

## Certification of Poliomyelitis Eradication in Singapore and the Challenges Ahead

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### Abstract

**Introduction:** This study reviewed the epidemiological trends of poliomyelitis from 1946 to 2010, and the impact of the national immunisation programme in raising the population herd immunity against poliovirus. We also traced the efforts Singapore has made to achieve certification of poliomyelitis eradication by the World Health Organisation. **Materials and Methods:** Epidemiological data on all reported cases of poliomyelitis were obtained from the Communicable Diseases Division of the Ministry of Health as well as historical records. Coverage of the childhood immunisation programme against poliomyelitis was based on the immunisation data maintained by the National Immunisation Registry, Health Promotion Board. To assess the herd immunity of the population against poliovirus, 6 serological surveys were conducted in 1962, 1978, 1982 to 1984, 1989, 1993 and from 2008 to 2010. **Results:** Singapore was among the first countries in the world to introduce live oral poliovirus vaccine (OPV) on a mass scale in 1958. With the comprehensive coverage of the national childhood immunisation programme, the incidence of paralytic poliomyelitis declined from 74 cases in 1963 to 5 cases from 1971 to 1973. The immunisation coverage for infants, preschool and primary school children has been maintained at 92% to 97% over the past decade. No indigenous poliomyelitis case had been reported since 1978 and all cases reported subsequently were imported. **Conclusion:** Singapore was certified poliomyelitis free along with the rest of the Western Pacific Region in 2000 after fulfilling all criteria for poliomyelitis eradication, including the establishment of a robust acute flaccid paralysis surveillance system. However, post-certification challenges remain, with the risk of wild poliovirus importation. Furthermore, it is timely to consider the replacement of OPV with the inactivated poliovirus vaccine in Singapore's national immunisation programme given the risk of vaccine-associated paralytic poliomyelitis and circulating vaccine-derived polioviruses.

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### Introduction

Paralytic poliomyelitis used to be a common childhood disease in Singapore. It was recognised as a major public health problem in the immediate post World War II period.<sup>1</sup> The epidemiological pattern was that of an endemic disease with periodic epidemics, indicating transition from the endemic behaviour characteristic of countries with low levels of environmental sanitation, towards the epidemic behaviour characteristic of countries with improved hygiene standards.<sup>2</sup> There was no seasonal pattern; cases occurred throughout the year, with epidemics recorded in 1946, 1948

and the end of 1950 and beginning of 1951.<sup>1</sup> Age-specific incidence showed that children below the age of 5 years were most at risk, particularly those between 6 months and 2 years of age. Laboratory investigations showed that poliovirus type 1 was responsible for the majority of cases and for the epidemic waves; poliovirus type 3 was of minor importance, while poliovirus type 2 relatively unimportant.<sup>2,3</sup>

Serological and faecal surveys conducted in 1960 showed that the rates of natural infection occurred extensively in very young children with over 50% having neutralising

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antibodies for all 3 poliovirus types by the age of 5 years.<sup>2</sup> In addition, over 20% of the children had natural non-poliovirus enterovirus infection which could interfere with the uptake of live oral poliovirus vaccine (OPV) should it become available for the control of paralytic poliomyelitis.<sup>2</sup>

### **Poliomyelitis and OPV in Singapore**

Singapore was among the first countries in the world to introduce live OPV on a mass scale. During the 1958 to 1959 epidemic caused by poliovirus type 1, monovalent Sabin type 2 attenuated poliovirus vaccine was administered on a voluntary basis to 200,000 children between 3 months and 10 years of age in an attempt to abort the raging epidemic of 415 paralytic cases.<sup>1</sup> At that time, inactivated poliomyelitis vaccine (IPV) was the only vaccine licensed for mass administration in the United States of America, and OPV had just been developed. However, IPV would have taken several weeks to confer protection, and would have been ineffective as an emergency measure once the epidemic had started.<sup>4</sup> In addition, there were concerns over the safety of IPV due to the Cutter incident of 1955, in which inadequately inactivated IPV led to an epidemic of poliomyelitis in the United States.<sup>5</sup> It was during this difficult period that Professor ES Monteiro (Dean of the Faculty of Medicine and Professor of Clinical Medicine, University of Malaya, Singapore) and Professor JH Hale (Head, Department of Bacteriology, University of Malaya, Singapore) decided to use OPV to try and stop the epidemic, and had to defend their decision before the Singapore Medical Association because of insufficient information and data about OPV at that time.<sup>6</sup>

The Singapore Medical Association eventually gave Professors Monteiro and Hale the mandate to use OPV, and the vaccine was obtained from the United States with the permission of Dr Albert Sabin (Professor of Research Paediatrics, University of Cincinnati College of Medicine, Ohio, United States) on condition that adequate laboratory control could be assured.<sup>1</sup>

It was hoped that the dissemination of large quantities of OPV throughout the community would interfere with the natural transmission and establishment of the epidemic type 1 poliovirus, thus providing protection to the susceptible population.<sup>1,3,7</sup> Moreover, to enable the safety of the vaccine to be assessed under field conditions, the use of a different serotype in the vaccine would enable cases of poliomyelitis caused by the wild poliovirus to be distinguished from those which resulted from the vaccine-derived poliovirus. The raging epidemic was brought under control and there was a substantial reduction in the risk of paralytic disease as a result of the vaccination.<sup>8</sup>

However, in 1960, another epidemic of 196 poliomyelitis cases occurred.<sup>3</sup> It became evident that this pattern of

endemicity with periodic epidemic peaks would continue unless the herd immunity of the population could be raised through a comprehensive childhood immunisation programme against poliomyelitis.

### **Disease Trend and Launch of the Immunisation Campaign**

In 1959, the Singapore Government appointed a Committee on Poliomyelitis to study the problems related to the prevention of poliomyelitis in Singapore. Professor Lim Kok Ann of the Department of Bacteriology and a member of the World Health Organisation Expert Advisory Panel on Virus Diseases, was invited to advise the Committee.<sup>2</sup> The findings of this committee led to the first phase of the poliomyelitis (OPV) immunisation campaign which began in March 1962.<sup>7</sup> Children between the ages of 6 months and 5 years who visited the Maternal and Child Health Centres for immunisation against diphtheria were offered OPV on a voluntary basis. Trivalent OPV was administered in 2 doses, 3 months apart, and it was hoped that repeated vaccinations would overcome the interference caused by naturally occurring enteroviruses. By November 1962, 205,000 children, comprising about 60% of the target population had received 2 doses. This led to a dramatic fall in the incidence of paralytic poliomyelitis at the end of 1962.<sup>2</sup>

A follow-up serological study revealed that 98.5% of the vaccinees possessed neutralising antibodies to poliovirus type 2, but only 50% to type 1 and 58.8% to type 3.<sup>2</sup> This was unsatisfactory since seroprotection against types 1 and 3 was considered of more importance epidemiologically compared to type 2. The children of the first phase of the immunisation campaign were recalled for a third dose of trivalent OPV, and eventually about a third of them completed their primary course of 3 doses.<sup>9</sup>

Based on the experience gained, the Ministry of Health (MOH) inaugurated a routine programme of immunisation against poliomyelitis on a voluntary basis with OPV in March 1963. Infants aged 3 to 4 months were offered 3 doses of OPV at monthly intervals when they turned up for vaccination against diphtheria.<sup>2</sup> In view of the varied serological responses to the different poliovirus serotypes, the first 2 doses of the immunisation schedule were changed from trivalent vaccine to bivalent vaccine comprising types 1 and 3 followed by a single dose of trivalent vaccine. Since types 1 and 3 polioviruses were responsible for the majority of cases in Singapore, it was considered desirable to immunise with these types initially; and to include them even when immunising with type 2 vaccine. Type 2 vaccine was omitted from the first 2 doses as type 2 in a trivalent mixture was found to interfere with the immune response of the other types.<sup>7</sup> To ensure long-lasting immunity, a booster dose of trivalent vaccine was given a year later and again

at the age of 4 years.

Unfortunately, an epidemic of 74 cases of paralytic poliomyelitis re-appeared in 1963, of which 64 cases occurred in the latter half of the year.<sup>7</sup> Of the reported cases, 77% were infants between 6 months and 2 years of age with type 1 poliovirus isolated from more than 50% of these cases. These findings led to the decision to increase vaccine coverage and the number of boosters to disrupt transmission of wild poliovirus (WPV) strains and to maximise the possibility of vaccine “take” given the high prevalence of naturally occurring enteroviruses in the community. In 1964, catch-up vaccination was offered to children attending primary school for the first time at age 6 to 7 years. Those who had never been vaccinated were given the primary course of 3 doses, while those who had had 2 doses in the 1962 campaign were given one dose of trivalent vaccine as a booster.<sup>2,10</sup>

To enhance and maintain the immunity of the population, the immunisation programme was further expanded in 1976 to include primary school and secondary school leavers aged 11 to 12 years and 15 to 16 years, respectively.<sup>10</sup>

With the successful control of poliomyelitis, the bivalent OPV of the first 2 doses of the primary course were substituted with the trivalent OPV in September 1982 to relieve the workload required in the preparation of both bivalent and trivalent vaccines.<sup>10</sup> The boosters given at 4 years and 15 to 16 years were also removed.

### Immunisation Coverage

The immunisation programme was implemented by the government-run Maternal and Child Health Services and School Health Services, as well as registered private medical practitioners in Singapore. The denominator used for the determination of coverage rate for preschool children was based on notification of births obtained from (i) duplicate copies of the 24-hour Notification of Birth Forms received from private medical practitioners and midwives; and (ii) the Preliminary Report of Birth Forms received from the Registrar of Births and Deaths. In the case of school children, it was based on the list of school entrants supplied by school principals. The immunisation records were subsequently computerised and managed by the National Immunisation Registry (NIR) which is responsible for the collection and maintenance of accurate, complete and current immunisation records of all children from birth to 18 years of age in Singapore till this day. Although notification of vaccination against poliomyelitis is not mandated by law, both public and private healthcare institutions routinely notify NIR of all immunisations that had been administered to preschool children. The records of immunisations carried out in schools are maintained by the School Health Services.

Since 1962, immunisation against poliomyelitis remained voluntary. However, as the immunisation schedule for poliomyelitis is the same as that for diphtheria which is compulsory by law, the uptake for poliomyelitis immunisation has been good. The immunisation coverage for the primary course of 3 doses ranged between 78% and 96.4% of the total live births during the period 1973 to 1977.<sup>10</sup> For the period 1978 to 1982, 84% of the total live-births completed the primary course under one year of age while an estimated 74.1% to 86.5% of preschool children (2 years of age) were given the first booster doses. During the same period, boosters were administered to 93.8% of primary school entrants 6 to 7 years of age, and 88.5%, and 91.4% of primary (11 to 12 years) and secondary school leavers (15 to 16 years), respectively.<sup>11</sup> During the period 2003 to 2007, the immunisation coverage for all age groups improved further. Ninety-five percent to 97% of infants below 1 year of age completed the primary course and 83% to 91% of 2 year olds received the first boosters. In addition, 92% to 94% of primary school entrants and 95% to 98% of primary school leavers were administered boosters.<sup>12</sup>

Singapore’s current National Childhood Immunisation Programme for poliomyelitis is described in Table 1.

The immunisation coverage for infants, preschool and primary school children has been maintained at around 92% to 97% over the past decade (Table 2).

### Poliomyelitis Situation from 1964 to 2000

Notification of poliomyelitis was made compulsory by law since 1939.<sup>13</sup> With the comprehensive coverage of the national childhood immunisation programme, the incidence of paralytic poliomyelitis dropped sharply from 74 cases

Table 1. National Childhood Immunisation Programme for Poliomyelitis, Singapore, 2010

Primary course	Booster doses	
	Preschool children (1 – 5 years)	Primary school students (6 – 12 years)
3 months (Types I, II + III)	18 months 1st Booster (Types I, II + III)	6+ years (Primary school entrants) Either:
4 months (Types I, II + III)		(a) Primary course for those who have never been vaccinated; or
5 months (Types I, II + III)		(b) 2nd Booster (Types I, II + III) for those who had been vaccinated.  10 – 11 years (Primary 5) 3rd Booster (Types I, II + III)

Table 2. Poliomyelitis Immunisation of Infants, Preschool and School Children, 1995 to 2010

Year	Coverage* for children at 2 years of age				School children		
	Completed primary polio course		Boosters given		School entrants	Boosters given#	
	No.	Coverage %	No.	Coverage %		No.#	Coverage %
1995	47,027	98	45,761	95	53,151	47,727	90
1996	46,345	97	45,382	96	48,075	43,355	90
1997	45,246	98	44,434	96	52,569	47,927	91
1998	45,932	97	44,917	95	49,793	44,191	89
1999	44,927	97	43,852	95	50,435	45,035	89
2000	41,244	98	40,085	95	50,912	46,397	91
2001	40,185	96	37,083	88	50,459	46,527	92
2002	43,227	96	39,887	87	49,657	46,052	93
2003	38,010	96	33,026	83	49,788	46,506	93
2004	36,548	95	34,211	89	47,918	45,085	94
2005	33,997	96	32,070	91	44,110	41,478	94
2006	31,935	95	30,009	90	44,572	41,312	93
2007	31,768	97	28,909	88	48,122	44,380	92
2008	30,964	97	27,679	87	43,548	40,055	92
2009	34,466	97	32,272	91	43,142	39,752	92
2010	32,496	96	30,299	90	39,465	37,037	94

\*Data refers to immunisation given to children of all Singaporean and Singapore permanent residents

#Coverage does not include booster immunisations done by private medical practitioners

in 1963 to 4 cases in 1968 and only 5 cases from 1971 to 1973. This decline in the number of poliomyelitis cases corresponded with the increase in immunisation coverage

(Fig. 1). It is important to note that the 5 cases reported from 1971 to 1973 were all children who had not completed the full course of primary immunisation.<sup>3</sup>

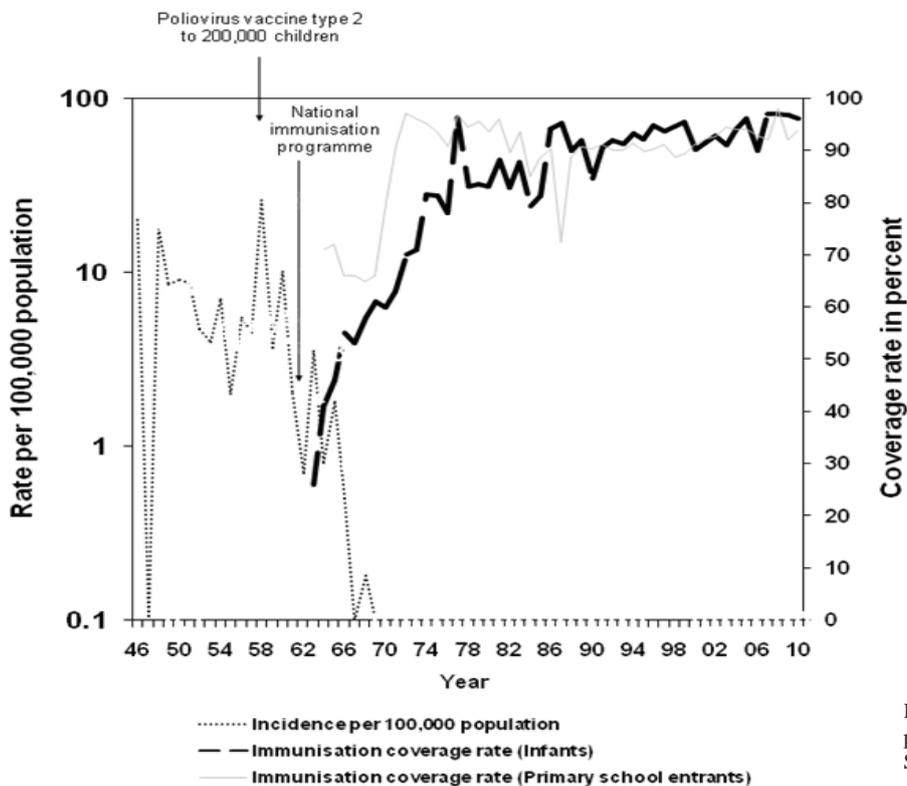


Fig. 1. Incidence per 100,000 population from poliomyelitis and immunisation coverage rates in Singapore, 1946 to 2010.

### *Pre-certification Surveillance of Vaccine-Associated Paralytic Poliomyelitis (VAPP)*

In June 1978, a case of acute flaccid paralysis was reported in an 8-month-old Indian boy.<sup>13</sup> He had been given the first dose of OPV (types 1 and 3) on 4 May 1978 and developed paralysis of the left upper limb 16 days later. Poliovirus type 1 was isolated from stool cultures, but there was no 4-fold rise in neutralising antibody titres. Another similar case in a 5-month-old Chinese baby was also reported in that same year.<sup>13</sup> The baby developed paralysis of the left lower limb one week after receiving the first dose of types 1 and 3 OPV. Although poliovirus type 3 was isolated from stool cultures, no 4-fold increase in antibody titres was again noted. Since live OPV was administered, the recovery of polioviruses from the stool of these 2 cases was not surprising as vaccine polioviruses, like the wild ones, replicate in the gut and could continue to be excreted in the stool for 6 weeks.<sup>14</sup> However, in the absence of a significant neutralising antibody rise in both cases, the paralysis was highly unlikely to have been polio. In any case, no test was carried out to differentiate if the viruses were vaccine or wild type, so if it was polio, whether or not the paralysis was due to the vaccine is not clear.

In 1999, a 4-month-old local Malay boy was admitted from 2 December to 16 December 1999 for meningoencephalitis complicated by seizures. The child presented with a history of fever, poor feeding and lethargy. He had received his first OPV dose on 1 November 1999. Physical examination revealed mild hypotonus with unsustained ankle clonus and normal reflexes. A computed tomography (CT) scan of the brain showed mild cerebral oedema, and microscopy of cerebrospinal fluid (CSF) showed increase in leucocytes but culture was negative for neurotropic viruses. Blood and urine cultures were also negative. Stool for enteroviruses revealed Sabin-like poliovirus type 1 with some mutations in all important antigenic sites. The child was well during follow-up, with power, tone and reflexes normal for his age. Since there was no residual paralysis, this child was not considered to be a case of poliomyelitis.

### *Pre-certification Surveillance of Imported Cases*

No other indigenous poliomyelitis case was reported from 1978 onwards. All the cases reported subsequently prior to poliomyelitis certification were imported, involving foreigners seeking medical treatment in Singapore.

In 1982, there was an imported case from India.<sup>15</sup> This was a 10-month-old male infant with no history of poliomyelitis immunisation. He developed fever and weakness of the left lower limb 2 weeks after he arrived in Singapore, and was admitted to hospital for treatment 3 days later. His stool culture was positive for poliovirus type 3. During active

case detection, 4 of his family members, aged between 2 and 10 years, were found to have no history of poliomyelitis immunisation. They were subsequently immunised.

Two imported cases of paralytic poliomyelitis and an asymptomatic case were reported in 1983.<sup>16</sup> The first was a 16-month-old male infant from Indonesia with a history of primary course of poliomyelitis immunisation. He developed fever and paralysis of the left lower limb while in Indonesia. He sought treatment in Singapore almost 4 weeks from the onset of fever. Poliovirus type 1 was isolated from the stool culture and 2 blood specimens showed high antibody titre to poliovirus. The second case, a 20-month-old male Vietnamese refugee, developed fever and weakness of his right lower limb while in Vietnam. Upon arrival to Singapore a month later, he was administered OPV at the Vietnamese refugee camp and subsequently hospitalised 2 weeks later. His stool culture was positive for poliomyelitis type 2, which was probably vaccine-derived. The asymptomatic case was a 25-year-old Chinese male resident living in Singapore. He presented with a sore throat and cough and was treated symptomatically at the outpatient polyclinic. A throat swab subsequently grew poliovirus type 1. Intratypic strain differentiation on the poliovirus isolate showed that the strain was vaccine-derived, which corroborated with the patient's recent history of primary polio immunisation and boosters.

In 1984, 2 imported cases of paralytic poliomyelitis from Indonesia were notified.<sup>17</sup> The first was a 14-year-old Indonesian girl who developed fever and weakness of both lower limbs. She was hospitalised in Indonesia and subsequently referred to Singapore for further treatment. Serological tests revealed poliovirus type 2 infection. She had no past history of immunisation against poliomyelitis. The second case was a 2-month-old Indonesian Chinese. He presented with fever and general paralysis in his home town and was treated by a general medical practitioner there. He sought medical treatment in Singapore a week later. Stool culture was found positive for poliovirus type 1. He also had no prior immunisation against poliomyelitis.

Two imported cases of paralytic poliomyelitis from Indonesia were reported in 1986.<sup>18</sup> The first was a 9-year-old boy and the second, a 9-month-old male infant. Both were not immunised against poliomyelitis and presented with weakness of the lower limbs in Indonesia. Upon seeking medical treatment in Singapore, poliovirus type 1 was isolated from the stool culture of the first case, and type 3 from the second case. Intratypic differentiation confirmed these were non-Sabin like wild poliovirus strains.

### **Assessing the Herd Immunity of the Population**

Given the high coverage of the national immunisation

programme, it was deemed unlikely that outbreaks of paralytic poliomyelitis would occur in the childhood population. However, there were growing concerns that there could be pockets of susceptible young adults who had missed the national immunisation programme and who congregated in close settings.<sup>19</sup> With the rapid decline in poliovirus transmission in the community, acquisition of natural immunity was minimal. Indeed, a 1978 serological study conducted in 127 national servicemen born between 1955 and 1958 showed that more than one third (35.4%) remained susceptible to at least one of the 3 poliovirus serotypes with the majority susceptible to poliovirus type 3, followed by type 2 and type 1.<sup>19</sup> Based on the findings, OPV was routinely offered to army recruits as a precautionary measure against adult poliomyelitis since 1978.

Serological surveys were conducted periodically to assess the herd immunity of the population against all 3 serotypes of poliovirus. A survey conducted in 1982 to 1984 among children from 6 months to adults above 45 years of age confirmed the high level of herd immunity in the population with 93.9% to 96.7% possessing neutralising antibody to all 3 types of poliovirus.<sup>20</sup>

In 1989, a rapid serological assessment was undertaken based on blood samples collected in a maternal and child health clinic from 30 infants below 1 year of age who had completed 3 doses of trivalent OPV. All 30 infants were found to possess neutralising antibodies to all 3 serotypes, thus confirming the immunogenicity of the trivalent vaccine

administered in the national immunisation programme.<sup>21</sup>

Another study conducted in 1993 confirmed the high level of herd immunity among the general population from 6 months to above 45 years of age with more than 99.0% possessing neutralising antibody to poliovirus types 1 and 2; and 97.8% to type 3.<sup>22</sup> Even adults above the age of 30 years had a relatively low level of susceptibility to poliovirus with 93.6% possessing neutralising antibodies to all three serotypes.

The last survey conducted from 2008 to 2010 showed that approximately 92% of children aged between 1 and 17 years had antibodies to poliovirus.<sup>23</sup>

### Preparing Singapore for Certification of Poliomyelitis Eradication

In 1988, the World Health Assembly adopted the goal of global eradication of poliomyelitis by the year 2000.<sup>24</sup> In 1996, the Regional Certification Commission of the World Health Organisation (WHO) Western Pacific Regional Office was established with the responsibility of determining when the Western Pacific Region could be declared free of poliomyelitis, in view of the WHO's target for global eradication by end 2000. The criteria<sup>25</sup> for regional certification are: (i) an absence of circulation of indigenous wild poliovirus transmission for a period of at least 3 years during which surveillance had been maintained at the level of performance needed for certification; (ii) a National

Table 3. Performance of AFP Surveillance System, 1996 to 2010

Year	Expected number of AFP cases*	Total AFP cases (< 15 years)	Total non-polio AFP cases	Non-polio AFP rate†	AFP cases with adequate stool samples‡		Cases with follow up at 60 days (%)
					No.	%	
1996	7	3	3	0.43	0	0	100
1997	7	7	7	1.00	4	57	100
1998	7	6	6	0.86	3	50	100
1999	7	8	8	1.00	2	25	63
2000	7	6	6	0.84	5	83	100
2001	7	9	9	1.24	4	44	78
2002	7	6	6	0.82	1	16	100
2003	7	5	5	0.70	4	80	100
2004	7	6	6	0.85	4	66	75
2005	7	10	10	1.44	8	80	100
2006	7	5	4	0.58	4	100	100
2007	7	10	10	1.47	11	100	100
2008	7	7	7	1.04	6	86	100
2009	7	7	7	1.05	6	86	100
2010	7	4	4	0.57	4	100	100

\*Base population of 700,000 is assumed.

†Per 100,000 population aged less than 15 years.

‡Two stool samples collected at least 24 hours apart, within 14 days after onset of paralysis, delivered to the laboratory packed in ice, with sufficient quantity for complete analysis and accompanied by proper documentation.

Certification Committee in each country has validated and submitted the certification documentation required by the Regional Commission; (iii) appropriate measures had been put in place to detect and respond to importation of wild poliovirus. Other prerequisites included a sensitive surveillance system for detecting all cases of acute flaccid paralysis (AFP) meeting standard performance indicators (e.g. the processing of all stool samples from AFP case-patients in WHO-accredited laboratories).

#### *Acute Flaccid Paralysis (AFP) Surveillance*

In December 1995, Singapore set up an AFP surveillance system to detect possible cases of poliomyelitis.<sup>26</sup> Under this system, all public acute care hospitals were requested to immediately notify all cases of AFP, including Guillain-Barré syndrome and transverse myelitis in any child below the age of 15 years. All AFP cases detected were required to have 2 consecutive stool samples for virus isolation taken 24 to 48 hours apart, within 14 days of the onset of paralysis. These cases would then be followed up for a duration of 60 days after the onset of paralysis for assessment of any residual paralysis.

This system did not initially meet the WHO's established criteria for the performance standards of a sensitive AFP surveillance system of detecting at least one AFP case per 100,000 population under the age of 15 years, even in the absence of wild poliovirus circulation. Based on Singapore's resident population, its AFP surveillance system should detect at least 7 to 8 cases of AFP per year. In 1996, only 3 cases of AFP were noted, which fell below the target.<sup>27</sup> The National Committee for the Certification of Poliomyelitis Eradication which was set up in 1996 thus revised the system in December 1996 in order to better meet these standards. The enhanced system required all public acute care hospitals as well as paediatricians and neurologists in private practice to notify all patients under the age of 15 years diagnosed with disease that could lead to AFP, regardless of whether AFP was present or not. These "at risk" diagnoses included poliomyelitis, all forms of encephalitis and myelitis, acute infective polyneuritis including Guillain-Barré syndrome, mononeuritis not due to physical causes, and monoplegia. Monthly returns, including "Nil" returns, were required. Further, checks on all hospital discharges (through public and private hospitals' computer databases) for AFP cases and cases with "at risk" diagnosis" were conducted periodically. This enhanced system was largely able to meet the WHO's performance targets.

Table 3 shows the initial results of the AFP surveillance system in 1996 and the performance from 1997 to 2010 after the system was enhanced with additional surveillance components.

#### *Supplementary Surveillance Activities*

To complement the AFP surveillance system and the surveillance activities of the National Polio Laboratory to prepare for Singapore's certification process, the Ministry of Health, Singapore undertook a retrospective case review of 95 cases admitted to the public hospitals in 1995 and 1996 with diagnoses that may have presented with AFP.<sup>28</sup> Similarly, another review was carried out in 1997 for 30 cases seen in the private sector over the period 1994 to 1996.<sup>28</sup> The first review on the public sector cases showed that 9 of the 95 cases had actually presented with AFP (6 with Guillain-Barré syndrome, 2 with encephalitis, and one with meningoencephalitis) but none with poliomyelitis. The second review on the private sector cases revealed that 9 of the 30 cases had indeed presented with AFP (7 with Guillain-Barré syndrome, one with transverse myelitis), and one was a possible case of paralytic poliomyelitis. This was a 2-year-old Bangladeshi female infant who developed AFP in her home country in March 1995, 5 days after receiving an OPV booster.<sup>28</sup> She came to Singapore for medical consultation where she was provisionally diagnosed as Guillain-Barré syndrome. Subsequently, a stool sample done back in Bangladesh isolated type 1 poliovirus, but there were no facilities for intratypic differentiation.

To further strengthen the AFP surveillance, the MOH also implemented a routine monthly check of its computerised database of hospital discharges. This practice has been in place since 1997.<sup>26</sup>

An event diagnosis of AFP would first be confirmed with the attending physician, before obtaining the case summary for further review. All cases of AFP which have not been notified are then identified, and hospital staff will be informed and reminded to notify all AFP cases in the future.

#### *National Laboratory for Poliomyelitis Eradication (National Polio Laboratory)*

In 1995, the WHO designated the Virology Section, Department of Pathology, Singapore General Hospital, as the National Laboratory for Poliomyelitis Eradication (National Polio Laboratory). The national surveillance of enteroviruses in Singapore has been carried out through this WHO-accredited laboratory since then.

Since 1996, all stools from AFP cases, suspected AFP cases, or cases defined under the enhanced AFP surveillance system have been cultured for poliovirus by the National Polio Laboratory. Initially, all poliovirus isolates, regardless of the source, were sent to the WHO Regional Poliovirus Reference Laboratory at the Victorian Infectious Diseases Reference Laboratory in Melbourne, Australia for differentiation between wild and Sabin type. However, since 2003, this function of intratypic differentiation has been

performed by the National Polio Laboratory in Singapore.<sup>29</sup> The laboratory has been notifying the MOH of test results within 28 days upon receipt of samples, and from 2010 onwards, within 14 days. Detection of any wild poliovirus is reported immediately to the MOH and the WHO.

#### *Laboratory Containment*

In November 1999, the National Coordinator for Containment of Wild Poliovirus implemented Phase 1 of the Action Plan of the Laboratory Containment in Singapore. The nationwide search to identify laboratories that may have stored wild poliovirus and infectious or potentially infectious material was successfully completed by the MOH and the National Polio Laboratory. From the national search, only one laboratory at the National University of Singapore was identified to have stored infectious wild poliovirus material which had since been destroyed by 2000.

The national inventory was updated in 2007. Survey questionnaires were sent out to all public and private institutions that might have laboratories containing any infectious material. Of the 211 laboratories listed, 28 institutions with no functioning laboratories were excluded. All of the remaining 183 laboratories confirmed that there was no infectious or potentially infectious material retained.

As part of the certification process, Singapore outlined a detailed response protocol to reported cases of poliomyelitis, whether indigenous or imported.<sup>26</sup> This protocol included the following aspects: (i) the establishment of a Steering Group of Experts to advise the National Committee for the Certification of Poliomyelitis Eradication and to co-ordinate activities nationwide; (ii) case investigation and contact tracing carried out by the Communicable Disease Centre, Tan Tock Seng Hospital; (iii) environmental inspection of water samples collected from rivers, waterworks and reservoirs; (iv) evaluation of immunisation response, determined by the epidemiology of the outbreak (if any) and other factors such as evidence of ongoing or potential for widespread transmission; (v) enhanced surveillance such as the AFP surveillance system, National Polio Laboratory activities and the MOH's supplementary checks for unreported AFP cases; and (vi) documentation of all of the above.

Based on the final documentation prepared by the National Committee for Poliomyelitis Eradication,<sup>28</sup> Singapore was certified poliomyelitis-free by the WHO on 29 October 2000, together with 36 other countries in the Western Pacific Region. This was the second region in the world after the Americas to achieve poliomyelitis-free status.

#### **Post-Certification**

Singapore's successful attainment of a poliomyelitis-free

status can be attributed to the high immunisation coverage as well as vast improvements in environmental hygiene and sanitation over the past few decades. Even though the Western Pacific Region to which Singapore belongs was certified poliomyelitis free in 2000, the problem is far from over. Continued vigilance is necessary because of the risk of importation of WPV from the remaining poliomyelitis endemic countries, including Pakistan which is connected to Singapore by trade and travel. During 2002 to 2006, 21 previously poliomyelitis-free countries in Africa had WPV importations originating from Nigeria and India with 4 countries (including Indonesia) reporting outbreaks of more than 100 cases.<sup>30,31</sup> Despite control efforts to interrupt WPV transmissions, multiple importations of WPV from countries with ongoing transmission resumed in Africa in 2008 to 2009.<sup>32</sup> In 2010, the first importation of WPV into the WHO European Region occurred since the region had been certified free of poliomyelitis in 2002. The outbreak in Tajikistan went on to spread to 3 other polio-free countries in the region.<sup>33</sup> In 2011, an incursion of wild poliovirus type 1 from Pakistan to the poliomyelitis-free Western Pacific Region resulted in an outbreak in Xinjiang Province, China.<sup>34</sup>

These events serve as reminders of the world's vulnerability to polio as long as poliovirus transmission remains in other parts of the world. While it is encouraging that India has recently been officially removed from the list of countries with active transmission of endemic polio on 25 February 2012 after being polio-free for one year, the country must continue this success for 2 more years in order to achieve polio-free status by the WHO.<sup>35</sup>

#### *Response to an Imported case of Wild Poliovirus*

Singapore encountered its first imported case of WPV post-certification in 2006.<sup>29</sup> This imported case was a 2-year-old Nigerian female from Jigawa, one of the 5 most endemic states for poliomyelitis in Nigeria. She presented with fever and paralysis of the left lower limb while in Nigeria. Subsequently, almost a week later, she sought medical treatment in Singapore. She apparently completed 3 doses of OPV with the last dose in June 2005. The patient was clinically diagnosed with polyradiculitis (likely due to poliomyelitis) and treated with a course of intravenous immunoglobulin. Poliovirus type 1 was isolated from her stool specimen; and intratypic differentiation conducted in the National Polio Laboratory confirmed that it was a wild strain of poliovirus. The viral samples were subsequently destroyed in accordance with the WHO's accreditation criteria.<sup>29</sup>

The outbreak response protocol was activated. Contact tracing efforts undertaken by the Communicable Diseases Division, Ministry of Health, Singapore showed that 8 children were likely to have come in contact with the case

during the time she was in the clinic in Singapore. Of these contacts, 3 were non-residents who had left Singapore. The WHO was informed to trace these contacts and had followed-up with the necessary precautionary measures such as immunisation and stool investigation. The next 4 contacts were Singapore residents, 3 of whom had up-to-date OPV immunisation records while the fourth was a 1-month-old infant who was not due for OPV vaccination. Stool investigations of these 4 children were negative for poliovirus. The remaining contact was a Taiwanese child who had not been contactable. However, immunisation records showed that the child had been up-to-date with OPV vaccination. Despite intensified surveillance, no secondary transmission was detected.

#### *Risk of Transmission Among Migrant Population*

Singapore has a highly mobile workforce and a large proportion of immigrant workers. As of December 2010, Singapore has 871,000 work permit holders, including foreign domestic workers.<sup>36</sup> A considerable number of these foreign workers come from the remaining poliomyelitis endemic countries. The immune status of these foreigners is by and large unknown, as they are not required to be vaccinated against poliomyelitis prior to entry into Singapore. Given the congregation of foreign workers in certain locales in Singapore, there is a potential risk of transmission. Thus, a close watch over the situation is being maintained.

#### *Choice of OPV Versus Inactivated Poliomyelitis Vaccine (IPV)*

The WHO has acknowledged that the eventual cessation of OPV use in routine immunisation programmes worldwide will become necessary to assure a lasting eradication of poliomyelitis.<sup>37,38</sup> Several countries, including the United States of America have switched from OPV to a full inactivated poliomyelitis vaccine (IPV) schedule, mainly to eliminate the risk of vaccine-associated paralytic poliomyelitis (VAPP).<sup>39</sup>

The risk of VAPP has been estimated to be 2 to 4 cases per million birth cohort per year in countries using OPV<sup>40</sup> with considerable variation between countries.<sup>14,41-45</sup>

The last city known to adopt an all IPV immunisation schedule in the WHO Western Pacific Region is Hong Kong in February 2007.<sup>46</sup> Some countries use sequential administration of IPV and OPV, which has been shown to be highly effective in inducing seroconversion,<sup>47</sup> and is also associated with substantially reduced risk of VAPP.<sup>47-49</sup>

Analyses of the incremental cost-effectiveness of switching from OPV to IPV have generally shown that such a change is not cost effective,<sup>50</sup> with cost per VAPP

case averted ranging from US\$740,000 (South Africa) to US\$3 million (USA) and AUS\$17 million (Australia).<sup>51-53</sup> However, cost effectiveness evidence plays a small role in the decision for the switch from OPV to IPV for most countries. VAPP prevention appears to be the main driver as even the extremely low risk of VAPP is deemed no longer socially acceptable in the absence of wild poliovirus.

To date, Singapore has so far not reported any indigenous cases of VAPP post-certification, except for an imported case which could possibly be vaccine-associated. This involved an Indonesian boy who had received BCG and OPV in Batam, Indonesia in 2001 at 19 days of age. He developed symptoms of gastroenteritis 2 weeks post-immunisation, followed by right leg monoplegia a week later. He came to Singapore for medical treatment and was noted to have persistent paralysis of the right leg on follow-up.

Given this low incidence of VAPP thus far, Singapore continues with an all OPV vaccination policy, although IPV has been licensed and is widely used in the private sector. The IPV is usually incorporated in the diphtheria-tetanus-acellular pertussis-inactivated poliomyelitis-*Haemophilus influenzae* type b vaccine (DTPa-IPV/Hib) in a single injection.<sup>54</sup> In fact, more doses of IPV than OPV have been administered in the last 5 years. With the exception of vaccinations by the School Health Services, about 75% of poliomyelitis vaccinations administered by private medical practitioners in 2009 were IPV.<sup>55</sup> There is increasing evidence that the rationale for continued use of OPV has become weaker, and IPV may ultimately be the preferred vaccine as it eliminates the risk of VAPP and outbreaks due to circulating vaccine-derived poliovirus (cVDPV). For instance, in October 2001, there was an outbreak of cVDPV in the Philippines, a close neighbour of Singapore, where there had been no cases of poliomyelitis in many years. These outbreaks occurred in provinces where immunisation coverage had been incomplete.<sup>56</sup>

Furthermore, a recent study of the largest documented cVDPV outbreak in Nigeria concluded that cVDPV is associated with an attack rate and severity of disease similar to that associated with WPV outbreaks.<sup>57</sup>

#### *Maintaining a Sensitive Surveillance System*

Singapore continues to strive to enhance its national surveillance system for AFP through constant engagement of medical practitioners and clinical laboratories. Furthermore, the quality of AFP surveillance and immunisation coverage is closely monitored and reviewed regularly. This is to minimise the risk of an outbreak from an imported WPV or cVDPV, of which several outbreaks have been reported in Afghanistan, India and Africa through late 2010 and 2011.<sup>58</sup> Singapore will continue to enhance its AFP surveillance

system with all surveillance standards kept at certification levels until global certification of poliomyelitis eradication is achieved.

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