Current Situation and Future Direction of Polio Prevention and Control in Taiwan

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Abstract

Poliomyelitis, often called polio or infantile paralysis, is one of the most serious communicable diseases in human history. In order to cut down on suffering and damage caused by polio, the World Health Organization (WHO) launched a worldwide campaign called the "Global Polio Eradication Initiative" (GPEI) in 1988. As a result of this campaign, the annual number of new symptomatic cases of polio had dropped to fewer than two thousand globally by the end of 2006. At this very moment, the epidemic areas are confined to only four countries worldwide, namely Afghanistan, India, Nigeria, and Pakistan.

Before the disease is eradicated in these epidemic regions, to prevent the disease from pouncing back, our polio surveillance system must remain on alert, and high completion rates of polio immunization need to be maintained. Also, attention needs to be given to the occasional imported cases to prevent the disease from spreading, laboratory management of of poliovirus specimens needs to be strengthened, and an appropriate polio vaccination policy for the post-eradication era should be developed in advance to ensure that polio stays eradicated and that

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the disease no longer poses a threat to the world. Now is a critical time for the on-going polio eradication process, and for the foreseeable future, we will continue to upgrade our polio surveillance and control system and to maintain the high vaccination rates so that the hard-to-come-by result of eradication, once achieved, can be effectively preserved.

Keywords: global polio eradication initiative, OPV, VDPV

A. Introduction

In human history, poliomyelitis (often called polio or infantile paralysis) has not only brought tremendous traumas to many individuals and families but also caused serious loss of human and financial resources for societies and nations. In order to lower the damage done by polio and to free all people from its intimidation, the World Health Organization (WHO) launched a worldwide campaign, the "Global Polio Eradication Initiative" (GPEI), in 1988. Due to the dedicated efforts of countries around the world, the accomplishment has been quite significant, with the annual number of new symptomatic cases dropping to fewer than two thousand globally at the end of 2006, which was already very close to the final target of eradication. At this moment, three major regions, including Europe, the Americas, and the West Pacific, have been certified by WHO as polio eradicated regions, and the persisting epidemic areas include only four countries, namely Afghanistan, India, Nigeria, and Pakistan.

In spite of many impediments such as geographic separation, disparities in economic strength, and differences in political stand, all countries joined forces under this great campaigning banner. During the course of the GPEI effort in the past two decades, it is estimated that hundreds of thousand children have been saved from possible havoc caused by polio. Now this Initiative is walking into

its 20th anniversary and reaching the final key moment. Every country should be extremely vigilant in making sure that its disease control network stay sturdy and invulnerable so that there is absolute no chance for the poliovirus to make a comeback and spoil the international effort in the final stage.

B. Polio control history of Taiwan

Since 1955, Taiwan has designated polio as a notifiable communicable disease. In those early years, Taiwan had about 400 to 700 confirmed cases each year. Because it was found that polio could be effectively prevented by vaccination, the government promulgated in 1966 the "Taiwan Province Polio Preventive Vaccination Program," which provided each newborn with two doses of oral polio vaccine (OPV) in their first year of life. In 1971, the program was modified so that one more dose was added to the vaccination schedule, with each baby now receiving three doses of OPV instead of two before turning one-year old. The result of the program appeared quite satisfactory as the annual polio case number was in decline after its implementation. However, an island-wide, large scale polio outbreak took place in 1982 and ended a ten-year period of no confirmed cases.

The cause of the large outbreak in 1982 was later attributed to gaps in the execution of the vaccination program that constituted loose ends in the chain of our polio prevention work. Therefore, the health authorities tried to mend the vaccination gaps and strengthen the surveillance system by adding one more dose of OPV to the vaccination schedule for children in their first year of elementary school. Besides, the government amended the statute to require the use of a standardized vaccination record card (Yellow Card) for every newborn and young child. Furthermore, in 1991, an Eradication Program for Measles, Congenital

Rubella Syndrome, Poliomyelitis, and Neonatal Tetanus was launched, and three years later in 1994, the government created a "Surveillance System for Acute Flaccid Paralysis (AFP)." As the record goes, Taiwan has had no polio cases caused by wild-type *poliovirus* (WPV) reported since 1983. Finally in year 2000, the West Pacific region to which Taiwan is a part was officially certified of polio successfully eradication. (Figure 1 chronicles the important events in polio prevention and control in Taiwan.)

C. Current global epidemic situation of polio

Quite like smallpox, polio is very swift in transmission from one person to another, but using vaccines can effectively intervene and prevent both diseases. In 1980 WHO announced that smallpox was successfully eliminated. The entire world was very much inspired by this great accomplishment and became highly confident in the eradication of polio through the introduction of the GPEI. Concerted efforts by all parties over the following eighteen years had resulted in a drop in the annual global total of new cases from some three hundred thousand in the early days of GPEI to fewer than two thousand cases, with the number of epidemic countries down from 120 to just 4 (i.e. Afghanistan, India, Nigeria, and Pakistan). As a whole, the world was very close to the ultimate target of eradication that the program aimed at.

According to the original plan, the completion date of GPEI was scheduled as sometime in 2000. However, in view of a number of countries that were obviously not able to get rid of WPV outbreaks in time, WHO modified the plan by changing the targets as well as the program duration. The completion date was rescheduled to sometime in 2004-2005, and the criterion changed to completely cut off the transmission of polio wild type strains (1). Unfortunately,

during the time period between 2002 and 2005, some epidemics in the northern part of Nigeria and India got out of control and spread over to Africa, Middle East, and even Indonesia. This made as many as 21 countries, which previously had no polio cases for years, suddenly fall victim to large scale outbreaks. Although an emergency inoculation strategy brought the outbreaks under effective control, the eradication target date had to be postponed again. As of 2007, there were still four countries (i.e. Afghanistan, India, Nigeria, and Pakistan) classified as WPV epidemic regions. Among those four countries, the epidemic situations in Nigeria and India are more serious with new cases continuously emerging.

Aside from WPV, vaccine-derived *poliovirus* (VDPV) happened to be another important factor leading to outbreaks (2). In order to interrupt the transmission of WPV, and due to economic considerations, most countries have chosen to use OPV as the regular vaccine type in their vaccination programs. This is because OPV has several advantages: the cost of vaccine itself is very reasonable; no special needles or tools nor specially trained personnel are needed to do the inoculation; plus it can effectively stimulate intestinal immunization, thus causing emission of virus and achieving herd immunity. Therefore, OPV has long been the first choice tool in polio prevention and control. However, in recent years when the eradication program was approaching its final stage of success, a string of problems derived from OPV unexpectedly appeared. Many VDPV outbreaks occurred in Egypt, the Dominican Republic, Haiti, the Philippines, Madagascar, Cambodia, Mainland China, and Indonesia. The reason was likely to be low completion rates of vaccination resulting in inadequate herd immunity and many so-called susceptible hosts, who were more sensitive than others to *poliovirus*. Meanwhile, if those vaccine strains of *poliovirus* previously discharged into the environment by the inoculated children

happened to undergo some kind of mutation and repossessed some pathogenicity capable of attacking the nervous system, then it might turn into the so-called "circulating VDPV" (cVDPV) and cause polio outbreaks. Another problem came from those inoculated individuals that have immunodeficiency (those with B cell dysfunction in particular) in the first place, as they would keep on emitting virus particles into the environment for a long time, even up to 10 years. During that time period, the virus discharged by these individuals might have gone through some mutation processes and evolved into some invasive or infectious, the so-called "immunodeficiency-associated VDPV" (iVDPV), and this could potentially lead to a polio outbreak. However, luckily such transmission has mostly led to single cases thus far.

D. The current global control strategy

According to its original plan, the GPEI promoted by WHO would have eradicated polio worldwide by the end of 2000, 12 years after it was launched. However, when the specified time arrived, there were still some countries troubled by new WPV outbreaks. In order to get around the obstacles encountered during the implementation of GPEI and solve the increasingly severe VDPV problem, WHO overhauled its original design of the program, changing its strategies, targets, and timetables. In the new scheme, the global spread of WPV is expected to be stopped between 2004 and 2005; then in the following three years (2006-2008), regions and areas are expected to be certified as polio free, and strategies for the post-eradication era will be developed. The entire world is expected to stop using OPV by 2009. According to the new timetable, the strategic targets for each stage were set as follows:

1. Stopping the global spread of WPV: It was agreed upon by all experts in the

field that to eradicate polio, circulation of WPV has to be stopped in the first place. How could we accomplish it? Theoretically, it could be done through thoroughly carrying out the regular vaccination program, raising the completion rate to as high as possible, and implementing extensive making-up vaccination in epidemic areas and their neighboring countries to enable local herd immunity to develop, thus effectively reducing the chances of being infected and interrupting transmission of the virus. Simultaneously, it is also necessary to keep a keen AFP surveillance system, so that suspected cases and poliovirus can be detected quickly and control measures can be taken in time.

2. Executing the global eradication-certifying process: During this stage, undivided attention shall be given to the following items: to ensure the polio-free status, to maintain the highly alert surveillance system and high completion rate of vaccination, to stock up monovalent OPV (mOPV, which contains only one single type of attenuated poliovirus), to establish its utilization protocol, to formulate a policy for using inactivated polio vaccine (IPV), and to set up a contingency plan for imported WPV cases. Besides, efforts shall be made to strengthen the quality of surveillance, enhance the virus intratypic differentiation (ITD) capability of local virology laboratories, and shorten the waiting time needed to get analytical results. In the meantime, all vaccine-manufacturing factories, R&D institutions, and laboratories that use and store poliovirus should be equipped with integrated protective mechanisms in order to prevent the virus from leaking out and causing outbreaks.
3. Stopping the use of OPV: In order to avoid vaccine-associated paralytic poliomyelitis (VAPP) cases, which are derived from the use of OPV, and outbreaks caused by cVDPV, we must consider to put a worldwide stop to OPV use. In this stage, we shall clearly locate the areas where cVDPV outbreaks

are likely to take place and the high-risk groups among the population once the use of OPV is stopped. An efficient response strategy and standard outbreak handling procedures need to be developed, and local herd immunity, capability of IPV production and overall cost-effectiveness need to be assessed in order to, work out the future policy for routine vaccination. At the same time, to be well prepared for a possible comeback of polio, not only should we maintain enough mOPV at all times, we should also make sure that our vaccine production is coupled with adequate laboratory security measures that help ensure proper storage and use of poliovirus specimens. The purpose of all these efforts is to minimize the risk of accidental release of the virus from the laboratories.

As mentioned before, since there were still four countries struggling to bring their WPV outbreaks under complete control at the end of 2007, the timetable of the Eradication Initiative had to be postponed again for another 3 years. Therefore, its latest target is to stop the global spread of WPV by 2009 and to stop the use of OPV worldwide by 2012.

E. The polio control strategy undertaken in Taiwan

1. Continuing thorough implementation of the “Eradication Program for Measles, Congenital Rubella Syndrome, Poliomyelitis and Neonatal Tetanus.”

   Since 1983, thanks to the dedication and hard work by all public health workers on this land, there has been no confirmed polio case derived from WPV infections in Taiwan. In order to preserve this hard-to-come-by achievement, in 1991, the health authorities followed the polio control measures recommended by WHO to regions wishing to maintain a polio-free status in formulating the “Eradication Program for Measles, Congenital

Rubella Syndrome, Poliomyelitis and Neonatal Tetanus," which was divided into several stages and constituted major guidelines for conducting disease control activities, including polio eradication. The program has gone through three stages all with flying colors so far. For the polio component, the target of eradication was achieved on October 29, 2000, and the next focus is to maintain this polio-free status. In 2007, the Program entered into its fourth stage of 5 years that will end in 2011. The following are the targets and implementation approaches (3) for this stage:

(1) Strategic targets:

a. Maintaining the status of no polio cases from WPV infection.
b. Maintaining the status of of no polio cases from VDPV infection.
c. Improving the quality of poliovirus diagnoses and biosecurity management at all laboratories dealing with polio in Taiwan.

(2) Implementation approaches:

a. Operating a rigorous surveillance system to meet the targets recommended by WHO and to constantly monitor the activity of poliovirus.
b. Maintaining a high completion rate for the polio vaccination program by encouraging young children to take vaccines in advance, tracking down children failing to show up for immunization, and getting them to receive a makeup dose. The completion rate for each township or district and for the national as a whole should stay above 95%.
c. Supervising all providers of vaccination to ensure the effectiveness and safety of vaccination.
d. Convening the "Taiwan Polio Eradication Certification Committee" (TPECC) and "Advisory Committee on Immunization Practices" (ACIP)

as necessary to discuss proper responses to the on-going international epidemic trends and future control strategies.

e. Conducting health educational campaigns through diverse channels.

f. Strengthening safekeeping and handling procedures of WPV, VDPV, and relevant specimens to guard against accidental release of the poliovirus from laboratories.

2. Priority tasks

In recent years, human sufferings and bodily harms caused by polio have greatly reduced worldwide along with the continuous drop in case numbers. However, to countries having already achieved eradication, the risk posed by imported polio cases would not completely disappear until global eradication has been materialized, as those WPV or VDPV circulating in the environment of polio epidemic countries could easily enter into any polio-free regions and result in outbreaks due to today's frequent international travels and exchanges if no defense lines were formed by efficient and tight surveillance systems and high immunization rates. Therefore, the focus of the prevention and control strategy at this moment is to keep on upgrading the efficiency and effectiveness of the existing monitoring system and further improving the completion rate of polio vaccination everywhere:

(1) Upgrading the efficiency and effectiveness of the surveillance system.

During the process of polio eradication and certification, the old disease control concept of "no outbreak, no notification," a passive approach to disease monitoring, was replaced by active reporting. According to WHO, the true meaning and spirit of "eradication" is not just about finding no more individual cases but is about being able to prove that there is a sound system in operation that can spot individual cases quickly

to minimize the size of outbreak or even to prevent any person-to-person transmission from occurring. In other words, "an apparent zero case count is not eradication, but being able to prove the zero-case status is." To fulfill this ideal and requirement, Taiwan has established a "Zero-Reporting System" and an "AFP Surveillance System" in 1991 and 1993, respectively. Both are still in operation.

According to the earlier disease control concept, if there is no suspected case, no reporting is needed. However, in order to meet the new definition and spirit of "eradication," an active way to conduct disease surveillance is required. The so-called "Zero-Reporting System" means that a local health unit will take the initiative to phone up physicians in its jurisdiction each week and ask them if they have found any suspected cases. The responses are employed as active proof of zero case. Other than case monitoring of acute flaccid paralysis (AFP), this system is also used in disease surveillance in elimination or eradication programs for measles, rubella, congenital rubella syndrome, and neonatal tetanus. (Figure 2 shows the monitoring results of the zero-reporting system for "Eradication Program for Measles, Congenital Rubella Syndrome, Poliomyelitis and Neonatal Tetanus")

The AFP monitoring system is a system based on symptom manifestation. Since polio in not the only cause of AFP, and various kinds of infection, nervous system diseases, and many other illnesses could also lead to AFP. That is why WHO recommended using AFP as a surveillance tool once the polio case number has greatly reduced. Such maneuver turns out to have significance for both clinical diagnoses and public health. In the aspect of clinical diagnoses, the AFP monitoring system can help find cases other

than polio yet with similar symptoms. Then through performing diagnosis, whether the AFP is caused by WPV can be ascertained to provide the basis for affirmation of the eradication status. On the other hand, from the angle of public health, we realize that a decrease in reported case number of polio can hardly tell if the real case number is indeed diminishing, because it might be just a phenomenon of underreporting. Besides, it was found that even in areas where WPV didn't exist, or its activity was very low, AFP still had a certain incident rate (It's called background rate. Among those 15 years of age and under, for instance, there was always one infected person out of one hundred thousand). So it can also be used as a tool to check the sensitivity of the surveillance system (4).

To each of those reported AFP cases under the age of 15, it is up to a pediatric neurologist to clinically examine the case's symptoms to decide whether the case fits the definition of an AFP case. The attending physician also has to do a follow-up examination 60 days after the onset of symptoms to determine whether there is a residual parasitic phenomenon. The diagnosis results are then submitted to TPECC for further assessment to decide the pathogenic cause of the AFP illness, especially if the diagnosis points to a poliovirus infection. (Figure 3 shows an the monitoring results of the AFP surveillance system)

(2) Conducting immunization

In the past decades, the Taiwan government has successfully promoted a mass multi-item immunization program. For the younger generation born during the last ten years, the annual completion rates of OPV3 immunization (i.e. the completion of 3 doses of OPV before in a child's

first year of life) have all been higher than 94% (from 94.7% to 97.0% to be exact). Although none of the past generations surveyed has ever reached a perfect completion rate of 100% – and because of this, the number of susceptible hosts would theoretically accumulate and rise in the long run – due to the facts that OPV has long been listed as a regular item in the immunization program and its completion rates have been kept remarkably high, the vaccine strains of the virus have established a dominant presence in our environment. Therefore, when some imported polio cases enter Taiwan, the endemic development will be quite limited, and the odds for them to evolve into massive disastrous epidemics like the one that took place in Indonesia and other countries in 2005 are very unlikely. However, in order to be able to completely evade the risk of an outbreak and go one step further to meet the targets set for eradicating vaccine-preventable diseases, it is necessary to maintain high completion rates of vaccine immunization of various kinds. The purpose of doing so is to preserve high levels of herd immunities.

Although Taiwan has been a polio-eradicated region since 2000, WPV is still in existence in a few other regions like Africa and India. In recent years, a few serious polio epidemics have unexpectedly broken out in countries like Yemen and Indonesia, which had not had WPV cases for years. Therefore, we are still facing the danger of possible imported polio outbreaks. Based on the considerations of enhancing herd immunities and disease prevention, Taiwan's ACIP passed a resolution to recommend giving 2 doses of monovalent IPV or multivalent or mixed vaccine containing IPV to the newborn first. Then as part of the subsequent immunization schedule, the young child is to be given at least 2 doses of

OPV, followed by one more dose of OPV when the child enters elementary school. The new scheme will further strengthen the protection against polio.

(3) Strategies for coping with imported polio outbreaks.

As we mentioned earlier, the possibility of large scale outbreaks caused by imported WPV or VDPV cases would be extremely slim, but in order to further ensure the effectiveness of domestic disease prevention, the health authorities responsible for disease control in Taiwan have already referred to past experiences and relevant guidelines both domestically and globally to formulate the "Guidelines for Poliomyelitis Epidemic Management 2006" (5), inside which measures to be taken against a major outbreak are as follows:

a. Conducting outbreak investigation right away without delay: to activate the epidemiological investigation system right away, and from various angles of clinical medicine, epidemiology, and virology to assess where the responsible virus strain might come from and if the outbreak would spread.

b. Reinforcing the surveillance system: to upgrade the mobilization level, intensify AFP and poliovirus surveillance activities, and recheck the quality of the surveillance system, which includes retrospective inspection and examination. The ultimate purpose is to find out if the manifestation is only derived from on-going but latent domestic endemics. Furthermore, extra active searches for other individual cases and surveillance activities with a broaden scope will be used to effectively prevent the imported virus from taking root.

c. Strengthening immunization effort: to call an urgent immunization

consultation meeting to evaluate whether it's necessary to launch a large scale immunization project, and to determine the proper schedule for the process and limits of the activity. In case the immunization project is deemed necessary, an inter-agency cooperative mechanism will be activated to mobilize and coordinate the joint endeavor with other government agencies, such as the household registration, home affair, social affair, and education authorities.

d. Launching health education campaigns: to make use of diverse channels and to combine private-sector and local resources to let raise public awareness about the severity of polio and the importance of immunization, so that people's willingness to corporate with the polio prevention and control tasks will be enhanced.

F. Current problems facing the world

Due to the increasingly frequent international economic and trade exchanges, borders between countries are no longer effective barriers against the transmission of diseases. According to global disease prevention and control experiences of many years, thoroughness in the implementation of immunization programs and high quality and capacity of the surveillance system stand out as the two most important factors in the course of successful polio eradication. However, negligence and slips, big or small, have occurred in many links of the global effort, often leading to accidental outbreaks that were hardly containable once they started, and their disastrous influence would even spread to neighboring countries. Therefore, the success of polio eradication depends first and foremost on all countries in the reaching a consensus. Due to various biological and disease-related characteristics of poliovirus, its prevention and control are harder

than many other diseases. This problem is complicated by the distinct geographic environment, economic conditions, and religious faith of each country, making it very difficult to synchronize the pace of national control strategies and to keep them all flawless in the process. It is thus not hard to understand why the Eradication Initiative has so far repeatedly run into unexpected barriers and difficulties.

1. Many covert or latent infected cases, through fast disease transmission

   Poliovirus is much the same as other types of enterovirus, in that about as many as 90% of those infected individuals do not display any apparent symptoms or just show some minor ones similar to those of the common cold. Only less than 1% of them do manifest paralysis. However, those asymptomatic cases are still full-fledged potential media for further virus transmission. At the same time, there is a long virus-emitting period of 3 to 6 weeks after a person is infected, plus the virus emitted is extremely infectious, and all these make the surveillance and control tasks much more difficult. Currently, those polio epidemic regions in the world consist of many areas with high population densities but inferior public hygiene conditions, making their local epidemic control extremely difficult. On top of that, because of the frequent international traffics, their hard-to-solve problems can easily spread to other countries.

2. Discrepancies in completion rates of immunization in different countries lead to gaps in the disease control front.

   Preventive immunization is commonly recognized as the most powerful tool for polio prevention. However, in the current global environment, promotion and implementation of immunization programs in many developing countries are hindered by wars, poverty, or even religious beliefs, and such hindrance

results in rather low completion rates of immunization, which then become the weak links in the prevention network. Furthermore, even when no such negative factors exist, both the completion rate of immunization and individual immunoreactions are not 100% anyway. Theoretically, there is bound to be a sizable group of susceptible individuals through accumulation over a period of time. This is another important reason why epidemic situations are so hard to put under control in current polio epidemic regions. Becau se of their high-density populations and high birthrates, continuous accumulation makes the number of those susceptible young children increase quickly, which helps the spread of the virus. To make the situation worse, some non-epidemic countries recently have relaxed their alertness by stopping their massive makeup vaccination programs, which provides poliovirus with opportunities for a comeback and is considered by many experts the biggest covert worry at present time. In comparison to those other countries, Taiwan has strived to push its nationwide OPV3 immunization completion rates to higher than 95% in recent years, which would render certain degree of safeguard to the Taiwanese population when wild-type poliovirus enters into Taiwan from epidemic areas, as the size and development of outbreaks will be limited if not completely averted. However, it does not mean that we have nothing to worry about. For instance, we still have a few remote areas (such as some mountainous rural areas in Hualien and Taitung Counties) with vaccination completion rates much lower than the national average due to their geographic remoteness, inconvenience in transportation, or high mobility of their residents. They are the weak links within our prevention and control network, and we have to pay much more attention and make every effort to strengthen these links.

3. Risk derived from using OPV

Poliovirus is an RNA virus, and in its evolution gene alterations happen all the time. Aside from being able to involve in gene recombination with different types of viruses, since RNA is not equipped with the functions of correcting the mistakes or damage that occur during its replication process like DNA is, mistakes that result in mutations are quite frequent (6, 7). In the attenuation process of OPV making, poliovirus undergoes gene alteration and becomes VDPV, but this alteration is by no means invariable under all circumstances. Depending on the extent of such alteration, there is possibility for the resulting vaccine strains to recover later its pathogenicity to attack the nervous system and human infection capability, which is especially threatening to those individuals having received no vaccine before or having not completed the immunization schedule. Now, as the world continues to rely on OPV as the only regular immunization vaccine and the widely used tool to stop occasional polio outbreaks caused by WPV, this downside effect of OPV is becoming more significant.

The global eradication effort is now in its final stage, but the frequency of polio outbreaks caused by cVDPV is apparently on the rise lately. Though the protective effect of OPV has been very good and it has played an undeniably important role in contributing to the polio eradication process, the fast, unpredictable and uncontrollable alterations of the virus means that we are fortunate so far to have not witnessed any more decisive alterations that could affect the expression of the virus' structural proteins and enable the neutralizing antibodies set off by OPV or IPV to lose their protective valence. However, this certainly does not guarantee such alterations would never happen in the future. If in the near future, some swift gene alteration happens

to cause significant changes in the structure proteins, the effectiveness of the existing vaccines will be greatly affected (8, 9), and this is likely to influence the course of the 20-year old Initiative in unpredictable ways.

Many countries have experienced cVDPV outbreaks in recent years. For example, in the Madagascan outbreak between 2002 and 2005, the responsible VDPV was formed through a recombination between the polio vaccine strain in the local environment and human enterovirus C (HEV-C). Because of the low completion rates of OPV immunization in the country (its annual OPV3 completion rates for years from 2002 to 2005 are 61%, 86%, 79%, and 87%, respectively), there were so many susceptible hosts who made it easy for the VDPV to reproduce and propagate, resulting in several waves of endemic outbreaks (10).

In India, the country has been listed as a polio epidemic region where outbreaks (caused by WPV) happen from time to time. Every time an outbreak occurs, the local health authority would launch a massive make-up OPV immunization project to stop the spread, which also result in an increasing trend of VAPP cases in recent years. This is another example showing the negative effect of OPV.

4. More financial support is urgently needed for carrying out the prevention and control measures

The spread of poliovirus has by no means been completely cut off – other than the few well known epidemic areas, even countries apparently free of polio for years can fall victim to polio outbreaks caused by imported virus without warning. Over the past years, many developed countries and non-governmental organizations have kept on donating money and manpower to support the GPEI, helping establish surveillance system in the epidemic

regions and carrying out strategic makeup vaccination projects of massive scale to boost local herd immunity and thus contain the spread of the outbreaks. Yet those epidemic regions are normally affected by conditions favoring the survival and prevalence of poliovirus, such as dense populations, poor environmental hygiene standards, economic plights, and religious interventions that severely hinder the execution of the policy and procedures of makeup immunization, thus making the eradication target impossible to be reached smoothly. In spite of those obstacles in the way, the international community is still quite optimistic about accomplishing the eradication goal. Therefore, before the entire world becomes polio free, all the relevant prevention and control measures will continue as they are, and that means it will need a great amount of money to sustain the effort. According to WHO's statistics, between 1988 and the end of 2006, the world has dedicated about 5.3 billion US dollars to this Initiative. Whereas the expenditure for the years 2007 and 2008 is estimated to be 1.27 billion US dollars, the donations pledged by all countries currently total less than 0.7 billion, meaning that there is a 0.57 billion shortage needing to be filled. Since these two years happen to be the Initiative's most critical period in which we have a real opportunity to make polio a history by maintaining efficient surveillance systems and high immunization completion rates, we need to avoid wasting the efforts we have made over the past 19 years by making it a priority to to find enough money to mend the shortage gap.

G. Future trends and strategies

1. Preserving the eradication achievements

As mentioned above, there are still four countries identified as epidemic

regions at this moment, and their WPV can be exported to the rest of the world via international traffics. Therefore, Taiwan must remain vigilant at all time to fend off imported polio cases. To deal with this problem, WHO recommended procuring and storing enough mOPV. Besides, mOPV is a more efficient vaccine form since one dose of it can achieve a seropositve conversion rate of above 80%, which is more effective than the conventional trivalent OPV (tOPV) in terms of polio prevention and control. In recent years, this new kind of polio vaccine has been widely used with great success to treat emergency outbreaks in prevalent areas.

According to the original WHO schematic plan, we need to wait for 3 to 5 years after the propagation of WPV has completely ceased before the entire world stops using OPV simultaneously. Understandably the demand of IPV will greatly increase when that time comes, and not only those developed countries currently using IPV need to expand their production facilities, the developing countries will have to join the IPV manufacturing lineup. However, those vaccine factories or R&D institutions will have to constantly maintain a massive quantity of WPV propagative cultures, which will pose greater biosecurity risks for the laboratories and greater infection risks for the general public who have received no vaccine before, and this can potentially affect the preservation of the eradication achievement. In response to these concerns, WHO has not recommended a completely replacement of OPV with IPV after the use of OPV is stopped. An alternative being put forward by WHO is to use some safer strains of vaccine virus to replace WPV in the production of Sabin-IPV, and WHO also encourages vaccine manufacturers to engage in technology improvement and other R&D endeavors. In addition, WHO recognizes the need for continuous improvement of the laboratory

biosecurity mechanism and requires all operations involving poliovirus to be carried out under the conditions of biosafety level 2 (BSL-2) or above to prevent the virus from accidental release that can potentially trigger outbreaks (11).

2. Planning future immunization policy in advance

In view of the fact that VDPV is able to cause unexpected polio outbreaks in countries with low immunization rates, and this problem seems to have a trend of becoming more serious in recent years, international experts have been engaged in discussions about the proper timing for stopping OPV use and the kind of immunization policies that should follow. WHO has addressed similar concerns in a published document (11) that recommends on the timing and subsequent measures to go along with the stoppage to serve as a reference to the decision-making health authorities of all countries and regions.

Since 1983 there has been no confirmed polio case reported in Taiwan. Besides, a "Vaccine Injury Compensation Program" (VICP) was set up in 1988, and during its existence, only two polio cases, one in 2001 and the other in 2006, were brought to the attention of the Program's Assessment Committee and subsequently judged to be related to OPV immunization and warranted compensations for the two subjects. The case in 2001 was a patient of congenital immunodeficiency, whose cellular immunity and humoral immunity were both in bad shape, and who had twice suffered from severe bacterial infections during adolescence. When vaccine strain virus particles (possibly from a close contact having just taken OPV) entered his intestinal passages under a circumstance of insufficient amount of secretory immunoglobulin A (IgA), the virus particles rush into the blood and circulate all over his body. However, his T cell immunity was too weak to exterminate them, so the virus

particles invaded the nuclei of the motor nerve cells and caused bulbospinal poliomyelitis. Although the case had received 5 doses of OPV before as required by the immunization program, he fell sick with the typical flaccid paralytic symptom. Through follow-up monitoring, it was found that the case kept on discharging virus for about 10 months after he caught the disease (when healthy young children take OPV, the emission of virus usually lasts for a few weeks only). Further analysis of the gene sequence of the virus isolated from the case showed that there was about 3.5% of the VP1 region in the virus RNA that is different from the original vaccine strain. From this variation it was estimated that the virus strain had stayed in the patient for as long as 30 to 35 months, which means such chronic infection phenomenon might have taken place right after the case received his 5^{th} OPV dose (12).

The other case occurred in 2006. The patient was found suffering from anal abscess when being born, and subsequently received antibiotic treatments because of a persistent fever. During that treatment the infant turned 2 months old and so his parents followed the immunization regulation to bring him in for a dose of 4-in-1 combination vaccine against diphtheria, tetanus, acellular pertussis, and Hemophilus B (DTaP-Hib) and simultaneously for the first dose of OPV. Then since his fever didn't go away, he received an anal fistulotomy. Two days after the operation his arms and legs started to show flaccid symptoms. The case was reviewed by VICP, and the verdict indicated that the case's flaccid extremities and the anal operation indeed had something to do with OPV. Thus, VICP agreed that the government should meet the compensation claimed. To sum up, over the many years during which Taiwan has used OPV as the regular vaccine for immunization, only the above-stated two VAPP cases have been detected, which suggests that OPV does not have

severe negative consequences in Taiwan. Furthermore, recent polio outbreaks caused by WPV or cVDPV in our neighboring countries have created no significant impact on Taiwan, which indicates that our high completion rates of OPV3 are serving effectively to provide protection for the Taiwanese population against the threats posed by outbreaks overseas. In terms of the iVDPV question, since Taiwan has not implemented a program to screen newborn immunity, no one knows for sure the risk of iVDPV through OPV immunization. However, all in all it seems that OPV has not had any severe negative consequence.

Though VAPP cases are extremely rare in Taiwan, whether we should use IPV to replace OPV as the regular vaccine in our immunization program is an important issue to consider in our future immunization policy if we are to work out the best strategy for simultaneously avoiding injuries caused by immunization, cutting down the possible burden to the society, and lowering the incident rate of VEPV,. As a replacement decision will influence the timing and related components in the current immunization program, if we do choose to follow the evaluation protocol used by WHO (13, 14, 15), we must first proceed with an epidemiologic survey of this particular disease in Taiwan (to find out incident rates, prevalence rates, serological epidemiology, etc.) and analyze relevant domestic and international research reports (on various topics such as vaccine valence, safety, cost-effectiveness, effective period of protection, etc.) before getting on to revise the current policy.

Looking at the United States as an example, in the earlier days, the U.S. used to employ OPV as their regular immunization vaccine. However, because it resulted in about 6 to 8 VAPP cases each year, the United States Advisory Committee on Immunization Practices (ACIP) made a decision in June 1996 to

change the policy. They wanted to eventually replace OPV with IPV but relied on a gradual switch approach, the so-called "Sequential IPV-OPV," to do it. That is, starting from January 1997, they let each newborn baby receive a shot of IPV at the age of 2 and 4 months respectively, followed by a dose of OPV between the age of 12 and 18 months and another does of OPV between the age of 4 to 6 years. In their original design, they gave themselves 3 to 5 years to try out the new vaccine formula and make assessments, with the conclusion being that there was no decrease in the completion rates whatsoever. So starting from January 2000, they dropped OPV entirely (All-IPV). Now, each newborn will receive one shot of IPV when at the age of 2 months, 4 months, 6-18 months, and 4-6 years old, respectively, totaling to 4 shots. Ever since the U.S. started the implementation of all-IPV, there has been no VAPP case detected and reported in that country. Certainly, their switchover tactics, implementation procedures, and relevant experiences can serve as a reference for us in planning our future immunization policy (16).

Is Taiwan now in the right position and right time to adopt an all-IPV immunization program? This is not a simple question to answer. This is because the antibodies produced by IPV immunization are mainly serological ones that cannot effectively produce long-term gastrointestinal immunity and herd immunity. Therefore, when an individual who has received IPV is infected with WPV, the virus can reproduce and propagate in the host's intestinal ducts and be discharged in the feces. The final outcome is that the virus can keep on spreading. That is the reason why WHO stressed again in April 2006 that it would not recommend a complete switch to and thus a total reliance on IPV at this stage. Instead, the use of OPV should not be totally stopped until three years has passed after the end of the last WPV outbreak

globally (13). Our ACIP has also convened many times to discuss the issue, and their conclusions and recommendations are: firstly, OPV remains to be important as long as the global polio is not entirely eradicated; secondly, when assessing Taiwan's current control policy and all relevant variables, the protective effect of OPV remains the better option than IPV. Therefore, we should maintain the all-OPV policy, and the only exception being when dealing with those few infants suffering from immunodeficiency and thus not able to take OPV without adverse effects. To them, an injection type 4-in-1 combination vaccine that includes diphtheria, pertusis, tetanus, and inactivated poliovirus (IPV) is provided instead of the regular OPV. Having received the mixed vaccine, such infants should receive three doses of OPV afterwards to ascertain the infant can build up adequate immunity. According to an ACIP resolution reached at a meeting held on November 21, 2006, a multi-valence mixed vaccine of diphtheria, tetanus, acellular pertussis, invasive hemophilus B, and IPV (DTaP-Hib-IPV), or another vaccine of diphtheria, tetanus, acellular pertusis, invasive hemophilus B, IPV, and hepatitis B (DTaP-Hib-IPV-HepB), has been listed as the third priority vaccine to be added to the regular vaccination program in the future. As to whether and when an all-IPV approach should be adopted, it will depend on the international consensus and on the outcomes of our multi-valence vaccine policy

3. Strengthening VDPV surveillance

Our record shows that no cVDPV outbreak has ever taken place in Taiwan, nor did those taking place in our neighboring countries in the past constitute any practical threats to the safety of our domestic disease prevention and control system. For this great record, we have to give credit to our well-executed immunization policy, which has made the vaccine strain virus absolutely

dominate in the environment and thus safeguarding Taiwanese people against the threats of imported WPV and VDPV. In order to be able to detect mutated strains early on, other than strengthening the existing AFP monitoring and notification system, we should proceed with relevant studies to obtain a fuller picture of virus variations so that we can take appropriate measures when anomalies occur. Evaluation of the efficacy and effectiveness of existing vaccines should also be carried out to serve as a reference for new vaccine development efforts.

H. Conclusion

Today, three regions in the world have completely eradicated polio. However, until WPV outbreaks are completely wiped out in the few remaining polio epidemic areas, all countries should be on alert and continue to maintain high sensitivity of their surveillance systems and high immunization completion rates. They must also be vigilant in detecting imported polio cases and take swift and effective measures to stop them from further transmission. The biosecurity control of laboratory virus strains needs to be enforced, and national immunization policies need to be made in advance to for the post-eradication era. In short, measures need to be in place to ensure that polio, once eradicated, will never make a comeback to threaten the world again.

Now is a critical time if humans are to claim victory in the long war against polio. For our part, Taiwan will continue to upgrade its disease monitoring and control system and maintain high immunization rates. As a responsible member of the global community, Taiwan will continue to play the role of a strong supporter and contributor in this fight against polio. Hopefully in the nearest future, we will be able to share with the rest of the world the ultimate

accomplishment of GPEI.

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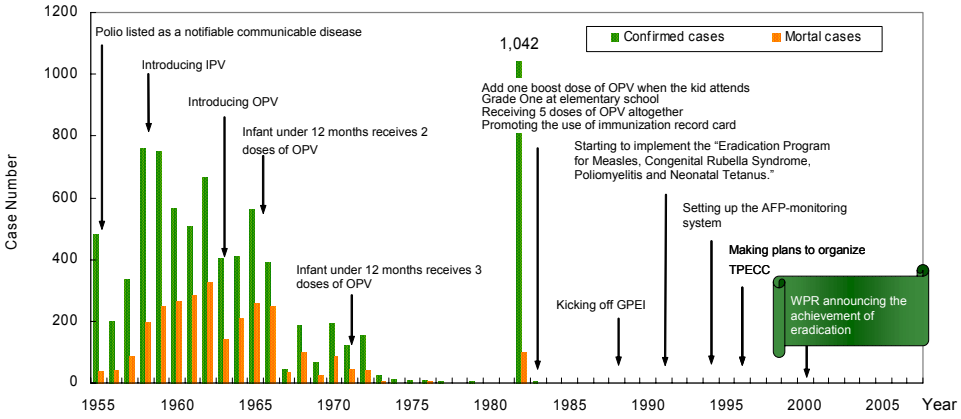

Figure 1. A Chronicle of Important Events in Polio Prevention and Control in Taiwan

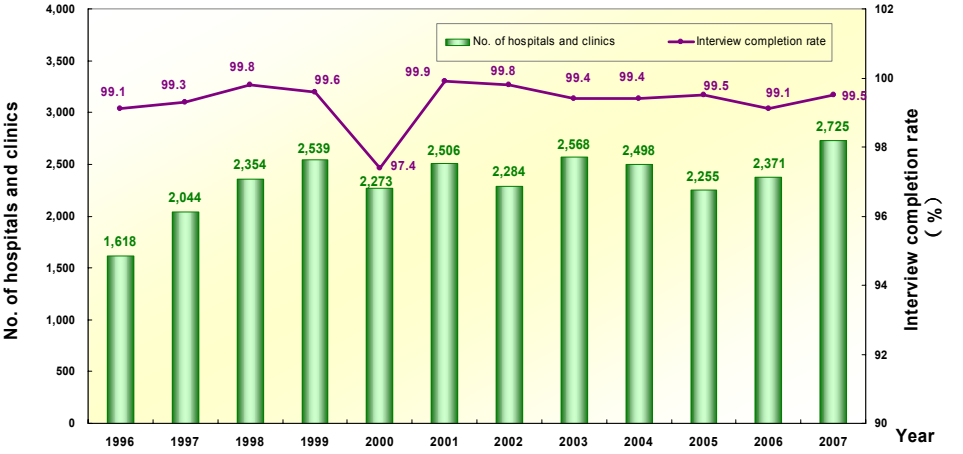

Figure 2. Monitoring Results of the Zero-case Notification System for Measles, Congenital Rubella Syndrome, Poliomyelitis and Neonatal Tetanus

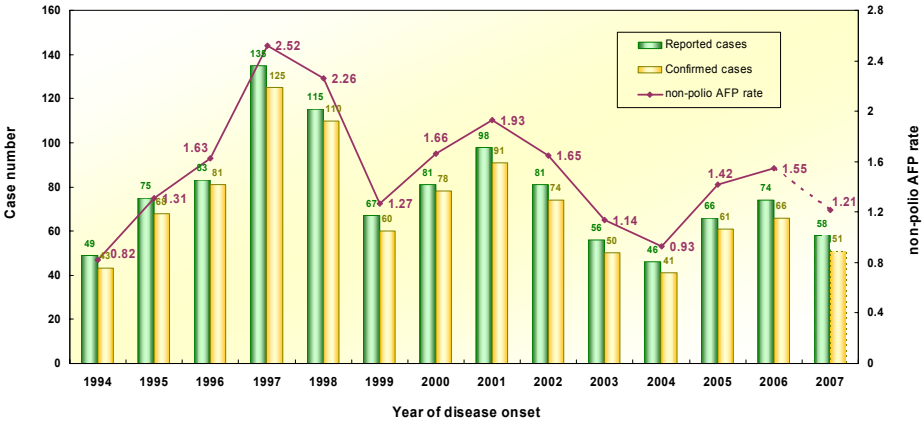

Figure 3. FP Monitoring Results