinations.

With respect to the diseases not covered by the routine vaccination program, surveillance results show that outbreaks are repeated every year, following similar patterns. Unfortunately, voluntary vaccines are not showing effectiveness in disease control since the vaccination rate of these vaccines are much lower than those of routine vaccines. Raising vaccination coverage will be the key to decrease disease incidence.

There are many issues we need to address in the vaccination system of Japan. The Hib vaccine, PCV7 (pneumococcal conjugate vaccine), and human papilloma virus (HPV) vaccine, all of which were recently approved in Japan, should be included in the routine vaccination program to achieve high coverage. Also, surveys, research, and surveillance to resolve these issues must start promptly.

Accurate data from well maintained surveillance studies provide us the information to understand current situations on vaccine-preventable diseases. Such information is also important when discussing issues on vaccine policy. Thus, it is important to maintain the high-quality surveillance, which will be achieved through cooperation between the people involved in the vaccination program and physicians.

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