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Consequences of Neglecting Epidemiology by Global Polio Eradication Initiative

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Abstract

Global Polio Eradication Initiative (GPEI) was assigned the task of eliminating polio in low income countries in Africa and Asia. GPEI did not apply epidemiological guidance in designing vaccination tactics while aiming to achieve the laudable goal of 'no child ever should get polio paralysis'. The force of infection of polio was even higher than that of measles, evidenced by its younger age distribution. Epidemiology taught that a vaccine of very high vaccine efficacy (VE) was required to prevent polio in vaccinated infants. GPEI chose to use trivalent oral polio vaccine (tOPV) exclusively (ignoring its very low VE in low income countries of Africa and Asia), instead of inactivated poliovirus vaccine (IPV) that has very high VE. The reasons were ease of giving and low cost. While every epidemiological observation pointed to respiratory transmission of wild polioviruses, GPEI maintained it was faecal-oral, ostensibly to justify the promotion of OPV.

Consequently, eradication of poliovirus type 1 is yet to be achieved; type 3 was eradicated 12 years beyond target; only type 2 could be eradicated before the set target year of 2000. These delays could have been avoided by using IPV (with or without OPV).
When using vaccines, not only VE but also safety had to be assured. GPEI ignored the safety problems of OPV. During the last 22 years vaccine-virus has caused polio outbreaks in 34 countries, the epidemiological warnings of which had been ignored by GPEI. Vaccine viruses are genetically unstable and regain virulence and transmission efficiency – the two properties that were minimised by attenuation. The many thousands of children paralysed by vaccine viruses remind the promoters and donors of GPEI that their goal ought to be that every child is hereafter protected from polio by giving just 3 doses of IPV.

Keywords: Force of infection, transmission vector, route of inoculation, herd immunity, herd effect.

Introduction

Polio control (community/country level), elimination (country/region level) and eradication (global), are public health projects. The foundation science of public health is epidemiology.

In 1974 World Health Organisation (WHO) launched an Expanded Programme on Immunisation (EPI) to prevent and control six childhood vaccine-preventable diseases (VPDs) including polio, in low income countries. Rich countries already had organised and functional public health, high standards of sanitation/hygiene and autonomously designed immunisation programmes to control VPDs.

Low income countries without such facilities availed of the common design of EPI. Although the intention was VPD control, disease surveillance or epidemiological skilling was not in its design.[1] Immunisation coverage surveys were recommended to monitor EPI's input-efficiency. Without outcome monitoring, EPI remained a 'vaccine-delivery platform'.[1]

EPI included three doses of trivalent oral poliovirus vaccine (tOPV), chosen for ease of administration and low cost.[2] There were three injected doses of diphtheria-pertussis-tetanus vaccine (DPT) – Inactivated poliovirus vaccine (IPV) entailed another injection at each clinic visit -- a possible deterrent for vaccine acceptance -- well worth avoidance.

In 1988 the World Health Assembly (WHA) resolved to eradicate polio by 2000, building on the foundation of EPI.[3] Most rich countries had controlled polio using IPV or OPV, but those using OPV had cases of vaccine-associated paralytic polio (VAPP), to avoid which, they switched to IPV during 1988 to 2000 or shortly thereafter, complying with the WHA eradication time-target.[4] WHO's role was in low income countries in Asia and Africa -- all other regions were already progressing towards polio elimination.

Progress during the 48 years of EPI and 34 years of eradication efforts is disappointing. WPV type 2 eradication took 11 years from 1988; type 3 eradication took 24 years; type 1 remains endemic in Afghanistan and Pakistan.[5]

Only 9 countries had WPV polio in 2001, requiring concerted efforts to complete global polio eradication immediately.[6] Yet, during 2002-2022 WPV polio (type 1 or 3) occurred in 14 countries and polio due to circulating vaccine-derived poliovirus types 1, 2 or 3 in 34 countries (see Table).[7]

Table. Countries reporting polio cases/outbreaks.[6][7]

2001: WPV polio outbreaks (n=9)	2002-2022: WPV polio cases/outbreaks (n=14)	2002-2022: cVDPV polio outbreaks (n=34)
Afghanistan	Afghanistan*	Afghanistan*, Angola, Benin
Angola	Cameroon*	Cambodia, Cameroon*, Central African Republic
Egypt	Egypt	Chad, China, DR Congo
Ethiopia	Ethiopia*	Dominican Republic, Ethiopia*, Ghana
India	Guinea* India*	Guinea*, Haiti, India*
Pakistan	Iraq* Pakistan*	Indonesia, Israel, Kenya, Pakistan*
Niger	Niger*	Laos, Madagascar, Niger*
Nigeria	Malawi* Mozambique* Nigeria*	Malawi*, Mozambique*, Myanmar, Nigeria*, Papua New Guinea, Philippines
Sudan	Sudan*, Syria*	Somalia, South Sudan, Syria*, USA, Ukraine, Yemen

* *Countries reporting both WPV and cVDPV cases/outbreaks during 2002-2022*

Role of epidemiology in the design of intervention tactics

Without disease surveillance – epidemiology's instrument to document disease distribution and determinants – country level polio control (reflecting vaccine effectiveness) and numbers of cases averted by vaccination (reflecting vaccine efficacy, VE) or not averted (vaccine failure) remained unknown in1988. Vaccine-safety problem remained hidden as incidence of VAPP was not monitored. These deficiencies in EPI had to be (but were not) corrected by the Global Polio Eradication Initiative (GPEI) for the quantum leap from control to eradication.

The Resolution said it *"invites member states which have covered at least 70% of their target populations with a protective course of poliomyelitis vaccine, and which continues to have cases of poliomyelitis, to formulate plans for the elimination of the indigenous transmission of wild poliomyelitis viruses….* and *encourages member states which have not yet attained a 70% coverage rate to accelerate their efforts so as to surpass this level as quickly as possible…"*[3]

The source of 70% benchmark was not EPI. When the last case of indigenous WPV polio occurred in USA, in 1979, the 3-dose tOPV coverage was ~70%.[8] In USA IPV was introduced in 1955 followed by IPV and tOPV till 1964, and tOPV exclusively thereafter. After 24 years of sustained immunisation pressure, polio due to WPV was eliminated.[8] Those who drafted the Resolution apparently expected 70% coverage would eradicate polio.
GPEI was cautioned, in 1993, about problems in India and other low income countries.

"Today we know that this expectation was naive, without understanding the complexities of two major factors. First, geographical variations in the response to, and efficacy of, oral poliovirus vaccine (OPV) occur in developing countries. Second, the power of poliovirus transmission is stronger in many developing countries than in developed countries. For these reasons the immunisation practices which caused interruption of virus circulation in the latter countries would not achieve the same in the former" [9]

Four elementary epidemiological parameters in low income countries were essential for designing eradication-quality vaccination tactics – (1) force of infection of WPV; (2) who infects young children? (3) route of transmission; (4) VE and herd effect of OPV and IPV.

Force of poliovirus transmission: how contagious is polio?

In 1970s and 1980s polio occurred exclusively in under-five children in low income countries. Both polio and measles began in infancy as maternal antibody waned, but while still on exclusive breast feeding; both had high speed of spread and low median ages – for polio ~15 months and for measles ~30 months.[10][11][12][13][14] Thus, polio appeared more contagious than measles.

Epidemiology's term for contagiousness is 'force of infection' (FoI), quantified by 'basic reproduction number' (R_0) -- the average number of secondary cases for one primary case, when all in contact are non-immune.[15] Such a situation exists only when a contagious disease pandemic begins. Otherwise, the population is a mixture of immune and susceptible individuals; their proportions determine the number of secondary cases per one primary case, which is represented by 'effective reproduction number', R_e.[15] During the steady state of endemic prevalence, one secondary case occurs for every primary case, for $R_e = 1$. During outbreak R_e would be >1, and as outbreak abates, R_e = <1. Immunisation, if applied on a large scale and sustained (by immunisation programme), R_e can be sustained at <1, resulting first in disease control and later in elimination (by interruption of transmission), illustrated by the example in USA.

Since all above 5 years and over half of those below 6 years in low income countries were already infected and immune for polio, R_0 had to be inferred from the median age and life expectancy, using the formula [1+ life expectancy/median age].[15] Taking 60 years as life expectancy in low income countries in the 1980s, the R_0 of polio was ~49 and that of measles ~25. Polio was more contagious than measles.

When immunisation is applied to counter high FoI, it must induce immunity more speedily than infection itself. Children should be immunised before they get infected. The needed immunisation coverage (by 6 months of age for polio and by 12 months for measles) for interrupting transmission rapidly (for eradication programme) could be calculated by applying the formula [1—$1/R_0$].[15] For polio it was 98% and for measles 96%. High birth rate plus high population density led to polio in very young age – immunisation tactics for eradication had to rely on very high VE and very early immunisation coverage.

The benchmark of ~70% apparently misled GPEI by instilling overconfidence that the task was very easy. Preparations for a United Nations Child Summit were under way, scheduled for 1990, when all low income countries were supposed to have reached 80% full immunisation coverage in infancy.[16] Apparently, GPEI expected eradication to happen rapidly.

When that did not happen supplementary immunisation (additional to EPI schedule) was started -- in India in 1995; polio surveillance was established only in 1997.[17] If GPEI had anticipated that 70-80% tOPV coverage and a few supplementary doses would not eradicate polio by 2000, surely surveillance and supplementary immunisation would have been started much sooner.

Transmission vectors of WPVs: who infects infants and young children?

Under-five children alone could not have sustained endemic circulation by infecting their coevals -- immunity-naïve under-fives constituted only less than half of them, or 5 to 7.5% of population, dispersed among older individuals.[18] Persons with regular contact with infected and uninfected infants and children, acting as transmission vectors, had to be adults. Their role in polio epidemiology was not explored by GPEI.

In 1969 one of us (TJJ) had tested 1000 adult stool specimens for viruses causing adult diarrhoea (then called sprue), and among several detected enteroviruses two were WPV (upublished). Importation of WPV from endemic to non-endemic countries were 'natural experiments' but the opportunity was not utilised for identifying transmission vectors.
In 2007 an Australian traveller returned from a visit to Pakistan, infected with WPV; this episode was discussed in a medical journal.[19][20]. Hull (who had earlier served EPI and GPEI) stated*: "children recently vaccinated with either OPV or IPV shed poliovirus following a challenge with OPV dose. Because secretory immunity falls rapidly, a high percentage of persons vaccinated years before or even decades ago will become transiently infected when exposed to poliovirus and will excrete virus for weeks. Lower vaccine efficacy in developing countries further compounds the issue"*[20] WPVs are much more infectious than vaccine viruses and re-infections as the crucial link is highly probable.

There were 24 WPV importations into polio-free countries during 2003-2006 and many more since then, but the crucial epidemiological question (who the transmission vectors were) was not asked. Circumstantial clues pointed to re-infected adults, themselves protected from disease.

Neither natural WPV infection, nor Immunisation with OPV, protects from breakthrough infection – but the immune individual sheds fewer viruses, for shorter duration, than during the first infection when non-immune. Since WPV could not be used for challenge studies, a susceptible species of monkeys have been investigated and the evidence was in complete agreement.[21] This is the basis of herd effect and R_e falling below 1, resulting in polio control, elimination and eradication (described below).

Route of transmission of poliovirus

The strategy of polio eradication is 'goal-guided vaccination'. The tactical use of either or both (OPV, IPV) vaccines required clarity on the route of WPV entry into the child's body -- being highly contagious, the route had to be either

nostrils (inhaling droplets/aerosol from throat fluids of infected individuals = respiratory transmission) or mouth (consuming faeces-contaminated water/food = faecal-oral transmission).

WPV is shed in throat and faeces; but that does not help in identifying which of the two is epidemiologically significant. Since experimental inoculation was not possible, epidemiological clues had to be interpreted for indirect evidence. Prior to WHO's revision (that WPV spreads by faecal-oral route), polio, measles, rubella, varicella, mumps, influenza, pertussis and diphtheria were known to be "*directly transmitted*" (without an intermediate vehicle, hence via air = respiratory).[15] The preferred vaccine against respiratory transmission was IPV; if faecal-oral, it was OPV.[4] Despite the critical need for identifying the route of transmission, GPEI assumed it to be faecal-oral and chose OPV, exclusively.
In the pre-vaccine era polio was prevalent ubiquitously. The 'sanitary movement' of the 19th century in the West had resulted in the control/elimination of all faecal-oral transmitted pathogens, but measles and polio did not decline in incidence. In USA typhoid fever was declining rapidly while polio outbreaks were increasing.[22] This paradox had to be explained.

Demography provided the answer. Journalist J S Smith observed:*"…from 1945 to 1955…two unrelated movements came together…The first was a steady, visible rise in the number of cases of polio. The second was the post-war …Baby Boom."*[23] Martinez-Bakkar and colleagues, expert biostatisticians, wrote: *"Our analysis show that the historical expansion of polio is straightforwardly explained by the demographic 'baby boom' during the post-war period…"*[24] If increasing proportions of children in the population pyramid led to increases in the incidence of polio, transmission had to be respiratory, not faecal-oral.

Further evidence for respiratory transmission was similar annual incidence of polio in the pre-vaccination era – 18-20/100,000/year in USA, Finland and India.[25][26][27] Respiratory-transmitted childhood infectious diseases can be prevented and controlled only by immunisation, not hygiene. Polio is exclusively vaccine-preventable. After introducing IPV, polio incidence fell dramatically to very low in several Western countries that earlier had high incidence of polio. Pathogens with faecal-oral transmission cause outbreaks when water supply gets contaminated by human excreta – cholera, typhoid fever, hepatitis A and E. Polio has never been reported in waterborne outbreaks.

Low income countries have several demographic and socio-cultural differences from high income countries, one of which is poor sanitation. Cherry-picking it, not determinant but confounder, was, we believe, only to reinforce faith in faecal-oral transmission. Alleging frequent faecal contamination of feeds of every infant and under-five child, in well-to-do and poor families, was not evidence-supported – it is not even plausible. The actual determinant of high polio incidence in young children in low income countries was high birth rate and high population density, not poor sanitation.[23][24][28]

Vaccine Efficacy and Herd Effect of OPV and IPV

When the WHA polio eradication resolution was passed, much was already known about the exquisitely high VE of IPV in rich and low income countries, the very high VE of tOPV in rich countries and disappointingly low VE in tropical/sub-tropical low income countries .[4] For eradication, the tactical use of polio vaccines had to be planned taking VE values into account.

The seroconversion frequency to tOPV (3 doses) was near-100% in rich countries -- in USA it was 97% to type 1 and 100% to types 2 and 3.[29] From the 1970s, sub-optimal antibody response had been reported many times in many low income countries.[30] Despite its epidemiological importance, GPEI did not explore which of the many demographic and sociocultural differences between the two sets of countries influenced the low take rate of vaccine viruses, before designing vaccination tactics for the affected countries. Malady determines remedy. We have argued that low sanitation/hygiene was the relevant determinant, with the many gastrointestinal infections enhancing innate immune responses that block cell-entry of attenuated poliovirus, while remaining powerless against fully virulent WPV.[4]

The GPEI's OPV paradigm was constructed on: (1) the fact of intestinal immunity; (2) assumption that intestinal immunity would prevent faecal WPV shedding when vaccinated children were infected; (3) the expectation that prevention of faecal shedding will interrupt transmission of WPVs. The IPV paradigm was that it does not to contribute to any reduction of WPV transmission (herd effect, in other words) because it does not induce intestinal local IgA antibody. The failure to monitor the epidemiological outcome of tOPV roll out in EPI that failed to fit the paradigm resulted in GPEI persisting with the same tactics for eradication. Both OPV and IPV paradigms had several anomalies.[31] Even after pointing them out, GPEI did not investigate them or revise immunization tactics.

VE is a critical factor for eradication through vaccination. For smallpox eradication, the only precedent to go by, the strategy was identical: 'goal-guided vaccination,' but vaccination tactics was unique -- to identify every case and 'ring vaccinate' around it so as to cut further transmission. That was possible for five reasons: case-to-infection ratio was 1 and disease exposed transmission chain; incubation period was about 2 weeks; VE was near 100%; post-exposure vaccination was effective in protection; R_0 was only ~7.[32]

For polio eradication vaccination tactics had to be vastly different – case-to-infection ratio was <0.01 with the vast majority of infections sub-clinical and invisible; R_0 was 49 and vaccine-induced immunity had to surpass it. Very high herd immunity (98%) had to be achieved -- skewed to below 6 months of age. If lower herd immunity was achieved, then herd effect (reduction of disease incidence in the unvaccinated segment of susceptible population) had to be relied upon to maintain $R_e < 1$ until zero transmission was reached.[33] Vaccine-induced herd immunity and consequent herd effect, had to be of reasonable levels, for which VE had to be reasonably high.[33]

While IPV had virtually 100% VE, achievable below 6 months of age, tOPV did not have the required VE. Monovalent OPV types 1 and 3 have far greater VE for types 1 and 3, compared to that of tOPV.[34] Retrospectively we can appreciate this since eradication using tOPV of type 2 took 25 years (1974 to 1999) from tOPV roll out in EPI; types 1 and

3 could not be eradicated with tOPV at all as its VE was too low. Using mOPV with two-and-half times higher VE, type 3 was eradicated in 6 years (2006 to 2012) from mOPV-3 roll out.[35] Using mOPV-1 WPV-1 was eliminated in 10years (2006 to 2016) everywhere except in Afghanistan and Pakistan where local anti-OPV sentiments prevented (and continues to prevent) needed coverage in early infancy. Choices are the hinges of destiny (Edwin Markham).

Conclusions

Facts can be stranger than fiction. The consequences of neglecting the foundation science of public health -- in twentieth century's most ambitious public health project of global polio eradication, have been tragic for the thousands of polio paralysed children in low income countries.

A disease targeted for eradication had to be observed through the lens of epidemiology. Without defining the force of infection or identifying transmission vectors and route of inoculation, GPEI proceeded with inexplicable hubris bringing the world to the imbroglio that has virtually replaced WPV with vaccine-derived wild-like polioviruses.

The way forward has to be guided by high VE to be pitted against highly contagious WPV and VDPVs. There ought to be 'accountability' that any infant contacted three times by health workers ought to be protected from polio (irrespective of WPV or VDPV) -- and that can be achieved, predictably, only with 3 doses of IPV. There are problems regarding availability and cost of IPV, but both are under human control and readily solved if GPEI and kind-hearted donors really want every child protected from polio. Where there is will, there will be ways, always. Eradication is the natural consequence of preventing polio in every child. The logic that eradication using OPV will eventually protect every child from polio is false, since it is the OPV-based eradication tactics itself that causes polio today.

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