The critical role of acute flaccid paralysis surveillance in the Global Polio Eradication Initiative

Rudolf H. Tangermann*, Christine Lamoureux, Graham Tallis and Ajay Goel

World Health Organization, Geneva, Switzerland

*Corresponding author: Tel: +41 79 244 6043; E-mail: tangermannr@who.int

Received 10 November 2016; revised 18 January 2017; editorial decision 23 January 2017; accepted 12 May 2017

Acute flaccid paralysis (AFP) surveillance is a key strategy used by the Global Polio Eradication Initiative (GPEI) to measure progress towards reaching the global eradication goal. Supported by a global polio laboratory network, AFP surveillance is conducted in 179 of 194 WHO member states. Active surveillance visits to priority health facilities are used to assure all children <15 years with AFP are detected, followed by stool specimen collection and testing for poliovirus in WHO-accredited polio laboratories. The quality of AFP surveillance is regularly monitored with standardized surveillance quality indicators. In highest risk countries and areas, the sensitivity of AFP surveillance is enhanced by environmental surveillance (testing of sewage samples). Genetic sequencing of detected poliovirus isolates yields programmatically important information on polio transmission pathways. AFP surveillance is one of the most valuable assets of the GPEI, with the potential to serve as a platform to build integrated disease surveillance systems. Continued support to maintain AFP surveillance systems will be essential, to reliably monitor the completion of global polio eradication, and to assure that a key resource for building surveillance capacity is transitioned post-eradication to support other health priorities.

Keywords: Acute flaccid paralysis, Environmental surveillance, Polio eradication, Poliovirus, Surveillance

Introduction

The Global Polio Eradication Initiative (GPEI) began in 1988, following a unanimous resolution by all WHO member states in support of global eradication1 at the World Health Assembly 1988, a year when 125 countries worldwide still reported endemic poliomyelitis (Figure 1). Progress towards interruption of poliovirus transmission since then has been impressive, and the GPEI is close to reaching the global eradication goal. Four of six WHO regions, comprising >80% of the world’s population, have already been certified as polio-free. As of the end of 2016, only three countries continue to report polio cases caused by endemic wild poliovirus type 1 (WPV1): Nigeria (WHO African Region) and Pakistan and Afghanistan (WHO Eastern Mediterranean Region).2

From the beginning of the initiative, the key strategy to detect transmission of poliovirus and monitor the impact of eradication activities has been surveillance for children <15 years of age presenting with acute onset flaccid paralysis (AFP), the lead symptom of paralytic poliomyelitis3; AFP surveillance was first used in the Region of the Americas during the 1980s.4 Following the reporting of the AFP case, stool specimens are collected and tested for poliovirus in WHO-accredited poliovirus laboratories that are part of the Global Polio Laboratory Network (GPLN).5 In specific situations, the sensitivity of AFP surveillance is enhanced by environmental surveillance for poliovirus (testing of sewage water) at selected sites,6 or collection of specimens from AFP case contacts. Poliovirus isolates detected in stool or environmental samples are further characterized through genomic sequencing, which yields programmatically important information on polio transmission pathways.7

AFP surveillance has become the world’s largest standardized disease surveillance system for an outbreak-prone disease. While the detection of wild and vaccine-derived polioviruses are reportable events under the International Health Regulations (IHR, 2005),8 there is no IHR reporting requirement for reporting AFP. Nevertheless, of 194 WHO member states, 179 conduct AFP surveillance and submit weekly AFP reports to WHO Regional Offices and WHO HQ, which, together with the lab results provided by the laboratories of the GPLN, allows timely outbreak detection and response. The only countries not conducting AFP surveillance are high-income industrialized countries in North America, Western Europe and the Western Pacific, all with high polio vaccine coverage and low risks of importation-related outbreaks. Most of these countries do use alternative surveillance methods to detect polioviruses.9,10

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This review describes the critical role of AFP surveillance in tracking progress towards global eradication, provides background on how the method was developed and is implemented, and how AFP surveillance quality is measured and assured. The review also highlights the contribution of the GPLN, discusses the significance of genetic sequencing for guiding programme decisions, reviews the use of AFP surveillance to strengthen surveillance for other outbreak-prone diseases and highlights the significance of maintaining high-quality AFP surveillance throughout the polio endgame.

Evolution of AFP surveillance

Surveillance for cases of AFP, backed up by virological examination of stool specimens, was first used during polio eradication efforts in the Region of the Americas. Unlike for monitoring polio control efforts, it was clear that clinical confirmation of paralytic polio cases would no longer be sufficient to monitor progress towards actually interrupting virus transmission. The main objectives of surveillance for the purpose of eradication were now to rapidly detect any remaining areas of poliovirus transmission, in order to effectively target large-scale immunization activities, and to reliably show where transmission had been interrupted.

As opposed to surveillance for smallpox or measles, surveillance for polioviruses is complicated by the fact that the great majority of infections in susceptible persons (>99%) do not result in paralysis. Also, the lead polio symptom of AFP may be caused by several other conditions that can mimic paralytic polio, most notably Guillain-Barré syndrome. Clinicians with experience during the polio-endemic era were familiar with polio, and it is likely that they were able, with reasonable accuracy, to distinguish polio from other causes of paralysis on clinical grounds. However, new generations of doctors no longer gained this experience as polio case numbers rapidly decreased in many countries, following vaccination and eradication efforts.

The non-specific initial presentation, as well as the decreasing experience of physicians with paralytic polio, meant that a certain proportion of true polio cases would be misdiagnosed, for example as Guillain-Barré syndrome, and so the reporting of clinical polio cases alone was not considered sensitive enough for achieving eradication. The surveillance case definition (‘Any patient <15 years of age with acute onset flaccid paralysis, or a patient at any age in whom a clinician suspects polio’) was expanded during eradication efforts in the Americas to include all cases of AFP since this would assure that all remaining cases of true paralytic polio would be included. Testing of stool specimens would then be used to separate true polio cases from cases of AFP not due to polio (‘non-polio AFP’).

AFP surveillance became one of the key polio eradication strategies, in addition to achieving the highest possible routine polio vaccination coverage and the conduct of large-scale supplementary immunization activities (i.e. national immunization days [NIDs], and ‘mopping-up’ activities, targeting the last remaining foci of transmission).

The main steps to implement AFP surveillance, as first established in the Americas, are still being followed today, in close coordination between vaccination programmes, public health surveillance teams and polio laboratories: reporting of all cases of AFP in persons <15 years of age (the majority of confirmed cases are still in persons <5 years old, but some cases may occur in older age groups up to 15 years), or at any age if a clinician suspects polio, and detailed epidemiological investigation of each reported case; collection of two stool specimens within 14 days of paralysis onset (since virus excretion in the stool may...
be intermittent, and because the probability of virus excretion in the stool of polio cases decreases rapidly beyond 2 weeks of onset of paralysis; virus isolation in a WHO-accredited polio laboratory; final classification of all AFP cases as ‘confirmed polio’, ‘discarded as non-polio AFP’, or ‘polio-compatible’ if polio could not be reliably excluded (i.e., specimens were not collected, or were collected late).\textsuperscript{13}

During the initial phase of the eradication initiative, polio case reporting remained incomplete and was still based on a clinical case definition. As AFP reporting and the timely collection of stool specimens improved, WHO regions switched to confirming as polio only those AFP cases as polio for which poliovirus had been isolated. While this switch occurred at different points in time in each Region, the change to a ‘virological case definition’ was completed globally by 2002.

Zero-reporting and active surveillance

Rather than relying on passive reporting of AFP cases from health facilities, the eradication programme in the Americas introduced the concept of weekly ‘zero-reporting’; i.e., health facilities at all levels were required to submit weekly ‘zero reports’ even if no AFP case had been seen. More than 10 000 health facilities in the Americas participated in weekly zero-reporting, which remained the key AFP surveillance strategy until the Region was certified polio-free in 1994. Zero-reporting was adopted by other Regions as eradication activities began there. However, it soon became clear that outside of the Americas, relying on zero-reporting alone would not assure complete enough reporting of all AFP cases.

‘Active surveillance for AFP’, consisting of regular visits by trained public health surveillance staff to priority health facilities in the AFP surveillance site network, was first used in the Western Pacific Region but was soon adopted in all other WHO regions and countries. Visiting public health surveillance staff enquire about any AFP cases seen and also conduct direct checks for AFP cases in all relevant hospital departments, including through the scanning of all relevant patient log books. The frequency of active surveillance visits is determined by the likelihood of AFP cases being seen at a facility, from weekly visits to the largest and highest priority hospitals, to bi-weekly or monthly visits to smaller health facilities.

Once an AFP cases has been detected, provincial or district surveillance teams conduct a detailed epidemiological investigation of the case, at the location of onset of paralysis.

Many countries began to use active surveillance visits to also detect and report other conditions, mostly other vaccine-preventable diseases such as measles and neonatal tetanus. AFP surveillance in industrialized and most middle-income countries is integrated into existing disease surveillance systems, implemented by national health staff. In 43 of 46 member states of WHO’s African Region, AFP surveillance is conducted as part of an Integrated Disease Surveillance and Response (IDSR) system.

Low income developing countries are provided with external technical and funding support to conduct AFP surveillance. In a number of these countries, the Ministries of Health and WHO built up a network of AFP surveillance officers to ensure that AFP surveillance quality is sufficient. Public health workers frequently conduct sensitization sessions and awareness seminars on AFP surveillance for clinicians and other health facility staff. Where health systems are fragile, providers working in the informal health sector, such as traditional health practitioners and quacks, as well as members of the community are also sensitized to report AFP cases.

AFP surveillance quality indicators

AFP surveillance became the most efficient and widely used method to monitor polio eradication efforts also because simple, standardized surveillance quality indicators were developed to monitor the quality and sensitivity of surveillance. These indicators can be used at all administrative levels to identify and address surveillance quality gaps, and to ensure that surveillance is sufficiently sensitive to detect circulating polioviruses. Regular monitoring of surveillance quality indicators is a critical tool to maintain and improve the sensitivity of AFP surveillance, at all levels.

The program uses two principal AFP quality indicators. The first is the ‘non-polio AFP (NPAFP) rate’; i.e., the number of cases per year per 100 000 population aged <15 years. The annual target rate set for all countries in three WHO regions (African, Eastern Mediterranean and South-East Asian Region) is \(\geq 2/100\ 000\), which is considered sensitive enough to detect any circulating poliovirus. Target in the three Regions already certificated as polio-free is to reach an annual rate of \(\geq 1/100\ 000\). The second main AFP quality indicator is the proportion of reported AFP cases for which ‘adequate’ stool specimens were collected: this proportion should be at least 80%. A stool specimen is considered adequate if it was collected within 14 days of paralysis onset, 24–48 hours apart, and arrived in the polio laboratory in a condition that is defined as ‘good’. This indicator is critical since the presence of poliovirus in a specimen can only be reliably confirmed or excluded through laboratory analysis. In this context, it is crucial for programs to assure reliable and timely transport of stool specimens to the laboratory in cold storage boxes, i.e., to maintain the ‘reverse cold chain’, which can present considerable logistical challenges and needs to be carefully monitored.

Other process quality indicators measure the timeliness of the initial notification of AFP cases, and the completeness and timeliness of active surveillance visits to all health facilities in the AFP reporting network. Likewise, there are several important process indicators that measure the completeness and timeliness with which polio laboratories process specimens and provide results.

Based on the experience during smallpox eradication, a system of regional and global certification of polio eradication has been established.\textsuperscript{14} The Global Commission for the Certification of Poliomyelitis Eradication has required that a period of 3 years without isolating wild poliovirus, with ‘certification standard’ AFP surveillance, is required before the interruption of wild poliovirus transmission can be certified in a WHO region. Certification standard AFP surveillance is defined as achieving an annual non-polio AFP rate of at least one non-polio AFP case per 100 000 population <15 years, with adequate stool specimens.
collected from at least 80% of all AFP cases. All WHO regions, and the majority of member states continue to achieve, maintain and often substantially surpass this standard (Table 1). Four of six WHO regions, containing >80% of the world’s population, have already been certified polio-free: the Region of the Americas in 1994, the Western Pacific Region in 2000, the European Region in 2002 and the South-East Asian Region in 2014.

Supplementary methods to increase surveillance sensitivity

With time, innovative surveillance methods and strategies were developed to adapt to settings where the application of traditional approaches could not yield satisfactory sensitivity. In countries affected by conflict or complex emergencies such as Afghanistan, Somalia and South Sudan, active surveillance cannot be conducted in many areas because of limited availability and usage of health facilities. Instead, AFP surveillance has successfully been extended into communities through setting up networks of community-level AFP focal points and AFP ‘informants’ (i.e., village leaders, teachers, pharmacy keepers, traditional healers, mullahs) who report the occurrence of AFP cases to district and province-level surveillance teams. Community surveillance for AFP is also successfully being used in hard-to-access areas of countries not affected by conflict.

Other supplementary methods to increase the sensitivity of surveillance include the collection of stool specimens from healthy direct contacts of AFP cases and/or from nearby communities, particularly when specimen collection from the index case is delayed beyond two weeks after the onset of paralysis. If poliovirus is isolated from a direct contact of a virus-negative AFP case, a scenario which does occur several times each year in the remaining infected areas, the index case is confirmed as polio. Also, in areas with low surveillance quality, or whenever surveillance needs to be enhanced such as following the detection of a new outbreak, national programmes may conduct special ‘AFP case search activities’ during supplementary immunization campaigns, or by visiting health facilities and conducting retrospective record searches. Such searches help to improve surveillance, particularly if they show that AFP cases were missed in the past.

Environmental surveillance for polioviruses

Environmental surveillance, i.e. the testing of sewage samples for polioviruses, is used to supplement AFP surveillance, with two main objectives. First, environmental surveillance is used to detect circulating polioviruses (wild, vaccine-derived and Sabin-like) directly from the environment, in order to identify residual WPV transmission in endemic and re-infected areas, particularly where WPV continues to circulate but does not cause paralysis. Environmental surveillance can also provide an early signal of new poliovirus importations into polio-free areas, or of the emergence of vaccine-derived poliovirus.

Environmental surveillance is conducted in the three remaining polio-endemic countries, Nigeria, Afghanistan and Pakistan, in India and in 34 countries without recent active
WPV transmission, including nine countries on the African continent. Environmental surveillance has played a key role in documenting the elimination of WPV in Egypt and India, and in detecting WPV or vaccine-derived polioviruses in several polio-free countries, such as Brazil, China, Egypt, Estonia, Finland, Israel and Mexico.

As the GPEI moves towards global eradication, data generated from continued high-quality environmental surveillance will provide important evidence to be considered before the decision can be made to certify the world as polio-free. Environmental surveillance also already proves to be an efficient tool to document the disappearance of Sabin-related vaccine viruses, such as following the cessation of type 2 oral polio vaccine (OPV2) use, through the April 2016 globally coordinated switch from using tOPV (types 1, 2 and 3 OPV) to bOPV (types 1 and 3 OPV).20

The Global Polio Laboratory Network

Global polio eradication would not be possible without the critically important contribution of the GPLN, which provides the GPEI with timely and reliable laboratory results to monitor progress towards eventual global interruption of poliovirus transmission.21,22 The network is comprised of 146 WHO-accredited poliovirus laboratories in all WHO regions. Of the 146 laboratories, 46 serve as primary virus isolation laboratory, 70 have the additional capacity for intratypic differentiation, 26 are able to sequence the viral genome, and 7 are considered global specialized polio laboratories (Figure 2). GPLN member laboratories follow standardized protocols to isolate and identify polioviruses; conduct intratypic differentiation to identify WPV or screen for Sabin-like or vaccine-derived poliovirus; and conduct genomic sequencing of detected poliovirus isolates.23 The accuracy and quality of testing at GPLN member laboratories is monitored through an annual accreditation program of on-site reviews and proficiency testing.

Poliovirus sequencing is used to monitor pathways of poliovirus transmission by comparing the nucleotide sequence of poliovirus isolates; its results allow to detect epidemiologic links between polio cases; identify local reservoirs sustaining polio endemicity; recognize imported polioviruses; but also to monitor progress toward eradication, as evidenced by decreasing biodiversity of the virus lineages in circulation; and characterize vaccine-derived polioviruses. The importance of genetic sequencing is illustrated in Figure 3, which shows how inferences from genetic sequencing results are used to track the international spread of WPV type 1—in this example the spread that occurred to polio-free from polio-endemic and other infected countries between January 2013 to October 2016.

Sequencing data allow polio programme managers at country, regional and global level to make critical programmatic decisions, such as on the need for large-scale outbreak response immunization and to assess progress towards eradication. Sequencing data also assists in assessing surveillance sensitivity. Poliovirus isolates for which the nucleotide sequence differs considerably from previously identified isolates are considered ‘orphan’ viruses which circulated undetected for a prolonged period, indicating gaps in AFP surveillance.

Figure 2. The Global Polio Laboratory Network.
Other vaccine-preventable disease laboratory networks have been built, following the example of the GPLN, and supported by much of the GPLN infrastructure. For more than 10 years, and as polio-free WHO regions and countries increasingly focused on measles control and elimination activities, a Global Measles Laboratory Network has been in existence, which supports the global measles mortality reduction and regional measles elimination goals.

Limitations and shortcomings

Despite the overall global utility of AFP surveillance, a number of caveats and limitations need to be kept in mind which can negatively impact on the sensitivity and reliability of surveillance results. AFP surveillance will be required until global certification, OPV cessation and beyond. Experience has shown that to maintain AFP surveillance of sufficient sensitivity requires the ongoing monitoring of surveillance quality indicators, at all relevant administrative levels. At regular intervals, desk and field reviews of surveillance quality are needed in order to detect surveillance quality gaps and to target measures to strengthen surveillance. Also, ongoing efforts are needed to train surveillance staff on AFP concepts and procedures and to sensitize clinicians and health workers in facilities likely to see AFP cases. Lastly, surveillance quality will decrease without regular supportive supervision of surveillance workers, especially those involved in critical strategies like active surveillance at major health facilities.

Effective quality control and maintenance for AFP surveillance requires sufficient government commitment to maintaining sensitive surveillance in the future, and also is not possible without the investment of considerable attention and time of national and provincial/state surveillance teams. This is easier in polio-endemic or recently endemic countries, or in polio-free low income countries still supported by WHO and UNICEF-supported polio teams. Middle- and high-income countries find it much more difficult to maintain AFP surveillance, both because there is no external support, and because of waning commitment to maintain surveillance for a disease that has been absent for a long time. It is for this reason that AFP surveillance quality indicators are decreasing in countries of the Americas, and of the European and Western Pacific Regions.

Situations of acute or chronic conflict and civil unrest, such as in Afghanistan, Somalia, South Sudan or north-east Nigeria, almost invariably lead to problems in accessing populations,
with strongly negative impact on the quality of vaccination campaigns. Of note, it has been possible to maintain surveillance quality in a number of conflict-affected areas, including in south-west Afghanistan or southern Somalia, at unexpectedly high levels—largely through the placement of full-time village-level polio workers, and involvement of ‘AFP informants’ at the local community level.

However, even with AFP quality indicators at high levels, evidence has repeatedly emerged that poliovirus transmission in some conflict-affected countries and areas was missed for prolonged periods of time (i.e., Chad and Sudan, 2004, and Borno, north-eastern Nigeria, 2016). In Nigeria, indigenous WPV1 was detected again in in Borno state in August 2016, 2 years after WPV1 was last reported in July 2014. Surveillance quality indicators in such scenarios are just one factor to take into consideration, and it is equally important to understand other determinants of surveillance quality, such as access and security, quality of supervision and monitoring, or population movement. Of note, the same factors are equally important as determinants of the quality of immunization activities. Furthermore, high rates of AFP reporting do not necessarily imply highly sensitive surveillance, because, in the absence of sufficient supervision, there may be considerable over-reporting of children as AFP cases who actually do not have AFP, while true AFP cases (i.e., Guillain-Barré syndrome cases) are missed.

**Expansion of AFP surveillance and innovative applications**

The establishment of national AFP surveillance programs has created a group of well-trained surveillance workers who, in most countries, also conduct surveillance for other vaccine-preventable diseases, assist in detecting and responding to other outbreak-prone diseases, or help in other health emergencies. This was demonstrated recently in Nigeria when the national polio team provided critical support to the Ebola outbreak response. Active surveillance visits for AFP cases can be used to also detect other vaccine-preventable diseases or infectious diseases, creating an opportunity to combine and integrate surveillance systems. Already in 2003, 131 of 194 WHO member states had added surveillance for measles and other vaccine-preventable diseases, depending on disease burden and national immunization schedule, to their AFP surveillance systems.

In addition to monitoring progress towards interrupting virus transmission, AFP surveillance data is routinely used also to generate other very useful risk and program effectiveness measures. An example for this is the routine analysis of the OPV vaccination history of AFP cases, which proved to be a useful proxy for the level of polio immunity in a population. Also, all WHO regions include an analysis of AFP surveillance performance in member states in their routine polio risk assessments.

It has also been proposed that the AFP surveillance system would provide a useful platform to achieve the objectives of the International Health Regulations (IHR, 2005) to strengthen global and national capacity to detect and respond to infectious disease and other health threats. More recently, it was suggested to strengthen surveillance for Zika virus infection, through screening of Guillain-Barré syndrome cases detected by AFP surveillance.

**Conclusions**

The maintenance of sensitive global surveillance for polioviruses is fundamental to achieving and sustaining global polio eradication. The unprecedented progress of the GPEI would not have been possible without AFP surveillance, which will remain the primary mechanism for poliovirus surveillance globally. As long as endemic polio transmission continues anywhere, polio-free countries and areas, particularly those with low-performing vaccination programs, remain at risk of outbreaks following WPV importation or following emergence of circulating vaccine-derived. Complemented by environmental surveillance, only sensitive AFP surveillance will enable programs to rapidly detect and respond to new outbreaks or emergence of circulating vaccine-derived poliovirus, allow to eventually certify that WPV transmission is finally interrupted, and assist in validating that all vaccine-related virus strains are eliminated following the cessation of OPV use.

AFP surveillance systems have become one of the most valuable assets of the GPEI, with the potential to use existing AFP systems as a platform to build integrated vaccine-preventable disease surveillance systems and to strengthen overall immunization programs, particularly in low-income countries. The GPEI’s Endgame Strategic Plan 2013–2018 stresses the importance of planning for transitioning and maintaining critical polio assets, including surveillance and outbreak response capacity, to support other public health priorities, such as national vaccine-preventable disease control programs. It is, therefore, essential that international partners and national governments continue to support AFP surveillance, both to reliably monitor the successful completion of global polio eradication, and to assure that existing key resources for disease surveillance are not lost but transitioned towards supporting other critical health programs.

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**Authors’ contributions:** RT, CL and GT jointly developed the structure of the manuscript; RT prepared the first draft which was reviewed and revised by CL, GT and AG. AG checked and confirmed all polio eradication data used in the manuscript. All authors read and approved the final manuscript. RT is guarantor for the paper.

**Funding:** None.

**Competing interests:** None declared.

**Ethical approval:** Not required.

**References**


