POLIOMYELITIS: CHOOSING THE RIGHT VACCINE FOR SAFER PROTECTION

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ABSTRACT

Program towards eradication of Poliomyelitis in developing countries is moving rapidly. Eradication of wild poliovirus from the Western Pacific region was achieved in October 2000. The key to poliomyelitis eradication in the world lies in the Indian subcontinent, and if success is achieved there, eradication elsewhere becomes a matter of time. However, the use of OPV is frequently followed by sporadic or even epidemic vaccine – associated polio. There are 2 excellent polio vaccines available. OPV has served us well, but the time has come to ask whether the risk of imported disease is greater or lesser then the sporadic and occasionally epidemic OPV associated poliomyelitis. The tradeoff seems to be between the safety of IPV and the secondary gain in immunization afforded by the spread of OPV strains to contacts. Public Health circumstances are not static when wild poliovirus strains were circulating abundantly, if made good sense to abort that circulation rapidly by the application of OPV. The cases of VAPP could be seen as the price that had to be paid in order to keep polio at bay. Now, in 2003, we face a different set of circumstances. Wild poliovirus no longer exist in the Western Pacific region and polio incidence is falling elsewhere. Therefore the substitution of IPV for OPV as has happened in North America and Europe, deserves new consideration for countries in this region including Malaysia.

Key Words: *Oral Polio Vaccine, Inactivated Polio Vaccine, Vaccine Associated Polio Paralysis, Vaccine Derived Polio Paralysis*

INTRODUCTION

Polio eradication program has shown significant progress since 1985. By year 2002, the number of endemic polio transmission countries declined to only 10 (Table 1) from about 20 in 2000. Rapid progress in poliovirus eradication owes its success largely to the widespread use of the oral poliovirus vaccine (OPV) developed by Albert Sabin. Eradication of wild poliovirus is possible because humans are the only hosts of human polioviruses, and because OPV has several major advantages. It is easily administered by mouth, which has facilitated the largest mass immunization campaign in history. OPV provides a long lasting high level of mucosal immunity, thus reducing transmissibility of wild polioviruses. The live attenuated poliovirus in OPV spreads to some contacts of vaccinee, increasing the impact of the vaccine beyond those actually vaccinated. Importantly, the elimination of wild polioviruses from much of the world is a testimony to the effectiveness of national and international public health programs.

Table 1 : Ten remaining endemic countries, highest to lowest transmission

India
Pakistan
Nigeria
Afghanistan
Niger
Somalia
Egypt
Angola
Ethiopia
Sudan

The progressive elimination of wild poliovirus begun in 1963 in Cuba, the first country to implement a National Immunization Day (NID). This type of campaign led ultimately to the eradication of poliovirus from Americas in 1991 and thereafter from European and Western Pacific region.

OPV OUTBREAKS

Unfortunately, there is a problematic side to reliance on OPV. This vaccine contains three attenuated strains of poliovirus, one for each of the major immunotypes (types 1, 2 and 3). Each attenuated strain of virus was derived by classical method of tissue culture passage and clonal selection for the attenuated phenotype. Detailed genetic analysis has revealed that the

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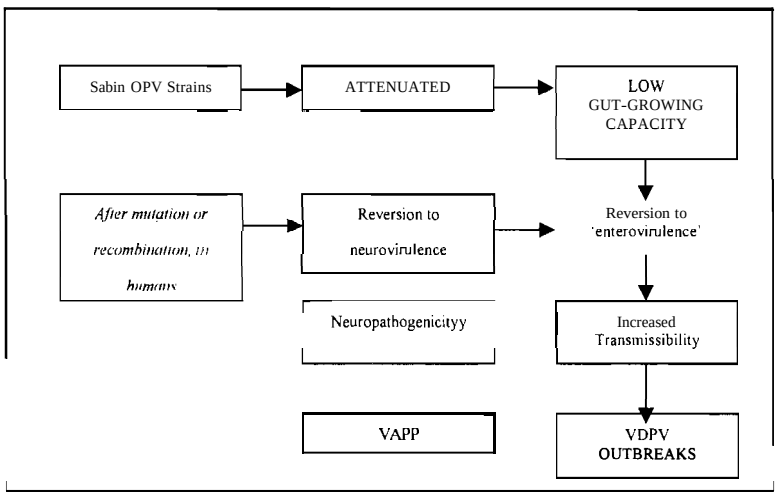
attenuation was due to a small number of critical mutative points (1). After ingestion, OPV replicates in the human intestine, with the generation of many mutants, some of which exhibit revertant phenotypes, which may resemble the neurovirulence of wild polioviruses (Figure 1). A high proportion of immunized subjects, perhaps 30% or more, excrete revertant straints of OPV, now called vaccine-derived polioviruses (VDPVs) (2,3). VDPVs are highly enterotropic and spread readily to non immune subjects.



OPV = oral poliovirus vaccine; VAPP = vaccine-associated paralytic poliomyelitis. Adapted from Crainic R. Benerits and risks of oral poliovirus vaccine. Presented at the 4th ASIAN Expert Bureau on Pediatric Vaccines: Poliomyelitis – Surveillance and Vaccination. September 2001, Beijing.

Figure 1: Mechanism Of Reversion of Sabin OPV Strains To Wild Poliovirus Phenotype

At a population level, these characteristics have important complications. If close to 100% of a population is immunized, the vaccinees are exposed to the attenuated vaccine virus and developed immunity before revertant strains can cause paralysis. However, if immunization coverage is incomplete and a large proportion of the population does not participate, then a VDPV may spread sequentially through non immunized persons, accumulating mutations and reversions, which will increase the livelihood that someindividuals will develop paralytic poliomyelitis. In essence, a vaccine program might inadvertently initiate an outbreak of poliomyelitis, similar to natural outbreaks in the past. The circumstances favourable to such anoccurrence, particular low coverage and poor hygiene, have been reviewed and discussed extensively (4-6). The report by Ken et al. (7) provides a detailed documentation of just such an episode on the island of Hispaniola. The authors provide impressive evidence that a single type 1 OPV virus underwent reversion and recombination with a wild enterovirus, and then spread to cause more than 20 virus-confirmed cases of paralytic poliomyelitis. Because there are usually 100 – 250 infections per paralytic case, it can be inferred that this virulent virus infected several thousand individuals. Most of the causes were documented in unvaccinated or incompletely vaccinated children under 15 years of age, where only about 30% of the population had received three doses of OPV. Thus the outbreak took place under exactly the conditions where it was postulated that OPV might spread (5). It is note worthy that at least two other similar small outbreaks have been observed, in Egypt and The Philippines, under similar circumstances (8,9).

WILD POLIOVIRUS ERADICATION

What are the implications of these observations for the poliovirus eradication? Currently, in

countries where wild poliovirus has been eradicated like Malaysia, children are still being immunized with OPV. High immunization coverage is maintained to protect children against the possible reintroduction of wild poliovirus or exposure to VDPV.

Progress towards eradication of poliomyelitis in developing countries is moving rapidly. Eradication of wild poliovirus from Western Pacific Region was achieved in October 2000. As has been marked by others, the key to poliomyelitis eradication lies in the Indian subcontinent, and if success is achieved there. eradication elsewhere becomes a matter of time.

If we then take the optimistic view that soon the question of certifying world wide eradication of polio will pose itself, how will that be done if OPV vaccine remains in use? The prospect of searching for wild poliovirus in a sea of excreted Sabin strains, many of which will be recombinants (10), is daunting, particularly as that search will be conducted in asymptomatically infected living in developing countries.The risk of importation is real, as exemplified by a Canadian child of Indian origin who returned from India excreting wild poliovirus type I, although she herself was asymptomatic with respect to paralytic disease (11). No doubt many such importations into polio free counties take place each year without being detected, but the empirical evidence is that spread has not occurred except in unvaccinated communities. Moreover, as mentioned above, spread from the focus is blocked whether the larger population was vaccinated with IPV or with OPV.

POLIO VACCINATION STRATEGIES

Which strategies should a country choose in eradicating the disease. The Asian Expert Bureau on Pediatric Vaccines on September 2001 in Beijing, China agreed on a consensus statement as an accurate reflection of the principal opinions, issues and ideas debated:-

OPV use is appropriate:

- ☐ In countries in which wild poliovirus has not yet been eradicated.

And should be considered:

- ❑ To control any outbreak of poliomyelitis

Sequential IPV-OPV use is acceptable in countries with:

- ❑ Certified eradication of wild poliovirus
- ☐ Adequate 3-dose DTP coverage rates (eg. at least 80%)
- ❑ A low risk of wild poliovirus importation, based on epidemiological assessments or eradication in the Southeast Asian region.

To completely eliminate the risk of VAPP, an all-IPV schedule will be acceptable when the above conditions are met and 3-dose DTP coverage rates are 90% or greater, or after the global eradication of wild poliovirus. Table 2 highlights the advantages and disadvantages of using all OPV, IPV-OPV (sequential) or all IPV schedule.

Table 2: Poliomyelitis Vaccination Schedules: advantages and disadvantages

	All OPV	IPV-OPV	All-IPV
Prevents wild-type paralytic poliomyelitis	Yes	Yes	Yes
Provides herd immunity	Yes	Yes	Yes
Induces intestinal immunity	High	High	Moderate
Provides contact immunity	Yes	Yes (some)	No
Approved for use in immunodeficient individuals	No	No	No
Risk of VAPP	Yes	Some	No
Other known serious adverse events	None	None	None
Heat sensitive	Yes	Yes (for OPV)	No
Requires extra injections	No	Not if combination vaccine used	Not if combination vaccines used

OPV = oral poliovirus vaccine; IPV = inactivated poliovirus vaccine; VAPP = vaccine-associated paralytic poliomyelitis

Polio Eradication Status And Vaccination Strategy In **Malaysia**

Surveillance Background

Where do Malaysia stand in this issue? Epidemiologically, we have been fiee fiom paralytic poliomyelitis since 1986 when we had 1 indigenous case. In 1992, there were **3** cases of paralytic poliomyelitis which the wild polio virus was believed to be imported from the lndian subcontinent (Figure 2). Together with the Western Pacific region, Malaysia was declared fiee fiom polio in October 2000.

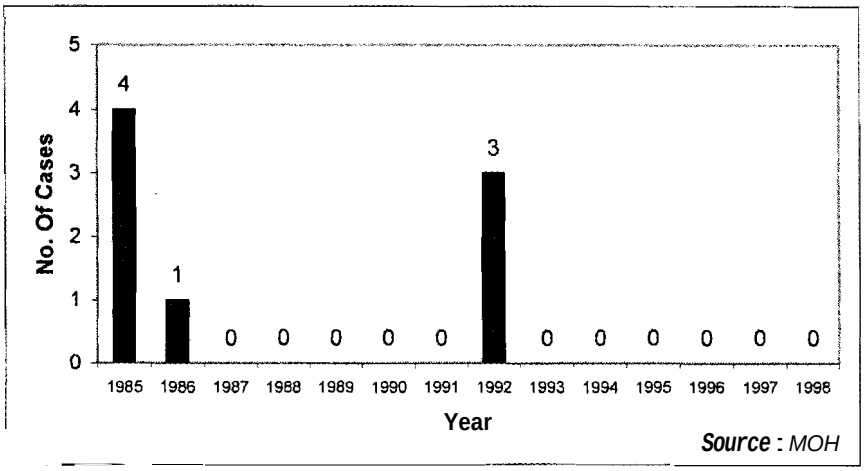


Figure 2: Incidence of paralytic poliomyelitis in Malaysia

Polio vaccines were available in Malaysia since 1960s and it was incorporated into the National Immunisation schedule in 1972. Immunisation coverage of polio vaccination has been more than 90% since 1991 (Figure 3). There were no cases attributed to VAPP reported. However, 11.8% of cases remained unclassifiable as non polio Acute Flaccid Paralysis (AFP).

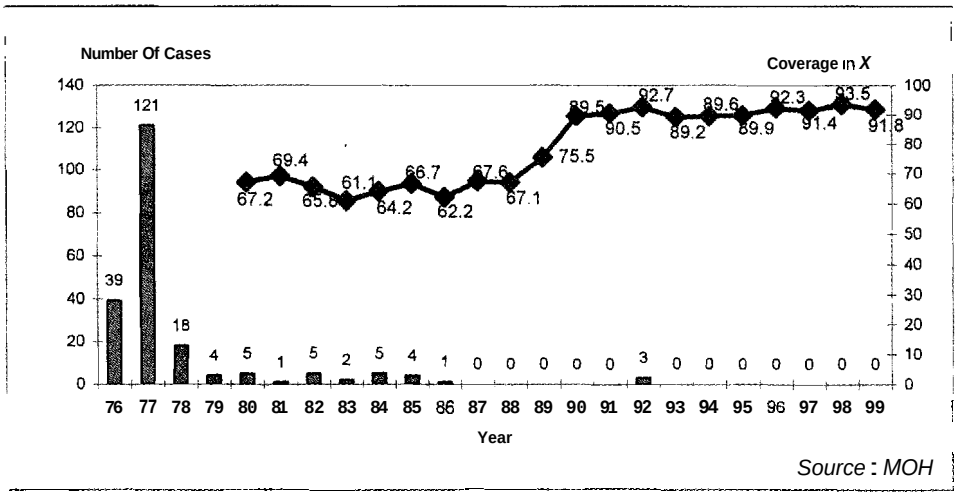


Figure 3: Reported Polio Cases and OPV3 Coverage – Malaysia 1976 – 1999

The incidence of VAPP reported at the average of 1 : 750,000 (12) on the first dose world wide. With a birth cohort of 550,000 per year, one would expect rhe occurrence of VAPP to be one case per every 2 years. Why then have there been no cases of VAPP reported in Malaysia?

There may be many reasons to that and one of it may be due to inadequate stool specimens in the AFP surveillance. WHO targeted 80% of two stool specimens within 2 weeks of the onset of paralysis and what has been achieved in Malaysia was between 50 - 60%. (Figure 4)

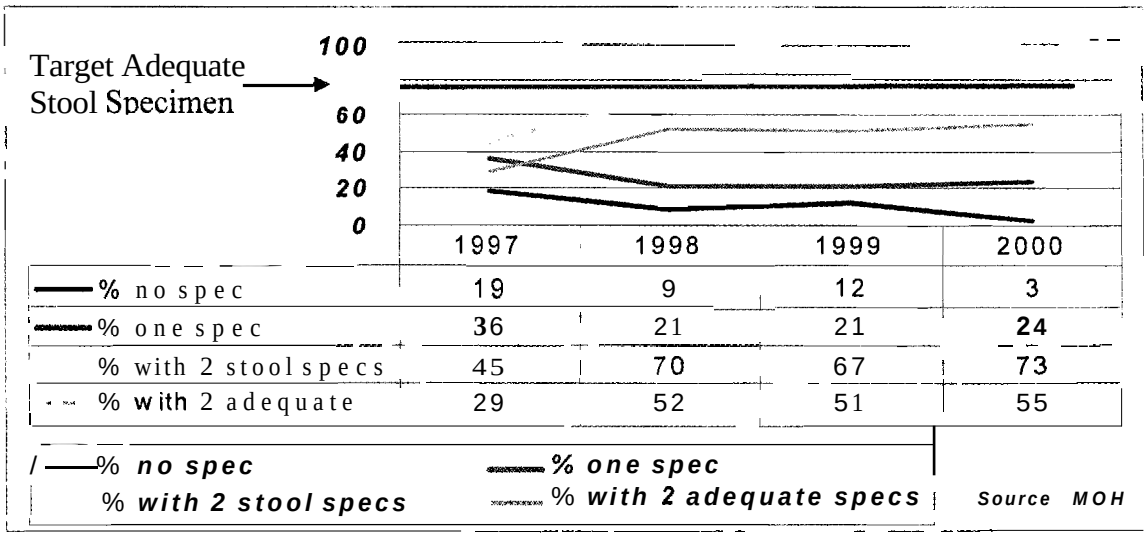


Figure 4: Percentage of stool specimen in AFP Surveillance in Malaysia, 1997 – 2000

VACCINATION STRATEGY ' FOR MALAYSIA

Based on the epidemiological scenario and high immunisation coverage, I feel that it is high time for Malaysia to review the current strategy of polio vaccination in the National Immunisation Program whereby Oral Polio Vaccine is used. To my opinion, the sequential IPV-OPV or all IPV schedule should be chosen soon in the future.

There are two main concerns with regards to the implementation of Inactivated Polio Vaccine in the National lmmunisation Schedule, they are (i) The reintroduction of cases as a result of importation of wild viruses from the few remaining zones especially Indian subcontinent and (ii) The implication of cost.

There have been many examples with regards to the herd immunity produced by IPV in countries that have implemented it - the IPV experience in Finland where a mass vaccination campaign has been conducted. Following this, poliomyelitis completely disappeared and did not return for a very long time despite the fact that scientist believe that poliovirus must have been re-imported back into the country countless times during this period. This experience shows that IPV induces very good serum immunity and also confers some protection against shedding, virus circulation and infection consequent of re-introduction. Two doses of IPV result in over 98% seroconversion. If a booster is given later, very high antibody levels will be achieved.

With regard to cost, although the cost of IPV is higher than that of OPV, the administration of IPV is more effective. The National Expanded Programme of lmmunisation (EPI) can be significantly improved especially since there is a combination vaccine with IPV available currently. The existing IPV combination vaccine that is registered in combination with DTP whole cell. In future, the combination with Acellular DTP and Hib is in the process of registration. With mass production, the cost of adding IPV into combination vaccines becomes marginal.

CONCLUSION

The choice of which polio vaccine to choose, whether it is OPV or IPV or both, very much depends on factors like epidemiological status of

the disease, immunisation coverage and the risk level of importation. The 'end game' poses another dilemma that is not easily addressed. The ultimate goal of the eradication program is the discontinuation of all polio vaccination. Inevitably , an increasing number of people would become susceptible to these viruses. To ensure that poliovirus is not introduced into a susceptible population, it would be necessary to destroy or contain all stocks of these viruses that include fecal samples, collected for many different reasons and held in freezers, world wide, may be inadvertently contaminated with wild or vaccine derived polioviruses.

Poliovirus eradication offer challenges to Public Health Specialists, Pediatricians and Health Policy Makers to come out with the best strategy that suits best to each country, region and hence the world.

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