Surveillance of immunity acquired from poliovirus immunization including
vaccination with the Sabin strain-derived inactivated vaccine

（Sabin 株由来不活化ポリオワクチンを含む予防接種で獲得されたポリ
オウイルスに対する免疫の推移）

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Abstract

In Japan, routine immunization for polio using the oral polio vaccine (OPV) was suspended in September 2012; subsequently, an immunization program with inactivated polio vaccines (IPVs), the conventional IPV (cIPV) derived from virulent strains, and IPV derived from Sabin strains (sIPV), was introduced. However, the immunity induced by sIPV is not well characterized. This study assessed and compared neutralizing antibodies produced against poliovirus in children who received doses of OPV or IPV. Serum samples were collected yearly between 2013 and 2016 as part of the National Epidemiological Surveillance of Vaccine–Preventable Disease. The neutralizing antibody titers for Sabin strain types 1, 2, and 3 in 224 children, aged between 0 and 90 months, were assessed. Seropositive rates after vaccination with OPV or IPV were more than 90%. Neutralizing antibody titers for Sabin type 1 after vaccination with IPV were lower than those with OPV, while those for Sabin types 2 and 3 after vaccination with IPV were significantly higher than those with OPV. Analyses of antibody titer dynamics revealed that the decay of antibody titers for Sabin types 1, 2, and 3 in cases vaccinated with IPV was steeper than those with OPV. Thus, our study showed that although IPV induced a sufficient level of neutralizing antibody, the immunity induced by IPV was not maintained as long as that by OPV. Our study suggested that a long-term survey should be conducted for polio vaccination using IPV and that it might be necessary to consider booster vaccination for IPVs.

Introduction

The world Health Assembly (WHA) adopted a resolution for the worldwide eradication of polio in 1988.[1] The Global Polio Eradication Initiative (GPEI) has reduced the global incidence of polio by more than 99%. The oral polio vaccine (OPV) comprising live attenuated poliovirus, such as Sabin strains, was used in the immunization program in most countries. The OPV induces effective immunity against poliovirus.[2]

However, the OPV is a live vaccine and carries the risk of causing vaccine-associated paralytic poliomyelitis (VAPP) and polio epidemics of vaccine-derived poliovirus (VDPVs).[3, 4] The Polio Eradication and Endgame Strategic Plan 2013-2018 is a strategy aimed at attaining a polio-free world by 2018. [2] The plan has four objectives, one of which is to strengthen immunization systems and withdraw OPV. Due to the risks associated with OPVs, globally synchronized switching from OPV to inactivated polio vaccine (IPV) has been set into motion.

The conventional IPV (cIPV) is derived from virulent strains of polioviruses, and as an alternative,[5] the Sabin strain-derived IPV (sIPV) has been developed and licensed.[6-8] Since the development of safer IPVs was recommended by the WHA and the Sabin strains are expected to reduce the overall biosafety risk, the sIPV has been approved for production in certain developing countries.[9]

In Japan, two doses of OPV were used to establish a polio-free status. The OPV was introduced into the national immunization program in 1964, and was discontinued in August 2012; subsequently, the OPV was replaced with standalone cIPV in September 2012. In November 2012, sIPV-containing diphtheria-tetanus-acellular pertussis combination vaccines were first introduced into the national immunization program, and polio vaccination schedule has been revised as four doses of IPV instead of the two doses of OPV.[10] Previously, children aged between 3 and 90 months were immunized with two doses of OPV at intervals longer than 6 weeks. After the introduction of the IPV in the national immunization program, children aged

between 3 and 90 months are immunized with three doses of IPV at intervals of 20-56 days, as the primary vaccination, followed by the fourth dose at least 6 months later. At present, no booster vaccination of IPV is included in the national immunization program in Japan. The booster vaccination with cIPV is being performed in several countries, but the booster vaccination for IPV is still under consideration in Japan. Japan was first to incorporate sIPV into routine immunization in 2012,[10] before it was marketed worldwide. Therefore, reports on the immunity induced by sIPV are limited. Thus, significant characteristics of sIPV, such as the time period for which the antibody titer must be maintained in order to confer sufficient protection, remain uncharacterized. We aimed to address these gaps in the understanding of the immunity resulting from vaccination using IPV.

This report is a surveillance study on the immunity induced by IPV and OPV, after the introduction of sIPV into the routine immunization program in Japan. This study assessed and compared the neutralizing antibodies produced against the poliovirus in children who were vaccinated with doses of OPV, cIPV, or sIPV, in order to verify the vaccination effect of sIPV on polio.

Results

Study population

From 2013 to 2016, Serum samples were collected from 1186 individuals aged between 0 and 69 years. A total of 224 children aged between 0 and 90 months were selected from the poliomyelitis immunization program. Profiles of children less than 90 months old are shown in Table 1. The children vaccinated with OPV were 34.8% (78/224), and those with IPV were 53.6% (120/224). The median age of children vaccinated with OPV, cIPV, and sIPV were 67.5, 35.5, and 17.5 months, respectively.

Seropositive rates and geometric mean antibody titers

The age distribution of seropositive rates and geometric mean antibody titers (GMTs) among the 1186 cases are shown in Figure 1. The seropositive rates for Sabin type 1 and type 2 were over 80% in most ages; however, those for Sabin type 1 among individuals in the age groups of 30's and 40's were less than 80% (Fig. 1a). The declining trend in seropositive rates and GMTs with age for Sabin type 1 and 2 was similar, but that for Sabin type 3 was different. Specifically, the seropositive rates of Sabin type 3 in individuals aged between 5 years and 50's were less than 80% (Fig. 1a), and GMTs in those aged more than 4 years were less than 32 (Fig. 1b).

Seropositive rates and GMTs in children aged between 0 and 90 months

Children aged between 3 and 90 months were included in the poliomyelitis immunization program in Japan. Seropositive rates and GMTs were analyzed for children aged from 0 to 90 months who were included in the immunization program.

As routine immunization for the poliovirus was switched from OPV to IPV in 2012, the cases vaccinated with OPV were compared to the cases vaccinated with IPV (Table 2). All

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seropositive rates were more than 90%, except for Sabin type 3 in children vaccinated with OPV (88.3%). There was a significant difference in the seropositive rates for Sabin type 1 between children vaccinated with OPV and those vaccinated using IPV. The GMTs for Sabin type 1 in children vaccinated with IPV (83.5) were lower than those with OPV (179.4), while GMTs for Sabin types 2 and 3 after vaccination with IPV (173.8 and 76.1) were higher than those of OPV (118.2 and 16.3). Significant differences were found in the GMTs for Sabin types 1, 2, and 3 between children with vaccinated OPV and IPV.

 Children vaccinated with two doses of OPV were compared to those vaccinated with four doses of IPV to confirm whether there are differences in seropositive rates and GMTs after the completion of vaccination. After vaccination with two doses of OPV, the GMTs were 69, and in the case of vaccination with four doses of IPV, the GMTs were 54. All seropositive rates after vaccination with two doses of OPV or four doses of IPV were more than 90% (Table 3). There were no significant differences between two doses of OPV and four doses of IPV in terms of the seropositive rates for Sabin types 1, 2, and 3. The GMTs for Sabin type 1 after vaccination with four doses of IPV (131.3) were lower than those after two doses of OPV (174.8); however, there were no significant differences. The GMTs for Sabin types 2 and 3 in children vaccinated with four doses of IPV (287.4 and 143.6) were significantly higher than those after vaccination with two doses of OPV (110.1 and 17.5) (Table 3).

 We compared the vaccination with four doses of cIPV with vaccination using four doses of sIPV to confirm the difference between the IPVs. Sixteen children were vaccinated with four doses of cIPV and thirty-two children were vaccinated with four doses of sIPV. The seropositive rates in children vaccinated with four doses of cIPV or sIPV were 100% (Table 4). The GMTs for Sabin type 1, 2, and 3 after vaccination with four doses of sIPV (173.3, 479.8, and 245.1, respectively) were higher than those after four doses of cIPV (94.5, 145.8, and 83.0,

respectively); the GMTs for Sabin types 2 and 3 were significantly higher after vaccination with sIPV.

We compared the vaccination with two doses of OPV with that using four doses of sIPV to confirm the difference between Sabin-derived IPV and OPV. Sixty-nine children were vaccinated with two doses of OPV, and thirty-two children were vaccinated with four doses of sIPV. All seropositive rates in children vaccinated with two doses of OPV or four doses of sIPV were 100%, except those for Sabin type 3 after vaccination with two doses of OPV. There were significant differences in the seropositive rates for Sabin type 3 between children vaccinated with two doses of OPV and those vaccinated with four doses of sIPV. The GMTs for Sabin types 2 and 3 after vaccination with four doses of sIPV (479.8 and 245.1) were significantly higher than those after two doses of OPV (110.1 and 17.5; Table 5)

Decay of neutralizing antibody titers induced by vaccination with two doses of OPV or four doses of IPV

Both vaccination with two doses of OPV and vaccination with four doses of IPV had high seropositive rates for Sabin types 1, 2, and 3. However, it is unknown for how long the neutralizing antibody titers need to be maintained after the vaccination. Therefore, we estimated the decay of neutralizing antibody titers induced by vaccination with two doses of OPV or with four doses of IPV by regression analysis using the least-square curve-fitting methods. The relationship between neutralizing antibody titers and elapsed time after the vaccination schedule completion was plotted for each Sabin type.

The regression lines of neutralizing antibody titers for Sabin types 1, 2, and 3 after vaccination with two doses of OPV and those after four doses of IPV are depicted in Figure 2. The slope of the regression line for children vaccinated with four doses of IPV was steeper than that in children vaccinated with two doses of OPV. There were significant differences in the regression

slopes ($p < 0.05$) between children vaccinated with four doses of IPV and those vaccinated with two doses of OPV. The decay of neutralizing antibodies for Sabin types 1, 2, and 3 after vaccination with four doses of IPV was faster than that after vaccination with two doses of OPV.

 As the cases vaccinated with four doses of IPV included those vaccinated with cIPV and sIPV, we compared the vaccination with two doses OPV with vaccination using four doses of sIPV to evaluate the immunity induced by sIPV. The regression lines of the neutralizing antibody titers for Sabin types 1, 2, and 3 after vaccination with two doses of OPV and after vaccination with four doses of sIPV are shown in Figure 3. The slope of the regression line for children vaccinated with four doses of sIPV was steeper than that in children vaccinated with two doses of OPV. The regression slope for Sabin type 3 was significantly different ($p < 0.05$) between children vaccinated with four doses of sIPV and those vaccinated with two doses of OPV. The decay of neutralizing antibodies for Sabin types 1, 2, and 3 after vaccination with four doses of sIPV was faster than that after vaccination with two doses of OPV, similar to that after vaccination with cIPV; however, decay of neutralizing antibodies for Sabin types 1, 2, and 3 after vaccination with sIPV was slower than that after vaccination with cIPV.

Discussion

 Since OPV was introduced as a routine immunization in 1964, OPV continued to be used until 2012, in Japan.[10] Routine immunization of poliovirus was performed using IPV instead of OPV from 2012 and during his time, OPV was completely removed from the routine immunization program. Following the introduction of cIPV in September 2012, sIPV was introduced in November 2012. In this report, we analyzed the seropositive rates and GMTs induced by OPV or IPV, after the introduction of routine sIPV immunization in Japan.

 The seropositive rates for Sabin type 1 and 2 were over 80% in almost all age groups, except the seropositive rates for Sabin type 1 in the 30's and 40's age groups, which was consistent with the low seropositive rates for Sabin type 1 in the population born in between 1977 and 1975 in Japan.[11] The seropositive rates for Sabin type 3 were less than 80% in groups aged between 5 and 50 years and less than 40% in groups aged between 9 and 10 years. The increased seropositive rates in groups aged over 50 years old might be a booster response due to the outbreak of poliomyelitis in 1960 and 1961 in Japan.[10]

 The GMTs for Sabin type 1 and 2 were over 8 in all age groups. On the other hand, those for Sabin type 3 in groups aged between 8 and 30 years were less than 8. Since the neutralizing antibody titer of 1:8 or more for poliomyelitis is sufficient for protection from infection[12], our results revealed that individuals of all ages possessed antibody titers sufficient for protection against poliovirus type 1 and 2 infection, but insufficient for protection against poliovirus type 3.

 Furthermore, both the lower seropositive rate and GMT for Sabin type 3 were considered to result from viral interference. Sabin type 3 is believed to be the most susceptible to viral interference among the various types of Sabin vaccines.[13,14] Furthermore, it was suggested that IPV has higher immunity-inducing ability in the case of Sabin 2 and 3 than OPV. IPV might elicit antibody responses against all vaccine antigens with no significant interference among

the types included in the live vaccine. The GMTs for Sabin type 1, 2, and 3 after vaccination with four doses of cIPV were lower than those with sIPV, which might be due to the longer periods post vaccination and the different challenge viruses that were used for the neutralizing tests.

The antibody titers for Sabin type 1, 2, and 3 after vaccination with four doses IPV decreased faster than those after two doses OPV and the antibody titers for Sabin type 3 after four doses of sIPV decreased faster than that after two doses of OPV. This suggests that the decay tendency of the neutralizing antibody titers differs between IPV and OPV. Since IPV, particularly sIPV, is the newly introduced vaccine, further assessment of antibody persistence is necessary. In countries such as the United States and Germany,[15-17] booster vaccination for cIPV is routinely carried out. In addition, it was shown that children given the booster vaccination at the age of 10 years maintained higher antibody titer at the age of 18 years than those given the same at the age of 6 years. On the other hand, most currently available reports on IPV are based on cIPV and there are no reports on the evaluation of the antibody titer during long-term follow-up after sIPV vaccination. A long-term survey is needed for the polio vaccination program using sIPV in Japan. Depending on the results of surveillance, it might be necessary to consider the booster vaccination for IPV and adding it into the list of routine vaccination.

There are some limitations in this study. The tested neutralizing antibody titers were against Sabin strains and not for the wild type strains. However, it has been reported that the neutralizing antibody obtained by sIPV exerts the same effect on the wild type strains in Phase II and Phase III clinical studies.[6]

WHO encourages the implementation of the WHO Polio Eradication and Endgame Strategic Plan 2013-2018. In this plan, WHO recommends stopping immunization with trivalent OPV and introducing immunization with bivalent OPV, removing the type 2, and using at least one dose of IPV. In order to maximize the effect of introducing IPV, it is important to ensure the

stable supply of IPV. For the manufacture IPV in middle- and low-income countries, sIPV derived from Sabin poliovirus strains, which are attenuated strains, is safer than the cIPV, derived from wild type poliovirus strains. The study and development of sIPV is needed for establishing a global supply system for these polio vaccines.

In conclusion, this is a surveillance study on the immunity induced by IPV and OPV, after the introduction of Japanese routine immunization program using the first licensed sIPV. Long-term surveillance needs to be conducted in order to evaluate the efficacy of sIPV. Our study highlights the necessity to consider booster vaccination for IPV.

Materials and methods

Study populations

This study was conducted as a part of the National Epidemiological Surveillance of Vaccine-Preventable Disease (NESVPD) in Japan. The NESVPD included the surveillance of poliomyelitis and was carried out by the National Institute of Infectious Diseases (NIID) and the Ministry of Health, Labour and Welfare, in collaboration with the prefectural governments and prefectural public health laboratories. Cases were collected at random between 2013 and 2016 in the Chiba Prefecture in Japan and the profiles included vaccination history, which were obtained from healthy individuals with their informed consent.

Ethical approval was not required for this study because the NESVPD is conducted for public health on the basis of the immunization law in Japan. However, the study procedures were conducted in accordance with the Helsinki Declaration of 1975.

Cell culture

RD-A, a Human embryo rhabdomyosarcoma cell line, gifted from the National Institute of Infectious Diseases, was used for the neutralizing test. Eagle's Minimum Essential Medium (M4655-500ML, Merck) supplemented with 10% fetal calf serum was used as the growth medium.

Titration

The neutralizing antibody titers against polioviruses were determined using the neutralizing test. Challenge viruses were Sabin strains of types 1, 2, and 3. The dilution ranging from 1:4 to 1:1024 were used. Serially diluted serum was incubated with challenge viruses at 50% cell culture infectious dose ($CCID_{50}$) of 100, at 36ºC for 3 hours; then, RD-A cells were added to each well. The titer of neutralizing antibody that exhibited 50% inhibition of the cytopathic

effect (CPE) was measured after 7 days. Neutralizing antibody titers of 1:8 or more were defined as seropositive.[12]

Statistics

Seropositive rates, geometric mean antibody titers (GMTs), and their two-sided 95% confidence intervals (CIs) were calculated. p values were calculated using the student's t test. The correlation between the neutralizing antibody titers and time elapsed after vaccination was plotted for each Sabin type. Each regression line was depicted by the least-squares curve-fitting method from the plot diagram. The differences between the regression slopes were analyzed using the student's t test. p values less than 0.05 were considered statistically significant.

References

1.   The Forty-first World Health Assembly. Global eradication of poliomyelitis by the year 2000. WHA41.28;1988:2-4.

2.   Polio Grobal Eradication Initiative. Polio Eradication & Endgame Strategic Plan 2013-2018. WHO;2013.

3.   WHO. Polio vaccines: WHO position paper – March, 2016. Wkly Epidemiol Rec. 2016;91(12):145-68. PMID:27039410

4.   Platt LR, Estívariz CF, Sutter RW. Vaccine-associated paralytic poliomyelitis: a review of the epidemiology and estimation of the global burden. J Infect Dis. 2014;210 Suppl 1:S380-9. doi: 10.1093/infdis/jiu184. PubMed PMID: 25316859.

5.   Murdin AD, Barreto L, Plotkin S. Inactivated poliovirus vaccine: past and present experience. Vaccine. 1996;14(8):735-46. PubMed PMID: 8817819.

6.   Okada K, Miyazaki C, Kino Y, Ozaki T, Hirose M, Ueda K. Phase II and III Clinical Studies of Diphtheria-Tetanus-Acellular Pertussis Vaccine Containing Inactivated Polio Vaccine Derived from Sabin Strains (DTaP-sIPV). J Infect Dis. 2013;208(2):275-83. Epub 2013/04/08. doi: 10.1093/infdis/jit155. PubMed PMID: 23568174.

7.   Liao G, Li R, Li C, Sun M, Li Y, Chu J, Jiang S, Li Q. Safety and immunogenicity of inactivated poliovirus vaccine made from Sabin strains: a phase II, randomized, positive-controlled trial. J Infect Dis. 2012;205(2):237-43. Epub 2011/12/08. doi: 10.1093/infdis/jir723. PubMed PMID: 22158682.

8.   Resik S, Tejeda A, Fonseca M, Alemañi N, Diaz M, Martinez Y, Garcia G, Okayasu H, Burton A, Bakker WA, et al. Reactogenicity and immunogenicity of inactivated poliovirus vaccine produced from Sabin strains: a phase I Trial in healthy adults in Cuba. Vaccine. 2014;32(42):5399-404. Epub 2014/08/12. doi: 10.1016/j.vaccine.2014.07.109. PubMed PMID: 25131734.

9.   Okayasu H, Sein C, Hamidi A, Bakker WA, Sutter RW. Development of inactivated poliovirus vaccine from Sabin strains: A progress report. Biologicals. 2016;44(6):581-7. Epub 2016/10/05. doi: 10.1016/j.biologicals.2016.08.005. PubMed PMID: 27720268.

10.   Shimizu H. Development and introduction of inactivated poliovirus vaccines derived from Sabin strains in Japan. Vaccine. 2016;34(16):1975-85. Epub 2014/11/21. doi: 10.1016/j.vaccine.2014.11.015. PubMed PMID: 25448090.

11.   National Institute of Infectious Diseases. Poliomyelitis, Japan, 1962-1995.IASR. 1997;18(1):28-29.

12   Plotkin SA. Correlates of protection induced by vaccination. Clin Vaccine Immunol. 2010;17(7):1055-65. Epub 2010/05/12. doi: 10.1128/CVI.00131-10. PubMed PMID: 20463105; PubMed Central PMCID: PMCPMC2897268.34.

13.   Okayasu H, Sutter RW, Czerkinsky C, Ogra PL. Mucosal immunity and poliovirus vaccines: impact on wild poliovirus infection and transmission. Vaccine. 2011;29(46):8205-14. Epub 2011/09/05. doi: 10.1016/j.vaccine.2011.08.059. PubMed PMID: 21896299.

14.   Maldonado YA, Peña-Cruz V, de la Luz Sanchez M, Logan L, Blandón S, Cantwell MF, Matsui SM, Millan-Velasco F, Valdespino JL, Sepulveda J. Host and viral factors affecting the decreased immunogenicity of Sabin type 3 vaccine after administration of trivalent oral polio vaccine to rural Mayan children. J Infect Dis. 1997;175(3):545-53. doi: 10.1093/infdis/175.3.545. PubMed PMID: 9041324.

15.   Knuf M, Vetter V, Celzo F, Ramakrishnan G, Van Der Meeren O, Jacquet JM. Repeated administration of a reduced-antigen-content diphtheria-tetanus-acellular pertussis and poliomyelitis vaccine (dTpa-IPV; Boostrix™ IPV). Hum Vaccin. 2010;6(7):554-61. doi: 10.4161/hv.6.7.11760. PubMed PMID: 20448468.

16.   Centers for Disease Control and Prevention (U.S.). Poliomyelitis. In: Epidemiology and Prevention of Vaccine-Preventable Diseases, 13th Edition. 2015;297-310.

17.   Böttiger M. Polio immunity to killed vaccine: an 18-year follow-up. Vaccine. 1990;8(5):443-5. doi: 10.1016/0264-410X(90)90244-G. PubMed PMID: 2251870.

Figure legends

Figure 1. Seropositive rates (a) and geometric mean antibody titers (GMTs) (b) of cases vaccinated with Sabin type 1, 2, and 3. Seropositive rates and GMTs were plotted by age and age groups. Seropositive was represented for titers of 1:8 or more. Age and age groups were plotted for age groups between 0 to 9 years and for every 10 years thereafter. Type 1: Sabin type 1; Type 2: Sabin type 2; Type 3: Sabin type 3.

Figure 2. Regression line of neutralizing antibody titers induced by vaccination with two doses of oral polio vaccine (OPV) or four doses of inactivated polio vaccine (IPV).

The relationship between neutralizing antibody titers and elapsed time after the vaccination schedule completion was depicted by least-squares curve-fitting method. p values less than 0.05 were considered significant. Each regression line was statistically significant. There were significant differences in regression slopes ($p < 0.05$). Circle: two doses of OPV; open circle: four doses of IPV; dotted line: regression line of two doses of OPV; dashed line: regression line of four doses of IPV; Type 1: Sabin type 1; Type 2: Sabin type 2; Type 3: Sabin type 3.

Figure 3. Regression line of neutralizing antibody titers induced by vaccination with two doses of oral polio vaccine (OPV) or four doses of Sabin strain-derived inactivated polio vaccine (sIPV).

The relationship between neutralizing antibody titers and elapsed time after the vaccination schedule completion was depicted by least-squares curve-fitting method. p values less than 0.05 were considered statistically significant. Each regression line was statistically significant.

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The regression slope for Sabin type 3 was significantly different ($p < 0.05$). Circle: two doses of OPV; open square: four doses of sIPV; dotted line: regression line of two doses of OPV; dashed line: regression line of four doses of sIPV; Type 1: Sabin type 1; Type 2: Sabin type 2; Type 3: Sabin type 3.

Table 1. Oral polio vaccine (OPV), conventional inactivated polio vaccine (cIPV), and Sabin strain-derived IPV (sIPV)-vaccinated cases of less than 90 months of age

Vaccination	Cases	Gender				Age (months)	
	n (%)	Male (%)	95% CIs (%)	Female (%)	95% CIs (%)	Median	Mean
OPV	78 (34.8)	43 (55.1)	44.0-66.2	35 (44.9)	33.8-56.0	67.5	65.1
IPV	120 (53.6)	81 (67.5)	59.1-75.9	39 (32.5)	24.1-40.9	21.0	26.6
cIPV	40 (17.9)	27 (67.5)	52.8-82.2	13 (32.5)	17.8-47.2	35.5	38.3
sIPV	72 (32.1)	49 (68.1)	57.3-78.9	23 (31.9)	21.1-42.7	17.5	19.5
cIPV and sIPV	8 (3.6)	5 (62.5)	26.6-98.4	3 (37.5)	1.6-73.4	24.5	32.8
Mixed*	11 (4.9)	4 (36.4)	6.6-66.2	7 (63.3)	33.5-93.1	51.0	55.0
unknown	15 (6.7)	9 (60.0)	34.3-85.7	6 (40.0)	14.3-65.7	49.0	43.7
Total	224 (100)	137 (61.2)	54.8-67.6	87 (38.8)	32.4-45.2	41.0	42.5

*OPV and cIPV, OPV and sIPV, or combinations of OPV, cIPV and sIPV

CIs, confidence intervals

Table 2. Seropositive rates and geometric mean antibody titers (GMTs) for oral polio vaccine (OPV) and inactivated polio vaccine (IPV)

Sabin strains	Seropositive* rate (%) (95% CIs)			GMTs (95% CIs)		
	OPV (n = 78)	IPV (n = 120)	p-value	OPV (n = 78)	IPV (n = 120)	p-value
Type 1	100.0	96.7 (60.6-132.7)	<0.05	179.4 (15.7-2047.4)	83.5 (2.9-2422.4)	<0.05
Type 2	100.0	99.2 (80.9-117.4)	0.16	118.2 (13.9-1007.1)	173.8 (8.2-3666.7)	<0.05
Type 3	88.3 (23.6-153.0)	92.5 (39.6-145.4)	0.16	16.3 (0.7-380.7)	76.1 (1.7-3492.4)	<0.05

*Seropositive: titers of 1:8 or more

**p-value: according to the student's t test; CIs, confidence intervals

Table 3. Seropositive rates and geometric mean antibody titers (GMTs) for two doses of oral polio vaccine (OPV) and four doses of inactivated polio vaccine (IPV)

Sabin strains	Seropositive* rate (%) (95% CIs)			GMTs (95% CIs)		
	Two doses of OPV (n = 69)	Four doses of IPV (n = 54)	p-value**	Two doses of OPV (n = 69)	Four doses of IPV (n = 54)	p-value**
Type 1	100.0	96.3 (58.2-134.4)	0.07	174.8 (17.8-1699.5)	131.3 (6.8-2539.0)	0.11
Type 2	100.0	98.1 (70.9-125.4)	0.16	110.1 (12.8-946.3)	287.4 (23.1-3580.8)	<0.05
Type 3	94.2 (47.1-141.3)	92.3 (58.2-134.4)	0.29	17.5 (0.8-399.1)	143.6 (5.3-3920.6)	<0.05

*Seropositive: titers of 1:8 or more

**p-value: according to the student's t test; CIs, confidence intervals

Table 4. Seropositive rates and geometric mean antibody titers (GMTs) for four doses of conventional inactivated polio vaccine (cIPV) and four doses of Sabin strain-derived IPV (sIPV)

Sabin	Seropositive* rate (%) (95% CIs)			GMTs (95% CIs)		
Strain	Four doses of cIPV (n = 16)	Four doses of sIPV (n = 32)	p-value**	Four doses of cIPV (n = 16)	Four doses of sIPV (n = 32)	p-value**
Type 1	100	100	-	94.5 (3.5-2510.2)	173.3 (15.9-1885.3)	0.07
Type 2	100	100	-	145.8 (12.7-1671.0)	479.8 (78.7-2925.4)	<0.05
Type 3	100	100	-	83.0 (2.6-2655.9)	245.1 (16.1-3744.1)	<0.05

*Seropositive: titers of 1:8 or more

**p-value: according to the student's t test; CIs, confidence intervals

Table 5. Seropositive rates and geometric mean antibody titers (GMTs) for two doses of oral polio vaccine (OPV) and four doses of Sabin strain-derived inactivated polio vaccine (sIPV)

Sabin Strain	Seropositive* rate (%) (95% CIs)			GMTs (95% CIs)		
	Two doses of OPV (n = 69)	Four doses of sIPV (n = 32)	p-value**	Two doses of OPV (n = 69)	Four doses of sIPV (n = 32)	p-value**
Type 1	100.0	100	-	174.8 (17.8-1699.5)	173.3 (15.9-1885.3)	0.49
Type 2	100.0	100	-	110.1 (12.8-946.3)	479.8 (78.7-2925.4)	<0.05
Type 3	94.2 (47.1-141.3)	100	<0.05	17.5 (0.8-399.1)	245.1 (16.1-3744.1)	<0.05

*Seropositive: titers of 1:8 or more

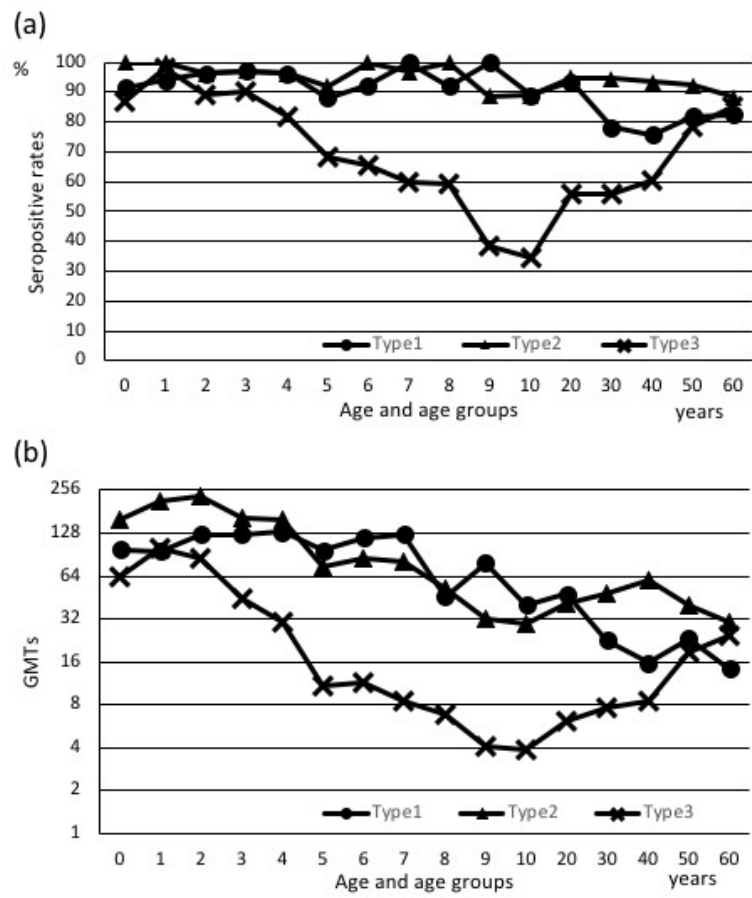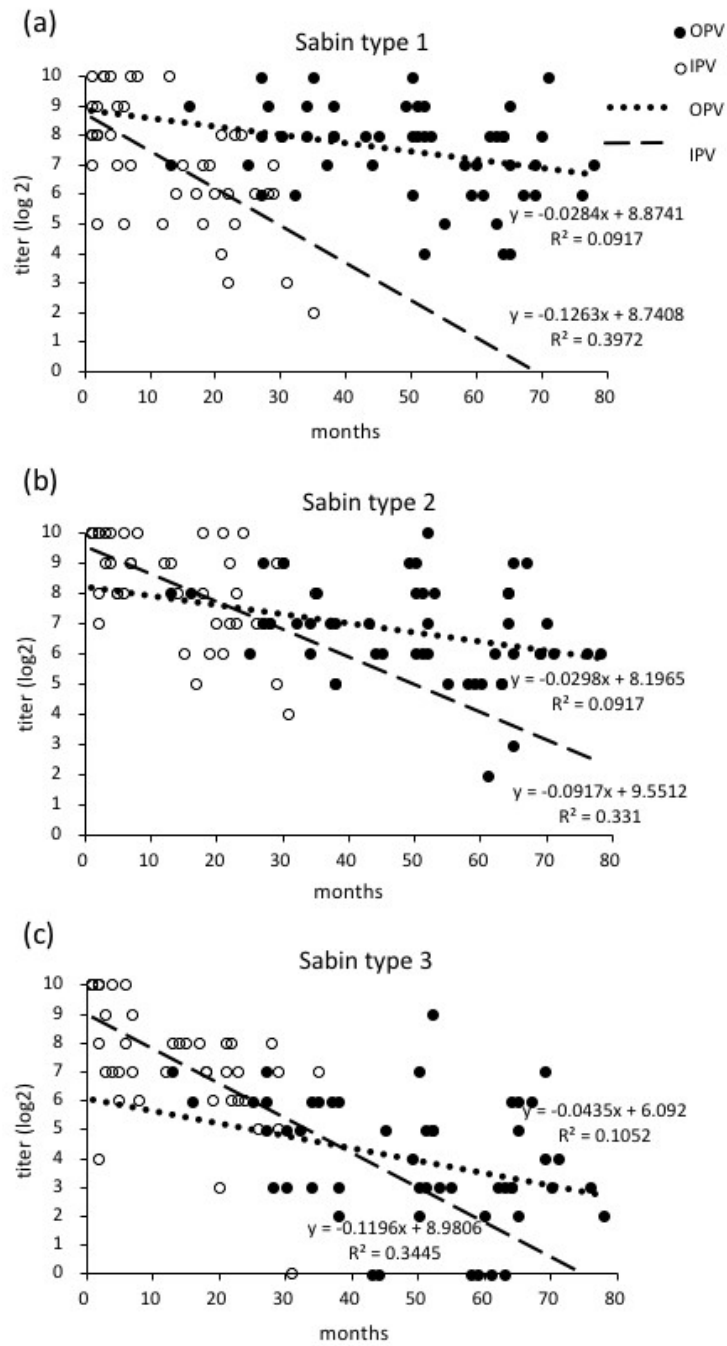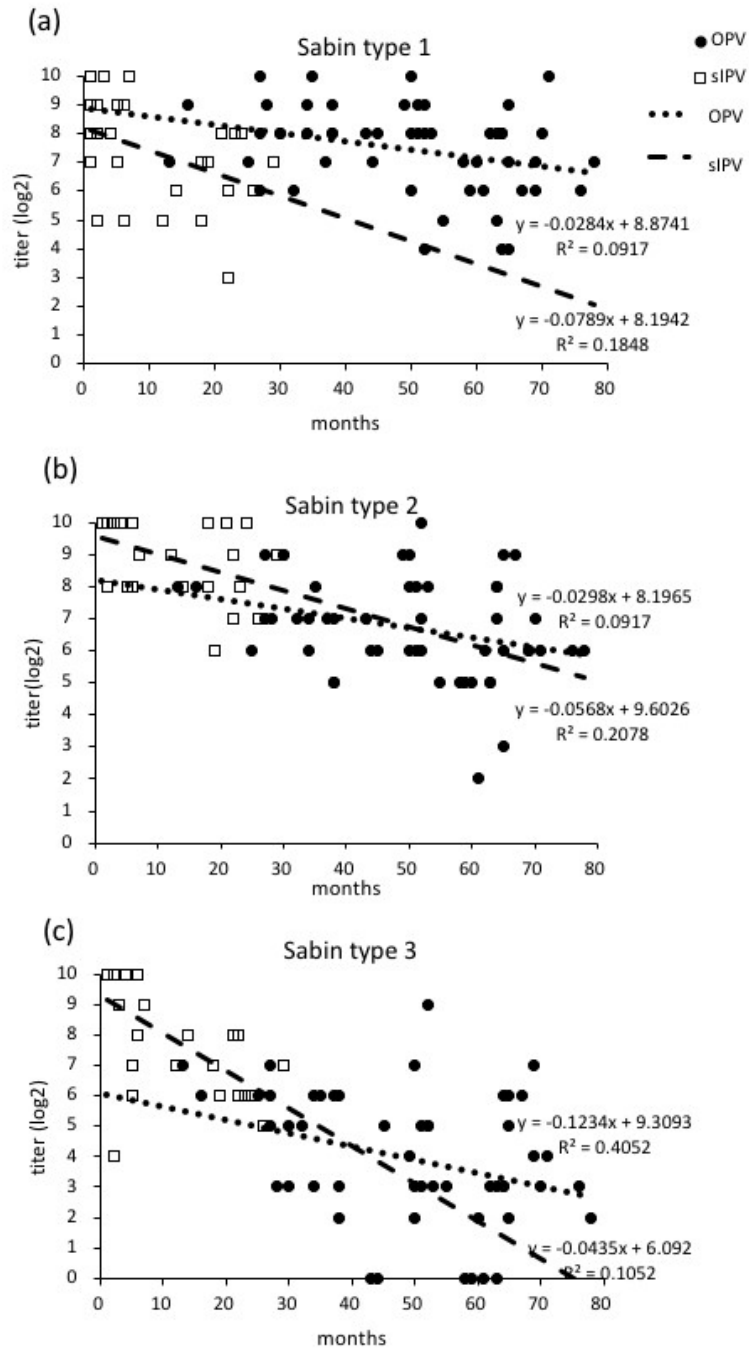**p-value: according to the student's t test; CIs, confidence intervals

Figure 1

(a)

(b)

Figure 2

Figure 2

Figure 3

(a)

Sabin type 1

● OPV
□ sIPV
⋯ OPV
— sIPV

y = -0.0284x + 8.8741
R² = 0.0917

y = -0.0789x + 8.1942
R² = 0.1848

(b)

Sabin type 2

y = -0.0298x + 8.1965
R² = 0.0917

y = -0.0568x + 9.6026
R² = 0.2078

(c)

Sabin type 3

y = -0.1234x + 9.3093
R² = 0.4052

y = -0.0435x + 6.092
R² = 0.1052

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