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A seroprevalence study of poliovirus antibody among primary schoolchildren in Korea

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SUMMARY

We aimed to determine the seroprevalence of poliovirus antibody in Korea by using the cell culture neutralization method recommended by the WHO. A total of 500 sera collected from children at eight primary schools in Kyunggi province were used for this study. We found that 82·2% of children were positive for all three types of poliovirus and antibody-positive rates for types I, II and III were 94·4, 96·6 and 86·8% respectively, indicating that seropositive rates for types I and II were considerably higher than for type III ($P < 0{\cdot}0001$). This result implies that the type III component of the oral polio vaccine should be evaluated further. Although a greater number of children, including young infants, need to be tested for seroprevalence, this study still provides us with valuable information on the effectiveness of vaccination against polioviruses in Korea.

INTRODUCTION

Other than the five cases of poliomyelitis that occurred in 1983, there has been no recent report of poliomyelitis in the Republic of Korea. Poliomyelitis was an endemic disease until the introduction of oral polio vaccines in the early 1960s. Since the introduction of Sabin vaccine in 1962, and the inclusion of polio vaccines in the National Immunization Programme in 1970, the incidence of poliomyelitis has dramatically declined in Korea. By the late 1970s, the incidence of poliomyelitis had decreased to only a few cases per year. Poliomyelitis is a notifiable class 2 disease requiring every physician to immediately notify a health centre under the Division of Communicable Disease Control in Korea. These reports are sent through the Internet EDI (Electronic Data Interchange) system from health centres to the National Institute of Health, Korea (KNIH), and included in the Communicable Disease Monthly Report (CDMR) that has been published since August 2000.

For three decades, the oral poliovirus vaccine (OPV) has been recommended by the Korean Advisory Committee on Immunization Practices (KACIP), together with other vaccines including diphtheria, pertussis, tetanus (DTP), measles, mumps, rubella (MMR), tuberculosis and hepatitis B for infants and younger children. The estimated coverage rate of OPV immunization in Korea is 90–95%. Following the recommendations of KACIP, the initial immunization for OPV is given three times to infants at 2, 4 and 6 months of age, followed by a booster before school entry at between 4 and 6 years of age. A polio

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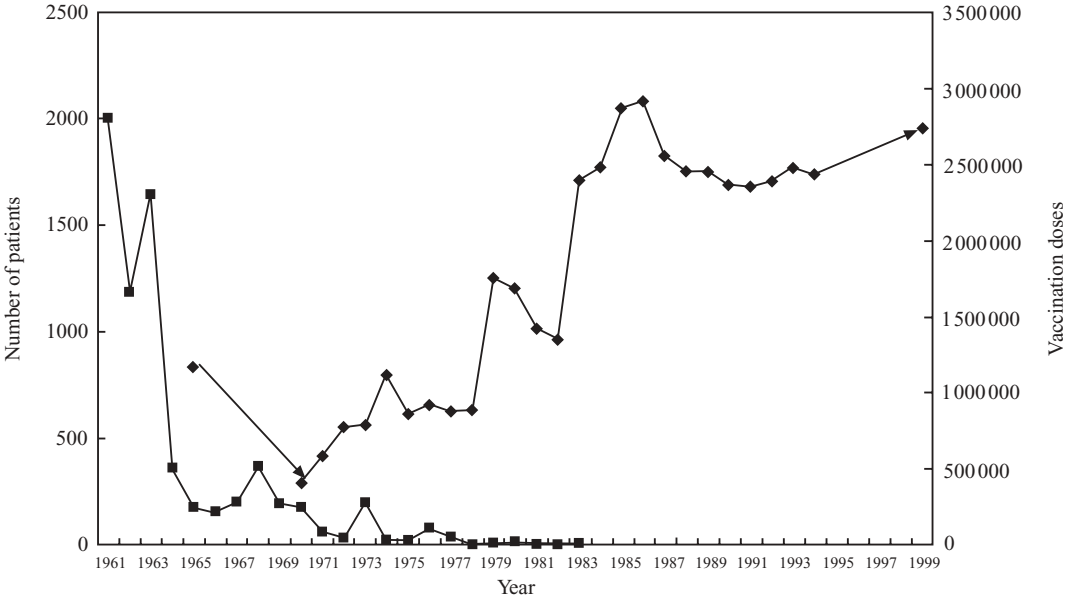

Fig. Poliomyelitis and OPV usage in Korea. ■, Poliomyelitis cases; ◆, OPV usage. (Data from *2001 Communicable Diseases Statistical Yearbook*, National Institute of Health, Korea.)

booster vaccination at 18 months was abolished in 1997.

For the production of oral polio vaccine, pharmaceutical companies in Korea import bulk materials for each poliovirus Sabin type and combine the appropriate titre of each type to produce the final vaccine product. The Figure shows the trend in the incidence of poliomyelitis and of OPV usage in Korea. As the usage of OPV has increased, the incidence of poliomyelitis has declined in Korea. The appropriate titre (N Log_{10} $TCID_{50}$) for each type included in the final product is: titre $>6{\cdot}0$ for type I; 5·0–5·3 for type II; and 5·3–5·7 for type III [1]. Inactivated polio vaccine (IPV) has only recently been introduced into the country. However, in accordance with recommendations for polio immunization issued by the Association of Korean Paediatricians, both OPV and IPV may be used from April 2002.

In this study, we aimed to provide supportive evidence of high OPV immunization uptake in Korea. We therefore decided to determine the seropositive rate of poliovirus antibody among 500 primary schoolchildren.

METHODS

Subjects

We tested sera from 500 children from eight primary schools in Kyunggi province, which is located in the north-western part of the Republic of Korea near the capital Seoul. Sera were selected from 2128 samples collected in 1999 using stratified random sampling in order to represent all grades of schoolchildren and to evenly represent children from eight primary schools. A total of 500 sera were collected representing all grades (ages 6–11 years) with even regional distribution from North, South, East and West. Tables 1 and 2 show the distribution of subjects in the various regions and age groups (grades). Unfortunately, the children's vaccination histories were not available. However, it is presumed that more than 90% of children had been vaccinated three times, since the average vaccination rate has continued to be high in this province.

Neutralization test

In this experiment, Sabin I, II, III strains and a rhabdomyosarcoma cell line were used for virus isolation and neutralization tests, in accordance with the *Polio Laboratory Manual* [2]. Sabin strains of poliovirus types I, II and III were obtained from the Korean Food and Drug Administration and used as the challenge viruses in the test. A 96-well microtitre plate was used for each test sera. Sera were inactivated at 56 °C for 30 min and then diluted twofold from 1/8 to 1/2048 using 50 μl of diluted sera for each well. A total of 50 μl of each virus sample, which corresponds to 100 $TCID_{50}$ of virus, was added to each dilution of sera and incubated at 37 °C for 1 h. Each well was filled with 1×10^5 cells and plates were

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Table 1. *Number of poliovirus neutralizing antibody-negative samples by region among the 500 sera tested*

Region	*n*	No. of neutralizing antibody negative sera						
		All	Type I only	Type II only	Type III only	Types I & II	Types I & III	Types II & III
South (urban)	91	0	3	1	13	3	2	0
South (rural)	79	0	1	0	10	0	4	0
North (urban)	66	0	2	2	5	0	1	0
North (rural)	28	0	0	0	6	0	1	0
East (urban)	64	0	3	0	3	0	2	0
East (rural)	68	0	3	1	4	0	1	3
West (urban)	72	0	0	3	5	1	0	3
West (rural)	32	0	0	0	2	0	1	0
Total	500	0	12	7	48	4	12	6

Table 2. *Seroprevalence of antibody to poliovirus among 500 sera tested*

School	*n*	Type I (%)	Type II (%)	Type III (%)	No. of fully immune sera (%)
South (urban)	91	83 (91·2)	87 (95·6)	76 (83·5)	69 (75·8)
South (rural)	79	74 (93·7)	79 (100·0)	65 (82·3)	64 (81·0)
North (urban)	66	63 (95·5)	64 (97·0)	60 (90·9)	56 (84·8)
North (rural)	28	27 (96·4)	28 (100·0)	21 (75·0)	21 (75·0)
East (urban)	64	59 (92·2)	64 (100·0)	59 (92·2)	56 (87·5)
East (rural)	68	64 (94·1)	63 (92·6)	60 (88·2)	55 (80·9)
West (urban)	72	71 (98·6)	65 (90·3)	64 (88·9)	60 (83·3)
West (rural)	32	31 (96·9)	32 (100·0)	29 (90·6)	29 (90·6)
		$P=0{\cdot}1952$	$P=0{\cdot}2309$	$P=0{\cdot}2446$	$P=0{\cdot}4033$

incubated at 37 °C in a 5% CO_2 incubator. The plate was observed each day until 7 days after infection and examined for the reduction in CPE. We interpreted the results according to the WHO's recommendation, with a cut-off titre of 8. The presence of neutralizing antibodies in sera at a dilution of 1/8 or higher were regarded as immune. Each sample was tested in duplicate. When there was a discrepancy in titre between two wells, the lower measurement was chosen as the titre for the corresponding sample. WHO/RIVM poliovirus antisera with known neutralizing activity were included in each test of sera to control the reproducibility of results. For each neutralization test plate, we also performed a back-titration by adding known titres ranging from 100 to 0·1 $TCID_{50}$ of Sabin viruses in duplicate.

Statistical analysis

A scored test for trends was performed using the Mantel–Haenszel χ^2 test. We assessed for independence using the χ^2 test and a P value of $<0{\cdot}05$ was considered significant.

RESULTS

The seropositive rates for all three types of poliovirus were analysed by region. The number of neutralizing antibody-negative sera by region are indicated in Table 1. The seronegative rate to type III was high, and 48 sera (9·6%) were found to be negative for polio type-III antibody. Fully immune sera to all three types of poliovirus were found in 82·2% (411/500). Seropositive rates to each type were 94·4% to Sabin I (472/500), 96·6% to Sabin II (483/500) and 86·6% to Sabin III (434/500). The seropositive rate for all three types ranged from 75·0% in the rural north to 90·6% in the rural west, and from 74·0% for grade 6 to 93·0% for grade 3. Otherwise, there was no regional difference in seropositive rate (Tables 2–4). There was no significant decrease in seropositive rate for all three types of poliovirus by

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Table 3. *Number of neutralizing antibody-negative samples by age among 500 sera tested*

Age* (grade)	*n*	No. of neutralizing antibody-deficient sera						
		All	Type I only	Type II only	Type III only	Types I & II	Types I & III	Types II & III
1	77	0	2	0	7	0	2	1
2	66	0	2	0	7	0	1	2
3	71	0	0	1	2	0	2	0
4	94	0	4	2	7	1	2	2
5	96	0	2	0	11	2	1	1
6	96	0	2	4	14	1	4	0
Total	500	0	12	7	48	4	12	6

* Ages for grades 1–6 range from 6–7, 7–8, 8–9, 9–10, 10–11 and 11–12 years, respectively.

Table 4. *Seroprevalence of antibody to poliovirus by age among 500 sera tested by cell culture neutralization*

Age* (grade)	*n*	Type I (%)	Type II (%)	Type III (%)	No. of immune sera (%)
1	77	73 (94·8)	76 (98·7)	67 (87·0)	65 (84·4)
2	66	63 (95·5)	64 (97·0)	56 (84·4)	54 (81·8)
3	71	69 (97·2)	70 (98·6)	67 (94·4)	66 (93·0)
4	94	87 (92·6)	89 (94·7)	83 (88·3)	76 (80·9)
5	96	91 (94·8)	93 (96·9)	83 (86·5)	79 (82·3)
6	96	89 (92·79)	91 (94·8)	78 (82·3)	71 (74·0)
Total	500	472 (94·4) $P=0·5896$	483 (96·6) $P=0·3118$	434 (86·6) $P=0·4617$	411 (82·2) $P=0·1824$

* Ages for grades 1–6 range from 6–7, 7–8, 8–9, 9–10, 10–11 and 11–12 years, respectively.
Mantel–Haenszel χ^2 test was used for trend analysis. For the trend analysis, the sum of grades 1 and 2, grades 3 and 4, and grades 5 and 6 was used.

age (Tables 3 and 4). We detected a relatively low seropositive rate for poliovirus type III compared to types I and II ($P<0·0001$).

DISCUSSION

The immunogenicity of OPV is lower in developing countries [3–5]. There has been substantial evidence of a low seroconversion rate to Sabin III [6–8]. The relatively low seroconversion rates to Sabin III compared to Sabin I and Sabin II have also been reported in the studies from developed countries, such as The Netherlands (96·6%), Germany (93·4%), and South Africa (89·7%) [9–11]. A seroprevalence study in the United States showed that the secondary spread of vaccine virus seemed to occur among children who had previously received one dose or less [12]. Some countries, including India, have recently introduced a titre of 5·8 for Sabin poliovirus type III in the production of oral polio vaccines, based on their survey results (Dr N. Withana, personal communication). However, a study performed in South Africa has showed that antibodies to type III were still lower than the other two types, in spite of the increase in the type III component to $1\times10^{5·6}$ TCID/dose [11]. A study conducted in Oman showed that the injection of the fourth dose of IPV, after three doses of OPV, was effective in enhancing the seropositive rate from 87·8 to 97·1% [13].

The seropositive rate required for maintaining population immunity to polio has not been universally determined by the WHO. However, the critical vaccination coverage needed to block transmission of poliovirus was determined to be 80–85% of the

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population by Anderson [14]. The level of full immunity determined in this study is therefore considered to be high enough to prevent the spread of wild poliovirus or vaccine-derived poliovirus if it is imported into Kyunggi-do. Serological studies using the cell culture neutralization test can be useful in defining regions of sub-optimal immunity, to enable special targeted vaccination programmes in countries that are almost polio-free.

Countries such as Japan and New Zealand in the Western Pacific Region or other regions have introduced, or are considering the introduction of IPVs [15, 16]. We have not yet seen many vaccine-associated paralytic poliomyelitis cases in Korea, and therefore the Ministry of Health and Welfare is not yet considering the inclusion of IPVs in the regular immunization programme, except for immunodeficient individuals for whom some practitioners prefer to use inactivated vaccines due to the risk of vaccine-associated paralytic poliomyelitis. However, we may consider the introduction of a combinational schedule of OPV and IPV in Korea, based on the results of a study in Oman [5]. We need to design a study to evaluate OPV and IPV/OPV immunizations in Korea in the near future, to assess whether the combinational schedule may be helpful in increasing the antibody-positive rate against poliovirus type III.

Despite the eradication of poliomyelitis in the Western Pacific Region, the level of acute flaccid paralysis surveillance and polio immunization coverage rate should be maintained at a high level in this region until the global eradication of poliomyelitis is achieved. Serological surveys, such as this study, can be a good indicator for determining and monitoring the immunization level in each country and ultimately supporting global activities towards the eradication of polio.

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