Original Article

Effects of a Public Subsidy Program for Mumps Vaccine on Reducing the Disease Burden in Nagoya City, Japan

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SUMMARY: Nagoya City initiated a public subsidy program for mumps vaccination using either the Torii or Hoshino strains in August 2010. To determine the effects of the program, we used publicly available information from Nagoya City to investigate the changes in immunization rates and numbers of patients who developed post-immunization adverse reactions, including post-vaccinal aseptic meningitis, in the 7 years since its initiation. We also investigated the numbers of mumps patients reported by sentinel sites in a national database during this period. The immunization rate in one-year-old children increased from 24.3% before the program to 91.0% after 7 years. The mean numbers of reported mumps cases per sentinel site in one-year-old to preschool children—the age groups targeted by the program—were 12.9 in the 7 years before the program and 4.93 in the 7 years after initiation of the program, showing a significant decrease of 1/2.6 ($p = 0.01$). The number of vaccinations during the 6.5-year period was 140,316, with only one case of aseptic meningitis reported (0.7 cases/100,000 vaccinations). No other serious adverse reactions were observed. The present findings demonstrate that the public subsidy program in Nagoya City is an effective and safe measure against mumps in children.

INTRODUCTION

In Japan, voluntary immunization with a monovalent mumps vaccine was initiated in 1981. At that time, 5 different vaccine strains (Urabe AM9, Torii, Hoshino, Miyahara, and NK-M46) were used. In April 1989, routine immunization started with the Japanese standard-type measles-mumps-rubella (MMR) vaccine, including the Urabe AM9 strain as the mumps vaccine (1). However, frequent occurrence of aseptic meningitis, higher than 1/2000, caused by the mumps vaccine strain (1), became apparent. Consequently, in October 1991, immunization with novel MMR vaccines from 3 vaccine manufacturers using the Urabe AM9 (Biken), Torii (Takeda), or Hoshino (Kitasato) mumps strains was started. However, the incidence of aseptic meningitis remained similar, leading to cessation of the use of all MMR vaccines in April 1993. Later, monovalent mumps vaccines involving the Torii, Hoshino, or Miyahara strains were again used for voluntary immunization. In recent years, the immunization rate has been 30–40% in children one to 6 years of age, and an epidemic of mumps occurs

every 4–5 years (2). The disease burden of mumps in Japan is still considered to be high. Kawaguchi et al. (3) reported a high hospitalization rate of 18% due to mumps in a local hospital. The Oto-Rhino-Laryngological Society of Japan reported at least 348 cases of hearing disturbances after mumps in 2015 and 2016 (4).

Nagoya City is the capital of Aichi Prefecture, located near the center of Japan. The estimated total population of Nagoya City was 2,311,132 (based on the statistics available from the Nagoya City and Aichi Prefecture websites) on April 1, 2018, making Nagoya City the 3rd largest metropolitan area in Japan. Nagoya City initiated a public subsidy program for mumps vaccination in August 2010, in which one to 6-year-olds could receive the vaccine at an out-of-pocket cost of 3,000 yen (5). With the initiation of the subsidy program, education for mumps vaccination to care givers was promoted in the same way as for routine vaccines by local pediatricians. It was expected that the introduction of this system would relieve children of the disease burden of mumps. However, there was concern that the resulting increase in vaccine recipients may also increase the number of post-vaccinal aseptic meningitis cases. In this study, we used publicly available information from Nagoya City to investigate the changes in immunization rates and the status of reported post-immunization adverse reactions, including aseptic meningitis, from the start of the subsidy program in fiscal year 2010 to fiscal year 2016. We also investigated the numbers of mumps patients reported by sentinel sites in the National Epidemiological

Received August 3, 2018. Accepted October 11, 2018.

J-STAGE Advance Publication October 31, 2018.

DOI: 10.7883/yoken.JJID.2018.276

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Surveillance of Infectious Diseases Program and examined the effects and safety of the public subsidy program for mumps vaccination.

MATERIALS AND METHODS

Vaccines: The vaccines administered in the public subsidy program are freeze-dried live attenuated mumps vaccines using the Hoshino strain (brand name: Freeze-dried Live Attenuated Mumps Virus Vaccine “Kitasato-daiichisankyo”; Kitasato Daiichi Sankyo Vaccine Co., Ltd.) (6) or the Torii strain (brand name: Dried Live Attenuated Mumps Vaccine (Torii Strain); Takeda Pharmaceutical Company Limited) (7). For both vaccines, one vial of vaccine is dissolved in 0.7 mL of accompanying solvent (Japanese Pharmacopoeia: water for injection), and 0.5 mL of the solution is injected subcutaneously once. Each 0.5 mL dose contains at least 5,000 50% cell culture infective doses of live attenuated mumps virus.

Sources of data: The number of vaccine recipients by age in Nagoya City were obtained from “Prevention of tuberculosis and infectious diseases” of the Annual Report on Health and Welfare in Nagoya City (8). For each age group, the immunization rate was calculated by dividing the number of vaccine recipients by the number of targeted children in that age group per year, and the results were expressed as a percentage. The accumulated immunization rate was calculated by dividing the total number of vaccine recipients in that year and the previous years by the number of targeted children, and the results were expressed as a percentage. In the Japanese National Epidemiological Surveillance of Infectious Diseases System, mumps is a disease that must be reported by sentinel sites (category V infectious disease defined by the Infectious Disease Control Law), and designated notification facilities (3,000 pediatric sentinel medical facilities in Japan) are required to report the number of mumps patients to public health centers every week. Over the relevant period, there were 70 to > 80 pediatric sentinel medical facilities in Nagoya City. For the numbers of mumps patients reported by the pediatric sentinel medical facilities in Nagoya City, “The number of patients reported from the National Epidemiological Surveillance of Infectious Diseases Program (weekly report), by disease, ward, month, and age group” of the Annual Report on Health and Welfare in Nagoya City was cited (8). Post-vaccinal adverse reactions to the mumps vaccine were obtained from the Annual Report of Control of Infectious Diseases in Nagoya City. These were spontaneously reported by medical institutions and/or guardians responsible for the immunization of children (9). For the numbers of mumps patients across Japan, the tables with the numbers of cases reported in the National Epidemiological Surveillance of Infectious Diseases (sentinel surveillance) by the National Institute of Infectious Diseases were cited (10).

Statistical analysis: To test the significance of differences in mean numbers reported by sentinel sites between the periods before and after initiation of the public subsidy program, the homogeneity of variance was initially checked, followed by a *t*-test. All tests were two-sided with a significance level of 0.05. The statistical analyses were performed with the SAS version 9.3 soft-

ware (SAS Institute Inc., Cary, NC, USA).

RESULTS

Immunization rates after the start of the public subsidy program: The immunization rates are shown in Fig. 1 and the changes in the accumulated immunization rates are shown in Fig. 2. The changes in immunization rates in one-year-old children and the accumulated immunization rates by age were evaluated. In one-year-old children, the immunization rate was 24.3% in 2010, the first fiscal year of the subsidy program, and then increased annually (Fig. 1). The rate reached 91.0% in fiscal year 2016, being 3.7-times higher than that of the first fiscal year (Fig. 1).

Fig. 1. Changes in immunization rates after initiation of the subsidy program. The immunization rate was 24.3% in 2010, the first fiscal year of the subsidy program, and then increased annually. The rate reached 91.0% in fiscal year 2016, being 3.7-times higher than the rate in the first fiscal year.

Fig. 2. Changes in accumulated immunization rates after initiation of the subsidy program. In fiscal year 2016, the accumulated immunization rates in 1–6-year-old children, as the targets of the subsidy program, were as follows: 91.0% in 1-year-old children; 91.4% in 2-year-old children; 94.4% in 3-year-old children; 93.3% in 4-year-old children; 88.1% in 5-year-old children; and 84.3% in 6-year-old children.

The accumulated immunization rate of 2–6-year old children was unidentified because the number of previous immunizations was unidentified in Nagoya city under the lack of a public subsidy program before 2009. In fiscal year 2016, the accumulated immunization rates in one–6-year-old children, as the targets of the subsidy program, were as follows: 91.0% in one-year-old children; 91.4% in 2-year-old children; 94.4% in 3-year-old children; 93.3% in 4-year-old children; 88.1% in 5-year-old children; and 84.3% in 6-year-old children (Fig. 2).

Changes in the numbers of mumps patients reported by sentinel sites before and after initiation of the public subsidy program: The mean numbers of reported mumps patients per sentinel site in the 7 years before and 7 years after initiation of the subsidy program in Nagoya City are shown in Table 1 and Fig. 3. In one-year-old children, the mean number of reported mumps patients per sentinel site in the 7 years before the subsidy program was 0.67, while the corresponding number in the 7 years after initiation of the subsidy program was 0.23, showing a significant decrease of 1/2.9 ($p = 0.01$). Similarly, the numbers of reported mumps patients per sentinel site decreased significantly from 1.45 to 0.48 in

2-year-old children (1/3.0, $p < 0.01$), from 2.48 to 0.83 in 3-year-old children (1/3.0, $p = 0.01$), from 3.10 to 1.19 in 4-year-old children (1/2.6, $p = 0.01$), from 3.10 to 1.30 in 5-year-old children (1/2.4, $p = 0.02$), and from 2.07 to 0.90 in 6-year-old children (1/2.3, $p = 0.01$). In the total population of one–6-year-old children, the age groups targeted by the subsidy program, the number of reported mumps patients per sentinel site decreased from 12.9 to 4.93, showing a significant decrease of 1/2.6 ($p = 0.01$).

The mean numbers of reported mumps patients per sentinel site before and after initiation of the subsidy program in all age groups are shown in Table 2. The mean number of reported mumps patients per sentinel site in the 7 years before the subsidy program was 17.0, while the corresponding number in the 7 years after initiation of the subsidy program was 7.5, showing a significant decrease of 1/2.3 ($p = 0.01$). In the whole of Japan at the corresponding times, the numbers of reported mumps patients per sentinel site were 39.5 and 29.9, respectively, showing no significant decrease ($p = 0.36$).

Reported adverse reactions after mumps immunization: The adverse events from unsolicited sources

Table 1. Comparisons of the numbers of reported mumps patients per sentinel site before and after initiation of the public subsidy program by age

Age	Item	Before public subsidy program							After initiation of public subsidy program							Rate of decrease
		2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	
1-yr-old children	No. of patients	46	103	72	38	34	50	38	44	24	19	19	9	7	13	1/2.9
	No. of sentinel sites	70	81	81	82	86	86	86	86	86	83	83	84	84	84	
	No. of reports per site	0.66	1.27	0.89	0.46	0.40	0.58	0.44	0.51	0.28	0.23	0.23	0.11	0.08	0.15	
	Mean				0.67							0.23				
	p-value								p = 0.01							
2-yr-old children	No. of patients	105	189	155	120	63	109	79	81	53	47	28	26	25	23	1/3.0
	No. of sentinel sites	70	81	81	82	86	86	86	86	86	83	83	84	84	84	
	No. of reports per site	1.50	2.33	1.91	1.46	0.73	1.27	0.92	0.94	0.62	0.57	0.34	0.31	0.30	0.27	
	Mean				1.45							0.48				
	p-value								p < 0.01							
3-yr-old children	No. of patients	180	395	270	171	97	161	131	142	79	93	69	30	36	43	1/3.0
	No. of sentinel sites	70	81	81	82	86	86	86	86	86	83	83	84	84	84	
	No. of reports per site	2.57	4.88	3.33	2.09	1.13	1.87	1.52	1.65	0.92	1.12	0.83	0.36	0.43	0.51	
	Mean				2.48							0.83				
	p-value								p = 0.01							
4-yr-old children	No. of patients	272	415	323	211	153	210	163	192	100	130	94	69	44	76	1/2.6
	No. of sentinel sites	70	81	81	82	86	86	86	86	86	83	83	84	84	84	
	No. of reports per site	3.89	5.12	3.99	2.57	1.78	2.44	1.90	2.23	1.16	1.57	1.13	0.82	0.52	0.90	
	Mean				3.10							1.19				
	p-value								p = 0.01							
5-yr-old children	No. of patients	247	486	270	216	149	214	171	194	111	147	116	69	49	83	1/2.4
	No. of sentinel sites	70	81	81	82	86	86	86	86	86	83	83	84	84	84	
	No. of reports per site	3.53	6.00	3.33	2.63	1.73	2.49	1.99	2.26	1.29	1.77	1.40	0.82	0.58	0.99	
	Mean				3.10							1.30				
	p-value								p = 0.02							
6-yr-old children	No. of patients	150	302	202	140	99	159	124	112	73	93	66	70	43	77	1/2.3
	No. of sentinel sites	70	81	81	82	86	86	86	86	86	83	83	84	84	84	
	No. of reports per site	2.14	3.73	2.49	1.71	1.15	1.85	1.44	1.30	0.85	1.12	0.80	0.83	0.51	0.92	
	Mean				2.07							0.90				
	p-value								p = 0.01							
1–6-yr-old children	No. of reports per site	14.3	23.3	16.0	10.9	6.9	10.5	8.2	8.9	5.1	6.4	4.7	3.3	2.4	3.8	1/2.6
	Mean				12.9							4.93				
	p-value								p = 0.01							

Effects of Subsidy Program for Mumps Vaccine

Fig. 3. Changes in the numbers of mumps patients reported by sentinel sites before and after initiation of the public subsidy program. The mean numbers of reported mumps patients per sentinel site in 7 years after the subsidy program decreased approximately 1/3 comparing to before this program. In the total population of 1–6-year-old children, as the age groups targeted by the subsidy program, the number of reported mumps patients per sentinel site decreased from 12.9 to 4.93, showing a significant decrease of 1/2.6 ($p = 0.01$).

Table 2. Numbers of reported mumps patients per sentinel site before and after initiation of the public subsidy program

Fiscal yr	Nagoya City ¹⁾		Japan ²⁾	
	No. of reported cases per sentinel site	Mean	No. of reported cases per sentinel site	Mean
2003	19.0	17.0	27.9	39.5
2004	30.5		42.3	
2005	21.0		61.3	
2006	14.4		66.6	
2007	9.5		22.5	
2008	13.6		21.7	
2009	10.8		34.6	
2010	12.2	7.5	59.3	29.9
2011	7.3		43.8	
2012	9.4		22.8	
2013	7.6		13.1	
2014	5.1		14.7	
2015	4.3		25.8	
2016	6.8		ND	
<i>p</i> -value	$p = 0.01$		$p = 0.36$	

ND, no data in the study term.

¹⁾: Annual Report on Health and Welfare in Nagoya City <Projects Part> (fiscal yr 2003–2016).

²⁾: The National Institute of Infectious Diseases: Tables for the number of reported cases in the National Epidemiological Surveillance of Infectious Diseases (sentinel surveillance). Diseases were monitored by pediatric sentinel surveillance for epidemic parotitis (fiscal yr 1999–2016).

Table 3. Adverse reactions after mumps immunization from fiscal year 2010 to fiscal year 2016¹⁾

	Case 1	Case 2
Fiscal yr when case was reported	2015	2015
Vaccine	Mumps	Mumps, chickenpox, measles-rubella, and influenza
Age	6 yr and 9 mon	1 yr and 6 mon
Sex	Girl	Girl
Adverse reaction	Aseptic meningitis	Possible exanthema associated with viral infection
Incidence rate of aseptic meningitis	0.7 patients/100,000 doses (1 patient/140,316 doses ²⁾)	—

¹⁾: Annual Report on Infection Control Measures in Nagoya City (fiscal yr 2010–2016).

²⁾: Annual Report on Health and Welfare in Nagoya City <Projects Part> (fiscal yr 2003–2016).

after immunization are shown in Table 3. The combined total number of the mumps vaccines administered between the start of the subsidy program and fiscal year 2016 was 140,316, with 2 cases of adverse reactions associated with immunization being reported. One case was that of a girl aged 6 years and 9 months, who developed aseptic meningitis in fiscal year 2015, and the other case was that of a girl aged one year and 6 months, who had post-vaccinal exanthema with mumps, chickenpox,

measles-rubella, and influenza vaccine by simultaneous inoculation, in fiscal year 2015. The incidence rate of aseptic meningitis after mumps vaccination was 0.7 patients/100,000 doses (one patient/140,316 doses).

DISCUSSION

In Japan, the use of MMR vaccines was stopped in April 1993. Thirteen years later, in April 2006, measles-rubella (MR) vaccination was included in routine immunization programs. Nevertheless, 25 years after MMR vaccination was stopped, mumps vaccination remains voluntary. In fiscal year 1993, the total domestic production of monovalent mumps vaccines was 388,000 doses. In fiscal year 2016, the production had increased 4.3-fold, to 1,661,000 doses (11), and there were over 200

municipalities with public subsidy of mumps vaccination as of May 27, 2016 (12). Calls for routine immunization with mumps vaccines are increasing (13–15).

According to the Subcommittee on Basic Vaccination Policy of the Committee on Immunization and Vaccines of the Health Sciences Council, a prerequisite for instituting routine immunization with a mumps vaccine is the availability of a vaccine that is expected to be safer than previous vaccines, and it was proposed that a new MMR vaccine should be developed (16). However, as of January 2018, no novel vaccine is expected to be approved. Meanwhile, among studies evaluating the safety (17,18), efficacy (13,17,19), and cost-effectiveness (14,15) of currently available monovalent mumps vaccine strains in Japan, the consensus is that the monovalent mumps vaccines are appropriate for routine immunization. Nevertheless, it is difficult to incorporate them in routine immunization which were previously excluded from use, without obtaining new safety data because of safety concerns in routine immunization.

In Nagoya City, the number of one-year-old children targeted for immunization in fiscal year 2016 was 19,755, the highest total among the municipalities that subsidize mumps immunization. The subsidy program was initiated in August 2010 (5) and covers children from the age of one year to children entering elementary school in the next fiscal year, who are registered residents in Nagoya City and have not previously received mumps vaccine or have a history of mumps. The subsidy covers one dose with an out-of-pocket cost of 3,000 yen (5). Since fiscal year 2013, individual notifications (information about immunization and sticker-type tickets for immunization) have been sent to the target families of the public subsidy program for mumps vaccination around the first birthday of the child (20). Mumps vaccination is recommended, and care givers are educated in a similar way to that used for routine immunization. We consider that this approach resulted in the immunization rate of > 90%. With the increase in immunization rates, the mean number of reported mumps patients per sentinel site showed a significant decrease from 12.9 in the 7 years before the subsidy program to 4.9 in the 7 years after initiation of the subsidy program ($p = 0.01$). Although the incidence of mumps epidemics differs between fiscal years and regions, we believe that the significant 62% decrease in the number of reported mumps patients between the 7-year periods before and after initiation of the public subsidy program reflects an inhibitory effect of widespread immunization on such epidemics.

When considering routine immunization for mumps, the greatest concern is the frequency of aseptic meningitis after immunization. Previous investigations used various calculation methods, making it difficult to compare their findings. When aseptic meningitis caused by the MMR vaccine became known and was discussed in public, its incidence was investigated prospectively and found to be > 50 cases/100,000 individuals (21). Meanwhile, between April 1, 2013, when the Subcommittee on Adverse Reactions of the Committee on Immunization and Vaccines of the Health Sciences Council started discussions, and April 30, 2017, 4,605,536 doses of monovalent mumps vaccines were delivered to medical facilities, and 96 cases of aseptic meningitis (75 cases of

aseptic meningitis; 7 cases of mumps meningitis; 3 cases of viral meningitis; and 11 cases of meningitis) in vaccinated individuals were reported by medical facilities and marketing authorization holders (22). This reflects an incidence of aseptic meningitis after immunization with monovalent mumps vaccines of 2.1 cases/100,000 doses, which is approximately 1/25 of the incidence rate recorded in the past. The main reason for the discrepancy may be differences in the investigation methods. It is also possible that the aseptic meningitis cases may have been caused by viruses other than the vaccine strains or wild-type strains of mumps virus that were not ruled out by rigorous virological tests. Hence, there is still a possibility of misclassification in diagnosis, although it is extremely difficult to demonstrate. At present, we do not have data regarding the true incidence rate, and, as there is no theoretical threshold of safety, it is very difficult to judge whether the current vaccines are safer than the previous ones based on the incidence of post-vaccinal aseptic meningitis. However, at least in the opinion of the above-mentioned Subcommittee on Adverse Reactions regarding the domestic monovalent vaccines, they were judged to be of “no serious concern for safety” (23). In the present study, the incidence rate of aseptic meningitis after vaccination in Nagoya City after initiation of the public subsidy program was 0.7 cases/100,000 doses. There were no other serious adverse reactions. As a reason for the lower incidence of post-vaccinal aseptic meningitis, a recent study has suggested that receiving the 1st dose of mumps vaccine at a lower age is associated with a lower risk of vaccine-associated aseptic meningitis (24).

With the public subsidy program for mumps vaccination in Nagoya City, which involves the education of potential mumps vaccine recipients in a similar way to those receiving routine immunization, the mumps immunization rate has increased to > 90%. In terms of safety, the program was found to have been performed with few reports of adverse reactions. Regarding efficacy, as in previous studies (14,25), we found that the number of mumps patients decreased significantly after the initiation of the subsidy program. We consider that the project contributed to a reduction in disease burden.

With the growing concern of mumps-associated hearing loss (4), the public subsidy program for mumps vaccine in Nagoya City presented here should be considered as a model case when discussing the risks/benefits of the currently available monovalent mumps vaccines, and whether routine immunization should be promoted for mumps.

Conflict of interest Nakano T has received honoraria from Takeda Pharmaceutical Company Limited, Japan Vaccine Co., Ltd., Daiichi Sankyo Company, Limited, Mitsubishi Tanabe Pharma Corporation, Denka Seiken Co., Ltd., Sanofi K.K., MSD K.K., and Astellas Pharma Inc. Kumihashi H and Kano M are employees of Takeda Pharmaceutical Company Limited. The other authors have no financial conflicts of interest to declare.

REFERENCES

1. Maruyama H, Tomizawa I. Status of aseptic meningitis after MMR immunization and countermeasures against it. *Clin Virol*. 1994;22: 77-82. Japanese.
2. The National Institute of Infectious Diseases and Tuberculosis and

- Infectious Diseases Control Division, Ministry of Health, Labour and Welfare, Japan. Mumps (infectious parotitis) in Japan, as of September 2016. Infect Agents Surveillance Rep. 2016;37:185-6. Available at <<https://www.niid.go.jp/niid/en/iasr-vol37-e/6836-idx440-e.html>>. Accessed May 11, 2018.
3. Kawaguchi M, Nishimura N, Kito S, et al. Disease burden of the pediatric mumps based on the clinical analysis of the hospitalized patients during 2008–2014. J Pediatric Infect Dis Immunol. 2017;29:227-33. Japanese.
4. Morimoto N. Present status of hearing loss due to mumps virus infection in Japan. Clin Virol. 2017;45:326-30. Japanese.
5. The Ministry of Health, Labour and Welfare. The 20th Subcommittee Meeting on Basic Vaccination Policy, Committee on Immunization and Vaccines, Health Sciences Council on 08 December 2017. Material 5: About vaccination programs (Explanatory material for Nagoya City, Aichi Prefecture), 2017. Available at <<http://www.mhlw.go.jp/file/05-Shingikai-10601000-Daijinkanboukouseikagakuka-Kouseikagakuka/0000187150.pdf>>. Accessed May 11, 2018. Japanese.
6. Kitasato Daiichi Sankyo Vaccine Co., Ltd. Package insert of freeze-dried live attenuated mumps vaccine (Hoshino Strain). Revised in March 2017 (6th version). Available at <<http://database.japic.or.jp/pdf/newPINS/00059369.pdf>>. Accessed May 11, 2018. Japanese.
7. Takeda Pharmaceutical Company Limited. Package insert of dried live attenuated mumps vaccine (Torii Strain). Revised in July 2018 (15th version). Available at <http://www.info.pmda.go.jp/downfiles/ph/PDF/400256_631340AD1040_1_19.pdf>. Accessed May 11, 2018. Japanese.
8. Nagoya City. Annual Report on Health and Welfare in Nagoya City (fiscal year 2003*–2016). Available at <<http://www.city.nagoya.jp/shisei/category/67-4-4-0-0-0-0-0-0.html>>. Accessed May 11, 2018(*No information on the web for the fiscal year 2003 report provided by Nagoya City). Japanese.
9. The Annual Report of Control of Infectious Diseases in Nagoya City. The report of post-vaccinal adverse reaction. 156. 2015. Japanese.
10. Ministry of Health, Labour and Welfare and National Institute of Infectious Diseases. Tables of the number of reported cases from the National Epidemiological Surveillance of Infectious Diseases (sentinel surveillance). Diseases monitored by the pediatric sentinel surveillance. Epidemic parotitis (fiscal year 1999–2016). Available at <<https://www.niid.go.jp/niid/ja/survei/2085-idwr/ydata/6565-report-jb2015.html>>. Accessed May 11, 2018. Japanese.
11. The Japanese Association of Vaccine Industries, General Incorporated Association. The 2017 basics of vaccines, from the manufacture to the distribution of vaccines. 2017. Available at <http://www.wakutin.or.jp/medical/pdf/kiso_2018.pdf#page=1>. Accessed May 11, 2018. Japanese.
12. Incorporated NPO Know VPD! Protect Our Children: Information on subsidy for pediatric vaccines in the country. Available at <<http://www.know-vpd.jp/>>. Accessed October 19, 2016. Available at <<http://www.know-vpd.jp/news/2235.php>>. Accessed December 1, 2017. Japanese.
13. Ihara T. Mumps vaccine: present and future situations. Clin Virol. 2010;38:386-92. Japanese.
14. Korematsu S, Akiyoshi K, Takano T, et al. The effects of publicly subsidized voluntary immunization and medical expenses deduction on pediatric care and the local community. J Jpn Pediatr Soc. 2012;116:1380-6. <www.jpeds.or.jp/journal/gakkaiza_back.html>. Japanese.
15. Sugawara T, Ohkusa Y, Taya K, et al. Cost-effectiveness analysis of routine mumps immunization in Japan. Kansenshogaku Zasshi. 2007;81:555-61. Japanese.
16. Ministry of Health, Labour and Welfare of Japan. The 20th Subcommittee Meeting on Basic Vaccination Policy of the Committee on Immunization and Vaccines of the Health Sciences Council on December 8, 2017. Material 8: The contents of discussion about candidate vaccines for routine immunization. 2017. Available at <<http://www.mhlw.go.jp/file/05-Shingikai-10601000-Daijinkanboukouseikagakuka-Kouseikagakuka/0000187158.pdf>>. Accessed May 11, 2018. Japanese.
17. Nishimura N, Ahn J, Watanabe N, et al. Clinical and serological studies on live attenuated mumps vaccines in healthy subjects: a 9-year survey at a pediatric clinic in Japan. Clin Virol. 2007;35:179-85. Japanese.
18. Nagai T. Natural infection of mumps and post-vaccination aseptic meningitis. Infect Agents Surveillance Rep. 2013;34:230-1. Available at <<https://www.niid.go.jp/niid/ja/iasr-sp/2254-related-articles/related-articles-402/3793-dj4027.html>>. Accessed May 11, 2018. Japanese.
19. Ochiai H, Ihara T, Nakano T, et al. Evaluation of effectiveness of mumps vaccine in an elementary school outbreak. Shonika-rinsho. 2007;60:489-94. Available at <<https://ci.nii.ac.jp/naid/40015334225>>. Japanese.
20. Nagoya City. About the individual notification of immunization (sticker-type ticket for immunization). 2017. Available at <<http://www.city.nagoya.jp/kenkofukushi/page/0000088911.html>>. Accessed May 11, 2018. Japanese.
21. Shishido A. Mumps vaccine. Clin Virol. 1980;8:319-26. Japanese.
22. Ministry of Health, Labour and Welfare of Japan. The 31st Subcommittee Meeting on Adverse Reactions of the Committee on Immunization and Vaccines of the Health Sciences Council. Material 4: About the status of reports on suspected adverse reactions due to freeze-dried live attenuated mumps vaccines. 2017. Available at <<http://www.mhlw.go.jp/file/05-Shingikai-10601000-Daijinkanboukouseikagakuka-Kouseikagakuka/0000186448.pdf>>. Accessed May 11, 2018. Japanese.
23. Ministry of Health, Labour and Welfare of Japan. The minutes of the 31st Subcommittee Meeting on Adverse Reactions of the Committee on Immunization and Vaccines of the Health Sciences Council on 29 November 2017, and the 9th Subcommittee Meeting on Drug Safety of the Committee on Drug Safety of Pharmaceutical Products of the Pharmaceutical Affairs and Food Sanitation Council of fiscal year 2017 (jointly held). 2017. Available at <<http://www.mhlw.go.jp/stf/shingi2/0000190696.html>>. Accessed May 11, 2018. Japanese.
24. Muta H, Nagai T, Ito Y, et al. Effect of age on the incidence of aseptic meningitis following immunization with monovalent mumps vaccine. Vaccine 2015;33:6049-53.
25. Ihara T, Suga S, Nagao M, et al. A clinical study of the efficacy of mumps vaccine. “A study to fundamentally solve a serious mumps vaccine gap”. Health and Labour Sciences Research Grants, summary report and study report in 2013. 2013: 19-24. Available at <<https://mhlw-grants.niph.go.jp/niph/search/NIDD00.do?resrchNum=201318077A>>. Japanese.