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The polio endgame

Philip Minor*

National Institute for Biological Standards and Control; South Mimms, Hertfordshire, UK

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Abbreviations: AFP, acute flaccid paralysis; cVDPVs, circulating vaccine derived polioviruses; IPV, inactivated polio vaccine; OPV, oral polio vaccine; tOPV, trivalent oral vaccine; VAPP, vaccine associated paralytic poliomyelitis.

Paralytic poliomyelitis is a disease that became a public health issue at the beginning of the twentieth century and was more or less eliminated in developed countries by the early 1970s. The Global Polio Eradication Initiative of WHO has now eradicated endemic polio from all but three countries although re-introductions occur. The progress in polio eradication is striking and has accelerated over the last few years. It is likely that it will be finally eradicated from the world soon, the looming issue will then be how to stop vaccinating or modify immunization programs safely so that poliomyelitis does not re-emerge. This review article discusses the history and pathogenesis of poliomyelitis. The progress made, and challenges in sustaining the eradication of this debilitating infectious disease are considered.

Introduction

The Global polio eradication program is the biggest public health intervention aimed at a single infectious disease in history. By 2003, the early programs had reduced the number of countries with serious endemic infection to four: India, Pakistan, Afghanistan and Nigeria. Further progress in these remaining areas seemed slow. In the last two to three years the momentum of the program has picked up; it appears that polio has been eradicated from India, and its complete eradication has come to seem an imminent possibility.[1,2]

History

The history of poliomyelitis in the world is roughly divisible into four periods. A funerary stele of the Middle Kingdom Egyptian priest Rom from about 1400 BCE shows the typical withered leg and down flexed foot of poliomyelitis but despite its striking clinical presentation there are fewer than a dozen instances identifiable in the medical literature until the end of the 19th century. The consensus is that there was very little disease until standards of living and hygiene improved when it began to occur in terrifying epidemics in western countries, a period that lasted from about 1900 to 1960. In the United Kingdom the peak period of incidence was the 1950s, after which the vaccine developed by Salk (Inactivated Polio Vaccine, IPV) and later the live attenuated vaccine of Sabin (Oral Polio Vaccine, OPV) eliminated it as a real public health problem. However it still occurred at high frequency in developing countries despite the apparently large amounts of vaccine being used, and for some time it was thought that OPV in particular did not work in tropical climates. This third phase began to come to an end in the mid-1980s when polio incidence was falling in certain South American countries. This was accomplished by mass OPV immunization campaigns, as recommended by Sabin, where colossal amounts of vaccine were given over a very short period so that the susceptible pool was reduced suddenly and transmission interrupted. This developed into the strategy of National Immunization Days, whose scale became vast. In the end stages India regularly immunized over 120 million children on a single day and repeated the exercise many times throughout the year. Developed countries had used a routine immunization strategy where children were vaccinated at a set age rather than all at once as a single cohort. In temperate climates polio transmission occurs almost exclusively in the summer so that the winter immunizations were eventually able to reduce the pool of susceptible individuals to a level too small to sustain circulation. Where exposure is year round, as in the tropics, the impact of this routine strategy on the size of the susceptible pool is insufficient to stop transmission so that massive campaigns are required.

The fourth and final phase is the cessation of vaccination after polio is eradicated, which is not trivial.

Pathogenesis

In 1909 polio was shown to be caused by a virus now classified as a species C enterovirus, a group that includes most of the Coxsackie virus A strains, within which the polio genome can recombine freely. Recombination may well have epidemiological significance in generating viruses with novel properties or removing regions of the genome that handicap growth or transmission.

The enteroviruses of which polio is the type member grow mainly in the gut where infection is entirely asymptomatic. However sometimes the virus can spread and infect unknown somatic tissues, where it can replicate and spread further to other regions including the throat, the regional nervous system and the central nervous system. In the central nervous system poliovirus

*Correspondence to: Philip Minor; Email: philip.minor@nibsc.org
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specifically targets and destroys the motor neurones leading to the classical clinical presentation. Typically the lower limbs are affected hemilaterally but infection further up the spinal cord can affect the respiratory centers leading to bulbar poliomyelitis where the victim will die unless respiration is assisted.

While paralytic poliomyelitis is the syndrome of concern it is in fact very rare, occurring in an estimated 1% or fewer infections. Mostly infection is confined to the gut, and as spread from there is by a viraemic phase, if the infected individual has circulating humoral antibodies disease will not occur. This is the accepted reason for the development of polio epidemics at the same time as hygiene standards improved. When babies were exposed to human waste and polio virus early in life they would have been protected by maternal antibodies and it was only when exposure occurred later that the virus could spread from the gut to other sites. The protective effect of humoral antibodies was demonstrated in trials in the 1950s.[3]

Implications for the Eradication Program

The pathogenesis of polio means that most infections are silent, so that counting cases is only an indirect measure of the presence of the virus. Thus if one country in the world has circulating poliovirus the entire world is at risk as it can be exported by asymptomatic individuals who are impossible to identify simply. This was graphically illustrated by events in Nigeria in 2002, where immunization in the Northern part of the country was halted because of a local belief that the polio campaign was harmful and would result in the sterilization of children. The virus spread from Nigeria to neighboring countries over a period of a few months and essentially the whole of Central Africa became re-infected. In addition pilgrims from Nigeria took the virus to Mecca and spread it to Yemen and Indonesia. Eventually the outbreak was brought under control by large scale interventions including mass campaigns across the whole of Central Africa. Export from endemic countries, including India has been repeatedly documented since.

In addition there has been silent circulation of a type 1 poliovirus strain in Israel detected by environmental surveillance of sewage. The virus has unusual antigenic properties and originated in Pakistan. This is particularly of concern as it appears to be happening in areas of good as well as poor hygiene and the vaccine coverage in Israel is well over 90% using IPV exclusively. Silent circulation may well have happened in Egypt where two isolates also derived from Pakistan have been made from environmental sampling with no associated disease. The data demonstrate that IPV cannot be relied on to interrupt transmission although it did so in some European countries including Scandinavia and the Netherlands. The consensus is that circulation could be stopped in Israel with OPV but there is a reluctance to introduce live virus into the population. The situation in Israel has parallels with that in the United Kingdom, where coverage is high and the switch to IPV occurred at roughly the same time. There is currently no environmental surveillance of sewage for polio in the UK and there are extensive contacts between the UK and Pakistan populations; it is conceivable that a virus is circulating undetected. The matter is particularly worrying because surveillance in the eradication program has usually focused on cases of acute flaccid paralysis (AFP) which could not detect silent infections of this type. Surveillance of sewage is taking a bigger role, and is performed routinely in Finland, India, Egypt and many other countries, and should almost certainly be initiated in the UK.[4]

Progress in Eradiation

Poliomyelitis remains an issue in Pakistan, Afghanistan and Nigeria where it has never been eradicated. There have been outbreaks in areas of conflict including Somalia, Ethiopia and Syria, and the current situation in Israel is cause for concern. Interestingly, polio occurs in three serotypes (types 1, 2 and 3) and all current activity is associated with type 1. There has been no case caused by a naturally occurring type 2 virus since October 1999 although there was a small cluster of cases caused by sabotage of OPV with a laboratory wild type strain in India. Similarly there has been no case of type 3 poliomyelitis since November 2011.[1]

A particular achievement was the elimination of polio in India, where the last case was reported in January 2011; while the prescribed three years had not yet elapsed at the time of writing it seems most likely that India is now polio free. The particular circumstances in India, where transmission seems to have been very forceful, make this particularly impressive. Part of the process was to vary the vaccines used; normally a trivalent oral vaccine (tOPV) containing all three serotypes would have been used in both campaigns and in routine use. The type 2 component of tOPV is particularly effective and outcompetes the other types, and so the type 2 component was omitted and either bivalent or monovalent OPV used with a greater effect. The program has thus become more flexible in the vaccines it uses.

Issues Associated with Vaccination and the Cessation of Vaccination: Vaccine Derived Strains

Given that there have been no polio cases caused by wild type 2 virus in the world since 1999 it seems strange that it is still included in the vaccine. The reason is that as oral polio vaccine strain virus replicates in the gut, typically for 30 d in first time vaccinees, it evolves rapidly to replicate more efficiently. For all three serotypes (but particularly types 2 and 3) the virus routinely becomes more virulent and can cause vaccine associated paralytic poliomyelitis (VAPP). In certain circumstances which are still not clear it may also regain transmissibility, circulating silently for one or two years before being identified as the cause of an outbreak. Such strains are termed circulating vaccine derived polioviruses or cVDPVs. Type 2 and type 1 are the commonest serotypes to do this and there have so far been no instances of a type 3 cVDPVs. Where type 2 has been omitted from the vaccines used in the mass campaigns it has so far been kept in the vaccines used in routine programs, which are less comprehensive

in their coverage. Thus a pool of individuals without immunity to type 2 builds up and cVDPVs, which occur anyway in areas of poor coverage, become even more of an issue. This has been a striking observation in Nigeria in particular. Modifying the vaccine to leave out the type 2 component completely is therefore a complex operation. IPV has been proposed as a possible way to prevent at least symptomatic polio, but this will require high coverage and at the moment IPV has not been used in mass campaigns in the same way as OPV.

As well as cVDPVs, hypogammaglobulinaemic individuals deficient in humoral immunity can become chronically infected when exposed to OPV by mistake or because they had not been diagnosed. This is rare, and even where virus shedding continues for prolonged periods of up to a year or more, it can stop spontaneously. Most long-term excreters have been identified when they get polio after several years of silent shedding. Virus isolates have been obtained from the longest known excreter of polio virus since 1995; the properties of the virus suggest that they had been shedding for at least 11 y before that, which is also consistent with the immunization history implying that the individual has been continuously excreting poliovirus for nearly 30 y at the time of writing. The patient remains healthy. In the absence of a high level of immunization coverage they would be a real source for introduction of polio after eradication.

The vaccine is therefore an issue for the endgame of eradication, and the use of IPV has become more important; no country in the European Union now uses OPV, the whole of North America (USA and Canada) has switched to IPV and other countries including Mexico, Russia and Argentina have either transferred to IPV or are planning to do so in the near future. However, the production of IPV currently requires the growth of colossal amounts of wild type polio viruses and in the past there have been escapes from production facilities on rare occasions. Currently there are possibly three producers of IPV, all in developed countries where production is very tightly contained. As countries such as India and China develop vaccine production capacity it is hard to believe that they will not also move into IPV production and the larger the number of producers the more likely an escape will be.

WHO have developed a number of relevant documents to address the issues which are very complex.[5-7] One possibility has been to use the live attenuated strains used in OPV to prepare IPV; apart from the fact that the strains create their own problems when used in immunisation campaigns, and are therefore not totally safe, they are also different in their immunogenicity in clinical trials raising problems for vaccine development. Alternative strains that are predicted to be both safe and stable are being explored. They would have the advantage that if the properties are really as thought, they could be used safely anywhere.

Conclusion

The progress in polio eradication is striking and has accelerated over the last few years. The looming issue is how to stop vaccinating or modify immunization programs safely so that poliomyelitis does not re-emerge.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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