Perspectives on the Future of Global Eradication of Polio, Measles, Rubella, and Congenital Rubella Syndrome

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Introduction

In 1985, the Pan American Health Organization (PAHO) with its member states and committed partners embarked on an initiative to eradicate polio by 1990. Funds from USAID and other partners such as Rotary International arrived in 1987. The Region, under the leadership of Dr. Ciro de Quadros, embarked on an ambitious plan of action to interrupt transmission on time three years later. The last case occurred on 23 August 1990, eight months, 23 days past the original target.

While polio was being eradicated, countries of the Americas also worked diligently to define the disease burden of measles. Many countries simultaneously administered polio vaccine to interrupt wild poliovirus transmission, and measles vaccine to prevent the large outbreaks of measles that they were encountering in the late 1980s and early 1990s. As a consequence of these efforts, the day polio eradication was certified in 1994, the Region embarked on the elimination of measles by 2000. The last case of endemic measles at that time occurred in November 2002 in Venezuela. Similarly, in September 2003 the Region launched the elimination of rubella and congenital rubella syndrome (CRS) by 2010.

In early 2017 at the time of this writing, the world has never been closer to achieving the global polio eradication goal. Five of the six World Health Organization (WHO) regions have measles elimination targets, and only three have rubella and CRS elimination targets. The Global Vaccine Action Plan (GVAP) calls for measles elimination by 2020 in five of six WHO regions. Progress is grossly insufficient to come close to the GVAP aspirations. The purpose of this chapter is to share perspectives on the future of the eradication of polio, measles, rubella, and congenital rubella syndrome (CRS), and potential actions required in order to achieve the targets.
Polio Pitfalls

For years, the global polio eradication initiative faced devastating set-backs, each with the potential to completely dismantle the program and commitment of governments and key partners. First, the global commitment was never fully recognized until 1998, two years before the global target. Success to that point, had been regionally driven, first in the Americas, followed by the Western Pacific Region (WPRO), and then the European Region (EURO). To work under conditions with insufficient global commitment was overwhelming for many Regions.12

However, India successfully eradicated wild poliovirus type 2 in 1999.13 The last wild poliovirus type 2 in the world was reported in western Uttar Pradesh, although at the time no one fully realized the substantial milestone that had occurred. By the end of 2000 which was the original global target date, the number of polio cases reported in India was at an all-time low.14 Prior, India was the country that typically reported two thirds of the world’s polio cases every year. At the same time polio in Africa, Pakistan, and Afghanistan continued to paralyze thousands of children.

However, a setback in India occurred in 2001 when the polio leaders decided to downsize the number of mass polio vaccination campaigns required to stop transmission. Polio came roaring back exceeding more than 1600 cases in 2002 in Uttar Pradesh, India, alone.15 To complicate matters, program leadership decided to conduct campaigns alternating between monovalent doses of oral polio vaccine (OPV) type 1 and type 3. Predictably, sequential outbreaks of wild poliovirus type 1 and type 3 occurred as a consequence of emerging pools accumulating from the sequential monovalent strategy. During the year OPV1 vaccine was not being used, wild poliovirus type 1 outbreaks occurred, and the same happened for outbreaks of wild poliovirus type 3.16

Almost simultaneously in Africa, the national immunization days required to maintain population immunity were canceled in African polio free countries largely because of insufficient funding and inadequate foresight. The decade of 2000 saw Nigeria continuing to export wild polioviruses to other recently free countries that were no longer protected with their national immunization days.17 Religious and other community leaders in Nigeria had yet to be convinced that polio eradication was good for their children and their communities. The exportations led to large outbreaks that spread extensively in previously declared polio free areas such as Southern Sudan, Yemen, and the Horn of Africa. It was in these countries that vaccinators had previously been killed while conducting their duties to achieve a polio free status.18

In retrospect it is quite remarkable that the program survived to fight another day, largely due to the credit of the Bill and Melinda Gates Foundation (BMGF) and unrelenting commitment of governments and other key partners such as the Centers for Disease Control and Prevention (CDC) and Rotary International. In particular, BMGF started committing the necessary resources that would not infringe upon the extent to which the necessary strategies were required, such as the size or number of mass polio vaccination campaigns, to carry the program over the finish line. Today, the world is as close as it has ever been to achieving the target. By the end of 2016, only 35 wild poliovirus cases were reported globally and only four cases due to circulating vaccine-derived polioviruses (cVDPV). But, as alluded to above, the world has been on the brink of success several times and hopefully the historical lessons will be applied and mistakes will not be repeated.
Polio Endgame

The eradication of polio is really the eradication of 2 viruses, the wild type poliovirus and the oral polio vaccine virus. Vaccine virus must also be eradicated because of its associated risks of vaccine paralytic poliomyelitis (VAPP), cVDPVs, and vaccine-derived polioviruses in immunocompromised individuals (iVDPV). If OPV use were to continue after wild poliovirus is eradicated in the world, then these risks would continue. Therefore, the cessation of OPV use must be addressed in the polio endgame strategy. Since wild poliovirus type 2 transmission was stopped in 1999, the OPV cessation process will be conducted globally in a phased manner. Such an effort was done in April 2016 by switching from trivalent OPV (tOPV) to bivalent OPV (bOPV) product that does not contain vaccine poliovirus type 2.

The switch to bOPV use required efficient and rapid global coordination and synchronization of activities. Ideally, the killed vaccine (IPV), which has none of the above described risks, would have been introduced 6 months before the start of bOPV, in order to continue to provide children with type 2 protection to mitigate the small risk of reemergence and spread of cVDPV2, or some other unexpected event. IPV would also boost mucosal immunity to those children previously vaccinated with tOPV.

PAHO conducted an aggressive planning process to ensure that no country was left behind. The PAHO region has remained polio free for approximately 25 years, at a cost that is actually quite substantial to individual countries if one considers the cost of surveillance and maintaining a trained work force. Unfortunately, the supply of IPV for PAHO’s Revolving Fund is limited to only one provider. Going forward supply issues will need to be urgently addressed. Because of multiple providers, the supply for bOPV looks more reassuring for PAHO member countries.

The cessation of the type 1 and 3 components of bOPV will be linked to the global eradication of the corresponding wild types. The work ahead at the time of this writing must be critically focused on stopping transmission of wild polioviruses existing in Afghanistan and Pakistan. The challenges in these countries because of security issues are enormous. From 2012-2014, 74 vaccinators were killed in Pakistan, including 41 in 2014. The government across all sectors, including military, are engaged. Military involvement in India led to smallpox eradication in the last most difficult areas to work. Parts of Afghanistan and Pakistan remain unreachable because of continued concerns about security.

An often overlooked risk are ongoing outbreaks of cVDPVs. Experts argue that these outbreaks are short-lived and more amenable to mass polio vaccination campaigns to stop their transmission. The data suggest that cVDPV is more responsive to OPV, compared to other circulating wild polioviruses. However, cVDPV does cause paralysis and can be transmitted from child to child causing unnecessary outbreaks. In Nigeria, cVDPV2 has persisted for several years. Transmission may be easier to interrupt, but persistent circulation of cVDPVs signify a critical error in the immunization system. Such cVDPV-caused outbreaks only occur in areas where OPV coverage has been very low.

One key programmatic challenge is to sustain the intensity of the end game efforts in spite of the fact that the polio eradication target date has been changed a number of times. Global interruption of transmission of wild poliovirus, as well as cVDPVs, did not occur at the end of 2015, the last selected target date. Eradication will occur, but the question is when. It may be challenging even in 2017. In the Americas, the last case was reported in 1991 in Peru, but 8 other cases were reported earlier in Colombia that year. In 1990, 18 cases were reported; and in 1989, 24 cases. The program did not go from 24 cases that occurred in 1989 to zero overnight. Recognizing the tremendous amount of work ahead in Afghanistan and Pakistan, partners and governments must “toe the line”. Additionally,
political commitment must remain even past the last wild case in order to carry out the three year work plan required to certify the target has been achieved. Funding these efforts must also continue.

The risk of the emergence of cVDPV relates to every country’s immunity profile. Where OPV was recently used with poor coverage results, cVDPV emergence remains a risk. The routine immunization program performance is more important than ever. To that end, resources from polio should be transitioned to support the strengthening of routine immunization and other services.26

Importantly, countries in the Americas will need to continue to maintain their guard against poliovirus importations and the emergence of any outbreak due to cVDPV until the world has reached the ultimate target of the eradication of wild and vaccine polioviruses. This issue will continue to challenge our resolve in the years to come.

Measles, Rubella, and Congenital Rubella Syndrome Opportunities

The opportunity to transition the assets of global polio eradication initiative to strengthen health systems, while eradicating measles and rubella, introducing new vaccines, and finishing the job with polio, is an ideal opportunity for the world to seize. The experience in the Americas demonstrates that it can be done, and GVAP provides an important roadmap for the world to use.27 WHO has been very proactive to develop a toolkit intended to help countries plan for these new challenges. Documenting lessons learned at the country level will be important to help other countries benefit from these experiences.

Current polio field staff number >30,000 globally, most of whom are actually local volunteers. The equivalent number for measles and rubella is >130. Most of the polio field staff are already spending almost half of their time on routine immunization, measles-rubella, and new vaccine introductions. The switch already happened.27 The potential for continued impact on reaching polio certification while eliminating measles and rubella is extraordinary. The areas of expertise that polio field staff provide other immunization services include: leadership and management oversight, policy and strategy development, planning, implementation and vaccine delivery, monitoring and evaluation, communications and community engagement, disease surveillance and data analysis and use for action, capacity building, and partnership coordination. Arguably, there is no better package of expertise to confront the GVAP targets, including the elimination of measles and rubella. The feasibility of global measles and rubella eradication has been assessed.28 One key guiding principle that programs have learned over and over again, is that simultaneous actions can be implemented. For example, more than one antigen can be provided in a vaccination campaign.29 This was demonstrated in Africa more than 40 years ago. When rubella is linked to measles elimination, achieving the goal results in the elimination of two infections, and one major disabling syndrome (CRS).

The global case needs to be packaged and communicated more strongly. The experience in the Americas consistently demonstrates that the elimination of CRS results in cost savings.30,31 Very few political leaders or ministers of health will turn down a cost savings benefit of eliminating a debilitating disease, particularly if supported by a core partnership. The last case of CRS in the Americas was in 2009, in advance of the 2010 target.7 It is not only cost savings, but very feasible even in a country as poor and challenged as Haiti.

One compelling argument for accelerating measles-rubella elimination is the cost of containing measles outbreaks. The import-related outbreak that spread nationwide in Ecuador in 2011-2012 cost the country...
approximately 8.5 million US dollars to contain.\textsuperscript{32} Infectious diseases are only a plane ride away, so a nation’s capacity to respond to measles will also be a litmus test on how well that particular country will respond to any emerging threat, such as new viral strains of influenza.\textsuperscript{33} Interestingly, we have learned that conducting one rubella mass vaccination campaign with measles-rubella containing vaccine, targeting all citizens, both men and women, aged <40 years will lead to the elimination of CRS. A one-time intervention leading to the elimination of a condition, in this case CRS, is unprecedented in global health. In addition, the population immunity provided to the expanded age groups also benefits measles prevention and control.\textsuperscript{33} The older aged immunity gaps that result from childhood vaccinations are covered in the rubella mass vaccination campaign. The arguments to accelerate measles and rubella elimination are compelling.

Unfortunately, WHO estimates that >50\% of the world’s children are currently not vaccinated against rubella.\textsuperscript{34} Any strategy that uses a single antigen measles vaccine anywhere in the world should be evaluated very thoroughly through an ethical lens. The hypothetical paradoxical response that including rubella antigen in the routine immunization program would increase the risk of CRS born infants has been dispelled by the wealth of global experience and data accumulated thus far. The world has a moral mandate to insure all children are protected from the devastating consequences of rubella, at only marginal incremental program costs.

In summary, like with polio, countries in the Americas will need to continue to maintain their guard against measles and rubella virus importations and the emergence of related outbreaks. The vast experience in the Americas dealing with measles importations every year reflects the very fact that this virus is the most infectious on the planet. This must reinforce our resolve to maintain high-quality surveillance and high levels of coverage. Follow-up MR campaigns conducted every 4 years are part of the elimination strategy and really should be maintained to ensure adequate population immunity is provided to prevent wide spread transmission when measles and rubella importations occur. Finally, immunization managers in the Americas should look for every opportunity to share their experience in other parts of the world.

**Conclusion**

Polio eradication will likely happen despite substantial challenges remaining, not to mention supply of IPV, the risk of cVDPV, the persistence of the wild poliovirus transmission in the remaining endemic areas, and immunity gaps. Progress has never been so close to achieving the goal. The transition of polio resources and assets to best practice opportunities like strengthening health systems, achieving universal immunization coverage and the elimination of measles and rubella, is a tremendous global opportunity to maximize the benefits of vaccines, and encompasses all the GVAP strategic objectives. A fundamental best practice is always building on the success of previous achievements, leading to no more polio, no more inequities, no more measles, rubella and CRS. The vision to accomplish these targets must also embrace the need for countries to increase ownership of their national programs by expanding the fiscal space of their own national budget allocations in order to guarantee the child’s right to vaccine protection. There is arguably no better way to sustain national programs than by becoming less donor dependent. To that end, other regions of the world would certainly benefit from a Revolving Fund-like mechanism to assure them a safe, more affordable supply of vaccines, especially the newer candidates that come at a much higher cost. Otherwise, countries may continue to struggle with the increasingly challenging issues of national sustainability and country ownership. However, these are challenges that have solutions. Indeed, even the countries of the Americas should never take their Revolving Fund for granted. The current pricing challenges of new vaccines is a call for them to remain committed to the same regional solidarity in the future that led to so many successes in the past. Finally, in the Americas we cannot lose sight of the fact that now more than ever we cannot drop our guard on sustaining the region free of endemic polio, measles, rubella, and CRS.
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