



## Outbreak, Surveillance and Investigation Reports

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### Polio Seroprevalence in Thailand: Assessment of Outbreak Risk by Age Cohorts

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#### Abstract

We conducted a serological survey to evaluate the population's antibody level against three types of polio virus and identify high risk groups. We analyzed stored serum samples from a hepatitis immunity study conducted in 2004 on people born between 1928 and 2004. These samples were categorized into nine age cohorts and selected by random sampling. Antibody titers were tested by micro-neutralization. A protective level was defined as greater than 1:8. Protective antibody level against poliovirus and geometric mean titer (log<sub>2</sub> reciprocal) were described by types of polio virus in the vaccine and birth cohorts. A total of 1,712 samples were tested. Protective antibody level against poliovirus type 1 was 90.9% while that of type 2 was 94.7% and type 3 was 83.9%. Means titers were 6.0 for type 1, 6.7 for type 2 and 4.9 for type 3. In the different birth cohorts, the antibody levels were the lowest against poliovirus type 2 (89.9%) in those who were born during 1955-1964. For poliovirus types 1 and 3, percentages in the 1975-1984 birth cohorts were less than 80%. Protective antibody level against the three types of poliovirus among the population in Thailand was assumed to be sufficient to generate herd immunity. People born during 1975-1984 were at risk and should be targeted for immunization if a polio outbreak occurred.

*Keywords:* polio, sero-surveillance, immunity, population, Thailand

#### Introduction

Polio is a viral disease which can cause muscle weakness and paralysis.<sup>1</sup> The World Health Organization (WHO) concerned about the possible spread of poliovirus and supports vaccination campaigns to eliminate the disease.<sup>2</sup> Oral polio vaccine (OPV), also known as trivalent oral polio vaccine, is a live-attenuated vaccine that contains types 1, 2 and 3 Sabin strain poliovirus.<sup>3</sup> There are other types of polio vaccine available such as monovalent OPV (one type of poliovirus), bivalent OPV (two types of poliovirus) or inactivated polio vaccine (three types of killed poliovirus). Since 1977, three doses of OPV (OPV3) have been given to Thai children aged two months, four months and six months under the expanded program on immunization (EPI).<sup>4</sup> During 1991-1999, an additional dose of OPV (OPV4) was given to children at age two. Since 2000, the fifth dose of OPV (OPV5) were introduced to the EPI for children at age four.<sup>5</sup> Additionally, National Immunization Days (NIDs), began in 1995,<sup>6,7</sup> provided supplementary dose of polio vaccine to children under 10 and five in 2001.<sup>7</sup>

The last case of wild-type poliovirus (WPV) in Thailand was reported in 1998. One case of type 2 immunodeficiency associated vaccine-derived poliovirus (VDPV), a vaccine strain of poliovirus that genetically mutates to cause poliomyelitis, was identified in Thailand in 2003.<sup>8</sup>

In 1980, the first national vaccine coverage survey carried out by the Ministry of Public Health found that the coverage of OPV3 was 21.2%. In the most recent survey completed in 2008, OPV3 coverage was 98.7% and OPV5 coverage was 79.4%.<sup>5</sup>

However, even with the successful EPI and NID programs, Thailand needs to continue to monitor the polio prevention and control program closely due to possible recurrence of the disease. There have been several re-emerging and cross-border polio outbreaks in the region. In 2005, Indonesia had an outbreak of 299 polio cases after 10 polio-free years.<sup>9</sup> In 2010, Myanmar had one imported polio case, as did China in 2011.<sup>10</sup> Additionally, China, Myanmar, Cambodia, and Philippines had experienced VDPV outbreaks since 2001.<sup>11</sup> Such events put Thailand at risk and raised the need to ensure that Thai population had

sufficient immunity to prevent reintroduction of poliovirus.

The objectives of our study, using secondary data and samples from a serological survey conducted earlier, were to evaluate the proportion of Thai population who had a protective antibody level against the three types of poliovirus, explore the mean titers among the population in different age groups and identify population at risk.

## Methods

### Serum Specimens

The serum specimens tested in this study were selected from samples of the hepatitis immunity study (HIS) conducted by Ministry of Public Health, Thailand in 2004. These samples were collected from four regions in Thailand, represented by Chiang Rai, Udon Thani, Chon Buri and Nakhon Si Thammarat Provinces.<sup>12</sup> Samples collected from one provincial hospital and two randomly selected community hospitals in each participating province were used. Healthy children attending well-baby clinics and every patient were included in the study, except those with chronic illnesses, undergoing immunosuppressive therapy, having clinical signs or symptoms associated with human immunodeficiency virus (HIV) or immunodeficiency diseases. Serum specimens were taken from the participants, coded with a sequential number and stored in a temperature-controlled freezer at the Faculty of Medicine in Chulalongkorn University. The serum specimens were thawed to determine seroprevalence of antibodies to measles, mumps and rubella in a study by another investigating team in 2009.<sup>13</sup>

Serum specimens were categorized into nine birth cohorts, spanning the years from 1928 to 2004. Estimated proportion of protective antibody for each birth cohort, ranging from 0.60-0.85, were used to calculate sample size with 10% margin of error. We

added 20% to the calculated sample size to compensate for attrition (Table 1). In each cohort, we randomly selected the first serum sorted by order of collection, and then selected the next serum at regular intervals. Serum with volume less than 0.35 mL were excluded and replaced by unselected samples.

### Antibody Assay

Polio antibody levels were tested by micro-neutralization assay conducted at the National Institution of Health (NIH).<sup>14</sup> Reference strains of Sabin types 1, 2 and 3 produced by the National Institute for Biological Standard and Control, United Kingdom were used. Serial two-fold dilutions of the serum were tested up to 1:1,024. The protective levels for poliovirus types 1, 2 and 3 were those samples with antibody titer greater than 1:8.<sup>15</sup>

### Data Analysis

Percentages of protective antibody against three types of poliovirus with 95% confidence interval (95% CI) were described for each cohort. Geometric mean titer (GMT) and 95% CI of GMT were presented as log<sub>2</sub> reciprocal titers (log<sub>2</sub> titer 1: 8 = 3). To obtain the average results for the total population, data was weighted by age distribution of Thai population in 2004.<sup>16</sup>

### Ethical Consideration

The code from the HIS, the identifier for the serum samples, could not be linked to individual person. The study was reviewed and approved by the Ethical Review Committee for Research in Human Subjects, Ministry of Public Health, Thailand (20/2554).

## Results

Among the 1,717 serum samples, five specimens were denatured and a total of 1,712 samples were analyzed for antibody level. Among Thai population, protective

**Table 1. Stored and tested serum by birth cohorts from 4 regions in Thailand, 2004**

Birth cohort	Number of stored serum	Estimated proportion of protective immunity	Calculated sample	20% plus calculated sample	Tested serum
1928-1954	840	0.70	165	198	197
1955-1964	760	0.70	165	198	198
1965-1974	789	0.60	256	307	308
1975-1979	407	0.60	256	307	303
1980-1984	396	0.60	256	307	306
1985-1989	569	0.75	128	154	154
1990-1994	649	0.85	68	82	82
1995-1999	966	0.85	68	82	82
2000-2004	850	0.85	68	82	82
Total	6,226	-	1,430	1,717	1,712

antibody level against poliovirus was 90.9% for type 1, 94.7% for type 2 and 83.9% for type 3 (Table 2). Thai people born during 2000-2004 had 100% protective antibody against all three poliovirus types. Percentages for poliovirus types 1 and 3 decreased in cohorts born before 2000. The lowest percentages were among the 1980-1984 birth cohorts for poliovirus types 1 (74.5%) and 3 (66.0%), then increased by age. People who were born after 1990 had 100% protection for poliovirus type 2, which then decreased by age. All nine birth cohorts had protective antibody against poliovirus type 2, with the lowest (89.9%) among the 1955-1964 birth cohort.

Log<sub>2</sub> antibody titers against poliovirus were 6.0 for type 1, 6.7 for type 2 and 4.9 for type 3. The titers had a similar trend with that of the percentages of protective antibody (Table 2 and Figure 1). The highest titers were in the 2000-2004 birth cohorts. Mean titers decreased to the lowest values in the 1980-1984 birth cohorts for polio types 1 and 3, and

the 1955-1964 birth cohorts for type 2. All mean titers were higher than three (log<sub>2</sub> titer of 1:8).

## Discussion

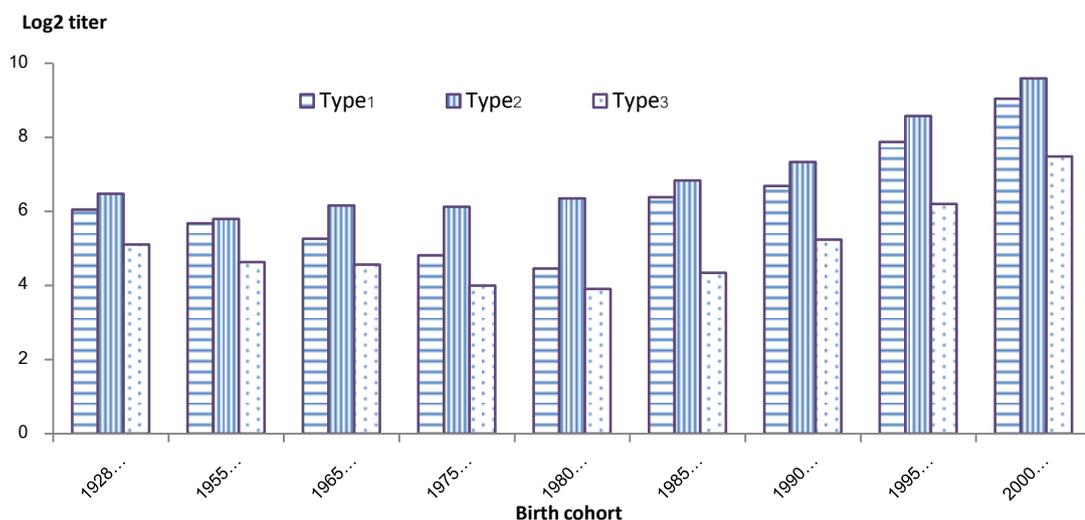
The protective antibody level against poliovirus among the general Thai population who had access to hospital was sufficient to prevent re-introduction of polio. However, this conclusion should be used with caution for population who lived in remote isolated areas or in areas with inadequate vaccine coverage. Additionally, this finding should not be assumed to apply to foreign migrant workers whom were not included in the study design. In other studies, protective herd immunity had been estimated between 80-86%.<sup>15,16</sup>

The protective proportion and mean titers of antibody among Thai people was less than those in high income countries such as Netherlands and Germany<sup>17,18</sup> possibly because of the interference from concurrent infections with other enterovirus or

**Table 2. Protective antibody level and 95% confidence interval (95% CI) against 3 types of poliovirus by birth cohorts in Thailand, 2004**

Birth cohort	Number of test	Type 1		Type 2		Type 3	
		Percent	95% CI	Percent	95% CI	Percent	95% CI
1928-1954	197	95.9	92.2-98.2	94.9	90.9-97.5	86.8	81.3-91.2
1955-1964	198	95.0	90.9-97.6	89.9	84.8-93.7	82.8	76.8-87.8
1965-1974	308	84.4	80.0-88.2	91.9	88.1-94.6	82.1	77.3-86.2
1975-1979	303	76.2	71.0-80.8	93.1	89.4-95.6	69.3	63.7-74.4
1980-1984	306	74.5	69.2-79.2	95.8	92.7-97.6	66.0	60.4-71.3
1985-1989	154	96.8	92.6-99.0	96.1	91.7-98.6	83.1	76.3-88.7
1990-1994	82	98.8	93.4-100.0	100.0	100.0-100.0	93.9	86.3-98.0
1995-1999	82	98.8	93.4-100.0	100.0	100.0-100.0	96.3	89.7-99.2
2000-2004	82	100.0	100.0-100.0	100.0	100.0-100.0	100.0	100.0-100.0
Total*	1,712	90.9*	-	94.7*	-	83.9*	-

\* Weighted by age distribution of Thai population in 2004 (Bureau of Policy and Strategy, Thailand)



**Figure 1. Mean and 95% confidence interval (95% CI) of antibody titers against 3 types of polio virus by birth cohorts in Thailand, 2004**

diarrheal diseases. Moreover, higher levels of maternal antibody in low to middle income countries could interrupt increasing of immunity during childhood.<sup>19</sup>

The proportion of persons with protective antibody was higher in the earlier birth cohorts, presumably because these age groups had been exposed to wild poliovirus. People born during 1965-1984 had a lower protective immunity than that of other birth cohorts. This might be due to the start-up of the EPI in 1977 when not everyone received the polio vaccine, yet the circulation of wild poliovirus decreased, and thus lowering the chance of natural infection. This result was similar to the Republic of Korea's seroprevalence data which immunity is lower among middle-aged population.<sup>20</sup> The proportion of the population with protective antibody also increased among later birth cohorts as polio vaccination coverage increased.

Among the three types of poliovirus, type 2 had the highest percentage of protective antibody at 90-100%. This finding was similar to other studies<sup>21,22</sup> that showed high immunogenicity of type 2 vaccines. The high percentage of protective levels of type 2 antibodies makes infection from type 2 VDPV less likely.

The low percentage of protective antibody against poliovirus type 3 was also similar to other studies<sup>20-22</sup>. This might be explained by low sero-conversion rate or potency of OPV type 3.<sup>23</sup> Other studies had shown that the level of protective antibody against poliovirus type 3 might be lower than other types of poliovirus.<sup>24,25</sup>

The protective titer for poliovirus types 1 and 3 for people born during 1975-1984 was lower than 80%, which put this population at risk of a polio outbreak. This underlined the importance of rapid OPV immunization in this group if there was a wild or VDPV outbreak in the country. The person in this birth cohort should also receive OPV or IPV vaccine if plan to visit high risk countries. A pre-outbreak OPV booster might be considered as a preventive measure. However, this would need to be weighed against the risk of polio importation, outbreaks and vaccine side effects in adults, especially vaccine associated polio paralysis (VAPP). The advantage of booster doses was supported by a study in Cuba in which eight OPV doses generated immunity against poliovirus higher than six OPV doses.<sup>26</sup>

Following the polio eradication and endgame strategy plan 2013-2018, replacing trivalent OPV with bivalent OPV (only poliovirus types 1 and 3) in routine immunization program of Thailand was likely

to have no problem from the switch because of globally eliminated wild type poliovirus type 2<sup>27</sup> and high immunity against poliovirus type 2 among population<sup>26,27</sup>. Advantages of the bivalent OPV include better immunity against poliovirus types 1 and 3, with at least 35% more effectiveness than trivalent OPV, and no VAPP from poliovirus type 2<sup>28</sup>.

There were some limitations in this study. First, as samples were collected from only four provinces, they might not be representative of the country. However, those provinces were located in four of the Thai geographic regions, so they captured a wide range of the population. Even though the serum samples were collected more than 10 years ago, the immunity results could represent the present situation because all the subjects would have or have not received OPV before 2004 and there has been no report of polio in the country since 2003.

In conclusion, Thailand was not at risk for polio outbreak. The protective levels for poliovirus types 1, 2 and 3 antibodies among Thai population were high enough to generate herd immunity. Because of the low percentage of antibodies to types 1 and 3, persons in 1975-1984 birth cohorts should be targeted for immunization if an outbreak occurred in Thailand or those persons plan to visit high risk countries.

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