Research Article

Relevance of Medical Ethics in Public Health: Case Study of Polio Eradication

T Jacob John[1], Dhanya Dharmapalan[2]

1. Professor in Clinical Virology, Christian Medical College Vellore, Vellore, India; 2. Apollo Hospitals Navi Mumbai, Mumbai, India

Global Polio Eradication began in 1988, with a time target of 2000, but it remains unfinished in 2023. Since 2000, polio caused by vaccine-virus-turned wild-like has been paralyzing many children in several countries that still use the live attenuated oral polio vaccine (OPV), according to the policy of Global Polio Eradication Initiative (GPEI). We have detected a fundamental flaw in GPEI's intervention tactics that began in 1988 with the exclusive use of OPV – which contravened the principles of medical ethics, namely beneficence, non-maleficence and justice – while a safe and highly efficacious alternative, the inactivated poliovirus vaccine (IPV), was already available. This flaw remained unrecognized as the common perception is that public health actions are 'public good,' hence outside the purview of medical ethics. We argue why medical ethics must apply to public health when a pharmaceutical substance is included in the intervention. Having identified unethical vaccine-choice as the root cause of both the failure to eradicate polio so far and causing widespread iatrogenic polio, it is imperative that the flawed policy is reversed at the earliest, for which we propose a way forward. We also advocate for financial compensation to be given to all individuals harmed by the unethical vaccine-policy of GPEI.

Introduction

Medical interventions involve interpersonal transactions and pharmaceutical substances; moral principles guiding them are codified as biomedical ethics [1]. Its basic elements are: do only what is beneficial (beneficence); avoid what causes harm unless benefit is greater than harm (non-maleficence), do only what is fair and just to the care-recipient (justice); and respect individual's right of choice (autonomy) [1].

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When public health interventions do not involve interpersonal transactions or pharmaceutical products, medical ethics is not relevant. When vaccine or drug is given, medical ethics necessarily applies. What is unethical in health-care cannot get ethical legitimacy through public health.

Whoever administers (or prescribes) pharmaceutical substance must be 'competent', knowing its benefits and safety. Considered choice is expected, as per established standards – erring is 'negligence'. Iatrogenic injury consequent to incompetence or negligence is justiciable under law regarding tort [2][3][4]. *Ipso facto*, iatrogenic injury in public health also ought to be justiciable under tort law.

People seek healthcare when ill. Choice of drug requires benefit-risk balancing for beneficence without non-maleficence. In clinical trials, medical ethics is enforced by mandatory Ethics Review Board (ERB) of experts with independent minds [5]. Participants have to give informed consent.

Vaccination in public health is for predicted societal benefit and should not cause more-than-trivial 'adverse event following immunisation' (AEFI) in vaccinees. Live attenuated oral poliovirus vaccine (OPV) causes, infrequently but with predictable probability, a serious AEFI (sAEFI), namely vaccine-associated paralytic polio (VAPP) which is a permanent disability for the affected children. Nobel Laureate Frederick Robbins wrote: *"An important issue is what to tell parents and vaccinees about the risk of OPV"* [6]. The availability of safe alternative, namely inactivated poliovirus vaccine (IPV), demanded 'considered choice' with risk-benefit assessment.

When the World Health Organisation (WHO) decided to eradicate polio, enabled by the World Health Assembly Resolution, it was not conditional on affordability [7]. Raising "extra-budgetary" funds was allowed [7].

VAPP occurred even in 'bystanders' *i.e* children uninvolved in immunisation process, violating right to life principle of universal human rights. Old public health philosophy allowed harm in a few if benefit was for many. Later it was revised: what is not in the best interests of individuals cannot be in the best interests of the community.

Moreover, 'health equity' is a core value of public health [8]. Equity refers to the fair distribution of both benefits and risks if any.

Exploring ethics in polio eradication

As a humanitarian mission, polio eradication is 'public good' -- we tend to value it above medical ethics [9][10]. The basis of such confidence is the perception that public health can do no harm to individuals.

In 2000 USA had eliminated polio by replacing OPV with IPV [11]. Yet, one person developed polio, caused by imported 'vaccine-derived poliovirus' type 2 (VDPV-2) in 2022 [12]. Syria, without wild poliovirus (WPV) since 1999, had a VDPV-2 outbreak in 2017, paralyzing at least 74 children [13]. Papua New Guinea, without WPV since 1997, had a VDPV-1 outbreak in 2018, paralyzing at least 18 children [14]. WPV-3 was eradicated globally in 2012, but Somalia had a polio outbreak caused by VDPV-3, in 2018 [15]. There were dozens of similar OPV-caused polio outbreaks since 2000. Harm through public health is stark. *Prima facie,* the vaccine choice was flawed; our question is if it contravened ethics -- if confirmed, immediate reversal is called for. No more polio should be caused in the name of eradication.

The beginnings and progress of Global Polio Eradication Initiative

In1987, domain-experts proposed polio eradication using IPV: *"OPV is capable of interrupting the transmission of wild polioviruses....On the other hand, the availability of an improved, more potent IPV since the late 1970s, offers the advantages of nearly universal seroconversion after only two doses and elimination of the small risk of paralysis associated with OPV"*[16].

In 1988, Robbins wrote: *"With the present OPV strains, rare cases of paralysis resulting from the vaccine viruses will occur in vaccinees and their contacts. Thus, on the one hand, with the available vaccine it does not appear that paralytic disease due to polioviruses can be totally eliminated with OPV. On the other hand, it has been pointed out that this elimination has been achieved with the sole use of KPV* [same as IPV] *or a combined regime, such as was used in Denmark"* and *"Data from countries that have used only KPV indicate unequivocally that poliomyelitis has been controlled and that, indeed, the virus can no longer be recovered from the environment"* [6].

Enhanced potency IPV combined with diphtheria-pertussis-tetanus vaccine (DPT) was available; it precluded need for additional contacts between vaccinators and children or separate injections, thus minimizing operational costs [17][18].

In 1988, polio 'control' with trivalent OPV (tOPV) through Expanded Programme on Immunisation (EPI), was upgraded to 'eradication' through Global Polio Eradication Initiative (GPEI). 'Initiative' is impersonal; policies are made by people. The onus of vaccine-choice had shifted from countries to GPEI in 1988 [7]. Experts had warned about tOPV's sAEFI [19][20]. Vaccine-choice for eradication had to take into account safety and efficacy characteristics of OPV and IPV.

Norway taught a crucial lesson – polio was eliminated using IPV during 1961-1969 [21]. In 1969, IPV was replaced with tOPV as it had become available. During 1969-1979, VAPP occurred at the rate of 8 per million birth cohorts, or 1/125,000 -- about half in vaccinees (mostly due to type 3) and the rest in the community (all due to type 2) [21]. Norway reverted to exclusive use of IPV in 1979 and remained polio-free since then [21].

This rate is probably its true frequency universally, as VAPP had been monitored diligently, not missing any case – without endemic WPV to confound. In India, limited data showed that VAPP's frequency was 1/143,000 babies born [22]. USA and Norway experiences proved that OPV was incompatible with polio eradication, confirmed by data from India.

Inadequate vaccine efficacy (VE) of tOPV in tropical low income countries (TLIC) was widely known prior to 1988 [23][24][25][26][27][28]. EPI had failed to control polio, despite ~ 80% 'full immunisation' coverage (one dose each of BCG and measles vaccine and three doses each of DPT and tOPV) in infants in low income countries [29]. Evidence showed that it would be a mistake to expect to eradicate wild polioviruses in TLIC -- particularly types 1 and 3, since VE was very low against them. We suspected some hidden reason why exclusive use of tOPV became GPEI's deliberate choice.

Failing to eradicate WPV 1 and 3 during 17 years since 1988, GPEI explored tOPV's per-dose VE [30]. It was merely 6-13% and 3-15% against types 1 and 3, respectively – despite feeding 1 million type 1 and 600,000 type 3 polioviruses [30]. Why did GPEI not explore the VE of the chosen vaccine, tOPV, until failure stared at it? If vaccine virus was very inefficient in initiating infection by the oral route in TLIC, the natural route of WPV poliovirus entry had to be carefully re-assessed. An explanation was needed how WPV saturated under-five children with the three types of WPV, while OPV could not infect a majority when massive doses were fed by mouth.

For OPV, per-dose efficacy remains constant for every subsequent dose [30][31]. So tOPV's 3-dose VE was only ~14-37% against types 1 and 3. In India children were getting WPV polio in spite of even 40 doses of tOPV [30].

In summary, the vaccine-choice did not conform to principles of medical ethics. Unknown to many, GPEI had changed the goal of eradication to fit whatever was possible using OPV (see below). The known safety risks of OPV were taken nonchalantly – which have boomeranged over time. The present situation can be likened to the proverbial 'sow the wind and reap the whirlwind.' Ethics exist for everyone's safety and the original vaccine choice should have been ethically correct.

Probable reasons for unethical vaccine-choice

IPV was licensed in USA in 1955, and became popular in USA, Canada and North European countries. Sabin's work on live attenuated vaccine was still in progress [32]. Intriguingly, WHO had established an 'Expert Committee on Poliomyelitis', which, in 1957, laid down *"criteria for* [live] *vaccine strains, designing field trials, and safety in manufacture"* [33]. Sabin was a member, not Salk who created IPV [33]. WHO was actually guiding the development of Sabin's virus strains into a vaccine [33]. Why would Sabin allow WHO's involvement?

In 1959-60, under WHO watch, USSR vaccinated 15 million children and observed drastic fall in polio incidence [6]. In the 'cold war' era, an American vaccine in Russian children became a political talking-point. USA licensed vaccine strains in 1961, without clinical trial for safety and efficacy, assuming the Russians had proved safety [34]. In 1962 OPV was found to cause polio in vaccinated children in the USA. Clinically indistinguishable from natural polio, it was named 'vaccine-associated paralytic polio' (VAPP) [34]. USSR and WHO Expert Committee had missed recognizing VAPP.

In 1988 Melnick wrote: *"Role of WHO: since the introduction of the vaccine, there have been significant improvements in a number of areas.... as a result of the* ***foresight of the WHO,*** *which serves as* ***custodian of Sabin's attenuated vaccine strains****... WHO inspection and approval of manufacturers of OPV [is necessary] to ensure that* ***stringent WHO standards are met****...At least 16 manufacturers around the world are engaged in....production based on the* ***WHO vaccine seeds"*** (emphasis added) [33].

Sabin had transferred his stock of vaccine strains to WHO in 1972; WHO stored them in the National Institute of Biological Standards and Control, UK (Information gleaned from letters between Sabin and WHO, in Sabin Archives in Cincinnati [35]. In 1973 a 'Consultative Group on Poliomyelitis' was established to manage OPV [33]. After Sabin's demise in 1993, WHO continued to promote OPV ignoring the serious consequences of its continued use. The potential 'conflict of interest' on account

of the long-standing involvement in the development of OPV and its eventual ownership, remains unresolved and generally unknown.

Sabin's theory of mouth as natural route of WPV entry, contradicting prevailing belief as nostrils became WHO dogma [36]. Sabin discovered that WPV colonized ileum and was excreted copiously. He surmised virus entry was oral, sourced from faeces; hence he put his heart and soul into creating live attenuated oral vaccine. Eventually pharyngeal colonization and virus shedding preceding intestinal infection were documented, and WHO added oral-oral transmission theory to accommodate pharyngeal shedding as a source of virus [36]. Polio epidemiology is inconsistent with faecal-oral transmission but consistent with respiratory transmission; oral-oral theory is weird, as it involves mouth-kissing [37][38].

We have described the history of the fast development of IPV and the crucial role that National Foundation for Infantile Paralysis (NFIP) had played in it [37]. As soon as Jonas Salk had proved the safety and immunogenicity of his killed poliovirus mixture of the three types, NFIP that had so far fully funded Salk's research, employed Thomas Francis to conduct the world's largest vaccine trial and the results were announced in a public function in April 1955 [37]. Now the role that NFIP played for Salk IPV was being re-enacted by WHO. The USSR "vaccine trial" involved 15 million children and a control group that was given Salk IPV, source undisclosed [37]. Strangely, IPV had no protective effect, as against high protection in Francis trial [37].

In 1969 the WHO Expert Committee started a multi-country investigation into safety of tOPV, mostly in Europe, which was reported in three consecutive publications [39][40][41]. VAPP, defined in USA in 1964, was re-named by the Committee as 'acute persisting spinal paralysis' (APSP), avoiding the word polio [39][40][41][42]. APSP (VAPP) occurred in all countries using OPV and none in IPV-using countries. All three reports asserted that OPV was *"one of the safest vaccines in use"* [39][40][41]. All other vaccines in general use then (BCG, DPT and Measles) were without sAEFI; OPV alone was unsafe. The assertion of safety patently misrepresented facts

Repeated shifting of goalpost of eradication

The 1988 Resolution stated: *"The forty-first World Health Assembly…declares the commitment of WHO to the* ***global eradication of poliomyelitis*** *by the year 2000"* [7]. The 1993 WHO report to the forty-sixth WHA stated the goal as *"****eradication of wild poliovirus*** *from the world by the year 2000"* [42].Shifting

from poliomyelitis to wild poliovirus was obviously to exclude VAPP from eradication-goal. GPEI must have believed that tOPV could eradicate WPVs and knew that VAPP would have to be accommodated in the goal. Shifting target to match outcome, is 'Texas sharpshooter bias.' [43].

In 1995, the 'Global Commission for the Certification of the Eradication of Poliomyelitis' (GCCEP), an organ of GPEI, reiterated the objective to eradicate *"all wild polioviruses"* with the qualification *"...The occurrence of* ***clinical cases of poliomyelitis*** *caused by other enteroviruses,* ***including attenuated polio vaccine viruses****, does not invalidate achievement of wild poliovirus eradication"* [44]. So, by unilateral definition, for GPEI, vaccine strains were not polioviruses; VAPP was not polio. GPEI has never reported cases of VAPP throughout the 34 years of polio eradication efforts [37][44].

The estimated annual VAPP number in OPV-using countries was 400-800 [45]. Since 2016, after tOPV to bivalent OPV (bOPV, types 1 and 3) switch, VAPP due to type 2 (annually ~100-200 cases) disappeared [45]. So, 10,300 to 20,600 children could have developed VAPP since 1988, all remaining unreported.

We found no evidence in public domain that these "shifts" were approved by WHA, despite GCCEP's claim that they were *"endorsed by the forty-fifth WHA in 1992"* [42].

In 1993, WHO report to WHA stated: (1)*"Polio endemic countries need to make a commitment to eradication at a high political level in order to accomplish the goal"*; (2)*"Most polio endemic countries will need to hold national vaccination days over a period of three to five years for polio-free zones to be created and expanded"* [42]. With transferred "commitment" from WHO to "polio-endemic countries", they themselves, not GPEI, are responsible for delay or failure. Countries had the new burden of supplementary vaccinations -- how many, could not be forecast.

Ultimately GPEI had, apparently, taken the stand that it would supply as much OPV as countries needed and wait for polio to disappear however much time it takes. With continued vaccination pressure, the effective reproduction number (R_e) of WPVs would continue to fall until it reached the point of interruption of transmission, when R_e reached zero [46]. This game plan was evolved through a series of internal resolutions resulting in wide deviation from the original eradication resolution [7].

Error or wrongdoing, consequences are the same

"People will learn from their mistakes if they weren't so busy denying them" (Harold J Smith). Repeated 'shifting of goalpost' indicated denial and cover up, entailing more mistakes.

VE of tOPV was higher against type 2 polio than types 1 and 3 [31][47]. In October 1999, world's last case of WPV-2 polio was documented in India [48]. So, globally, 'epidemiological' need for its vaccine vanished; moreover, type 2 was the commonest cause of VAPP in bystanders [48]. GPEI had to remove type 2 from tOPV [47][49]. An added advantage was the removal of the dominant strain in tOPV that was interfering with VE against types 1 and 3 [47]. But GPEI dithered and continued tOPV until 2016, presumably to avoid linking tOPV with VAPP. Thus, once again, the choice clearly contravened ethical principles of beneficence (by distributing an unsafe vaccine in the absence of its target disease), non-maleficense (for violating human rights by causing outbreaks of polio due to VDPVs paralysing children not protected by the safe and effective IPV) and justice (for causing injury exclusively in children in TLIC). Polio outbreaks caused by cVDPV-2 have been occurring in several countries every year, since 2005.

GPEI's refusal to switch to IPV, which was available in 1988, and to protect children in TLIC, seems to fit the pattern of its previous path, flouting medical ethics repeatedly. Compassion was conspicuously absent. GPEI hopes to eradicate cVDPV-2 by 2026, using a 'novel type 2 OPV' that will not spread to bystanders [49][50]. But ethics will be satisfied only if all children are given equal opportunity for IPV, now, not to be procrastinated.

Eradication of WPV-2 had proved that the highest possible tOPV coverage was reached in 1999 – and it became obvious that WPV-1 or 3 will not be eradicated by tOPV. GPEI attempted to eradicate them by repetitive tOPV campaigns, giving 40 and more doses per child [30]. The 'Vellore school' had anticipated the inability of tOPV to effectively control polio due to WPV-1 and 3, as VE of tOPV was too low to protect the majority of vaccinated children with 3 or 5 doses [24][26][31][47]. One practical solution, proved successful in 1976, was to use monovalent OPV-1 and 3 (mOPV-1 and 3), which showed 2.5 times higher VE against their respective target WPVs [47]. GPEI introduced them only in 2006 – as a result, WPV-3 was eradicated in 2012 [51]. This delay, when innumerable children had already developed vaccine-failure polio, was clearly due to incompetence and/or negligence – unfortunate under GPEI.

In 2013, suspecting that repeated feeding of OPV had hidden motive, Pakistan and Afghanistan faced opposition to house-based campaigns from a militant group [37]. Everywhere else WPV-1 was eliminated, but not yet in Pakistan and Afghanistan. Had mOPVs been given out in 1990s, or soon after 1999, GPEI could have eradicated WPVs on target or before the militant opposition manifested in 2013.

Withholding mOPVs, apparently just to protect tOPV's prestige, or perhaps due to negligence or incompetence, contravened beneficence, non-maleficence and justice. Ideally, in 1999 and thereafter, IPV should have been the mainstay of eradication.

Honesty is always the best policy

The Western Hemisphere had eliminated WPVs in 1993 without taking VAPP seriously [52]. Vaccination coverage slowly slipped. In Hispaniola Island, a paralytic disease began occurring probably in 1999 and continued into 2000 and 2001. After an unknown number of children were paralyzed, virological investigation conducted in USA proved it to be polio due to type 1 vaccine-virus variant [53]. The terms 'vaccine-derived poliovirus' (VDPV) and circulating VDPV (cVDPV) were coined by the investigators [53].

Alarmed by this twist in polio vaccinology/epidemiology, GPEI established systematic molecular screening of all polioviruses recovered from children with paralytic illness and classified them as WPV or vaccine, and vaccine-progeny viruses as, Sabin, 'Sabin-like', VDPV and cVDPV, Immunedeficiency associated (iVDPV) and Ambiguous VDPV (aVDPV) [37][54]. The next episodes of cVDPV-1 polio outbreaks were in Madagascar (2001 and 2014-2015); Indonesia (2005); Myanmar (2006-07); Mozambique (2011); Ukraine (2015); Laos (2015-16); Papua New Guinea (2018) [55].

Polio-eliminated countries had to continue giving tOPV, as GPEI counted all countries together as one population unit for eradication. VAPP was paralyzing children all along. It hopes to develop a separate process for verifying the absence of cVDPV in the 'post-certification era' and 'after cessation of oral poliovirus vaccine use [56].

Was polio eradication public health or clinical trial?

Public health uses proven interventions. No country had eliminated polio using tOPV, but several had, using IPV. So, what GPEI attempted was an experiment. The hypothesis seemed like: 'with intestinal IgA immunity in children in TLIC, the environment will be sanitized from WPV contamination, leading to interruption of WPV transmission.'

The hypothesis had three assumptions, all disproved along the way. One, WPV transmission was faecal-oral; two, intestinal IgA immunity was durable, protective against infection; three tOPV was

safe and effective in TLIC. Every assumption is invalid and the consequences of the trial masquerading as public health have been disastrous.

The faecal-oral transmission theory was Sabin's own idea, all contrary epidemiological evidences notwithstanding [4,8]. GPEI was perhaps justified in believing it to begin with, but not verifying it during the course of eradication efforts was not justifiable because it involved health of children. Intestinal IgA immunity is neither robust, nor long-lasting and irrelevant in polio prevention, even in control and elimination [4,8]. In TLIC tOPV was unsafe and inefficient. The experiment went awry, resulting in the present imbroglio.

Ethical need for compensation for injury due to unethical vaccine policy

The present state of polio eradication goes against even the core value of public health, namely equity, which means even distribution of benefits, and risks, if any. Today rich countries enjoy zero incidence of polio while many poor countries suffer iatrogenic polio due to unethical vaccine-choice.

There are three categories of polio-paralysed children deserving compensation, with effect from January 2000 -- vaccine-failure polio despite three doses of tOPV; VAPP; VDPV polio (including immunodeficiency-related).

GPEI has vaccination histories of all children with WPV polio; hence identifying vaccine-failure polio is easy. VAPP is polio with faecal samples positive only for vaccine virus. GPEI has data on every person with laboratory-confirmed VDPV polio.

We suggest that a group of economists be asked to recommend the quantum of compensation and method of payment.

Conclusion

Medical ethics must ensure protection of the vulnerable against unjust injury in 'the binary' of powerful decision-makers and choice-less, voice-less, people, in every public health programme.

The former group is educated and privileged, to which we also belong, and we live without risk from polioviruses. WHO being a specialized agency of United Nations Organisation (UNO), it is the duty of UNO to hold a review as we have done in this paper. We, as pediatricians, have a moral duty to be

children's advocates. The immediate need that we have identified is to stop polio, for which we have the wherewithal and the vaccine. Policy shift is urgently needed. Vaccine production will be up-scaled only if policy shifts to IPV. It is wrong to argue that enough IPV is not available now, because the volume of manufacture is guided by anticipated demand, which in turn is determined by policy.

We recommend that future public health projects of any international organization including WHO should be reviewed by an ERB, if it involves giving of a vaccine or drug.

On the part of the WHO, there ought to be a policy that all country level public health projects that distribute pharmaceutical products should have a mandatory ethics review.

Disclaimer:

The views presented are our personal opinions and do not necessarily represent those of the institutions with which we are affiliated. We have made every effort to ensure that all information is correct. We welcome correction if any error of facts is detected.

Additional References

- Global Polio Eradication Initiative. Polio Eradication & Endgame Strategic Plan 2013–2018. Available from: https://polioeradication.org/wp-content/uploads/2016/07/PEESP_EN_A4.pdf. Accessed on 23rd Jan 2023.
- John TJ, Devarajan LV, Balasubramanian A, 1976. Immunisation in India with trivalent and monovalent oral poliovirus vaccines of enhanced potency. Bull WHO. 54:115-7.

References

1. [a], [b] *Beauchamp EL, Childress JF. Principles of Biomedical Ethics. Second Edition. New York: Oxford Unive rsity Press;1983.*
2. [^] *Sampath R. When is iatrogenic harm negligent? AMA J Ethics 2022; 24(8): E735-739. DOI 10.1001/ama jethics.2022.735.*

3. ^American Medical Association. Council on Ethical and Judicial Affairs. Competence, self-assessment and self-awareness. Report 1-I-19. Available at https://www.ama-assn.org/system/files/2019-12/i19-ceja-report-1.pdf.
4. ^Twerski A, Cohen NB. Informed decision-making and the law of torts: the myth of justiciable causation. U Ill L Rev 1988; 607-665.
5. ^Idanpaan-Heikkila. WHO guidelines for good clinical practice (GCP) for trials in pharmaceutical products: responsibilities of the investigator. Ann Med 1994; 26(2):89-94. doi: 10.3109/07853899409147334
6. a, b, cRobbins FC. Polio – Historical. In: Plotkin SA, Mortimer EA, editors. Vaccines. WB Saunders, Philadelphia; 1988. p. 98-114.
7. a, b, c, d, eWorld Health Assembly. Forty-first World Health Assembly, Geneva, 2-13 MAY 1988. WHA41.28 Global eradication of poliomyelitis by the year 2000. Available from https://www.who.int/ihr/polioresolution4128en.pdf.
8. ^Liburd LC, Hall JE, Mpofu JJ, Williams SM, Bouye K, Penman-Aguilar A. Addressing health equity in public health practice: Framework, strategies, and measurement considerations. Annual Rev Pub Health 2020; 41: 417-432
9. ^Skrabanek P. Why is preventive medicine exempted from ethical constraints? J Med Ethics 1990; 16: 187-190.
10. ^Wilson J. The ethics of disease eradication. Vaccine 2014; 32: 7179-7183.
11. ^American Academy of Pediatrics Committee on Infectious Diseases. Prevention of poliomyelitis: recommendations for use of only inactivated poliovirus vaccine for routine immunization. Pediatrics. 1999;104:1404-140610585998
12. ^Global Polio Eradication Initiative. Updated Statement on Report of Polio Detection in United States, 29 July 2022. Available online: https://polioeradication.org/news-post/report-of-polio-detection-in-united-states/ Accessed on 10 January 2023.
13. ^WHO EMRO. 2 Dec 2018. Polio outbreak in Syria successfully stopped. Available from: https://www.emro.who.int/syria/news/polio-outbreak-successfully-stopped.html
14. ^World Health Organization. Polio outbreak in Papua New Guinea. Geneva:WHO; 2018. Available from https://www.who.int/westernpacific/emergencies/papua-new-guinea-poliovirus-outbreak. Accessed on 5th Feb 2023.
15. ^GPEI. Somalia: formal closure of the cVDPV3 outbreak. Available from: https://polioeradication.org/news-post/somalia-formal-closure-of-the-cvdpv3-outbreak/

16. ^Hinman AR, Foege WH, deQuadros C A, Patriarca PA, Orenstein WA, Brink EW. The case for global erad ication of polio. Bull WHO 1987; 65(6): 835-840.
17. ^Cohen H, Nagel. Two injections of diphtheria-tetanus-pertussis-polio vaccine as the backbone of a si mplified immunization schedule in developing countries, Rev Infect Dis 1984; 6(Sup2): S350-351 doi: 1 0.1093/clinids/6.supplement_2.s350.
18. ^Drucker J, Soula G, Diallo O, Fabre P. Evaluation of a new combined inactivated DPT-polio vaccine. De v Biol Stand. 1986; 65:145-51.PMID: 3030861.
19. ^Henderson DA, Witte JJ, Morris L, Langmuir AD. Paralytic Disease Associated With Oral Polio Vaccines. JAMA. 1964;190(1):41–48. doi:10.1001/jama.1964.03070140047006.
20. ^Nkowane BM, Wassilak SG, Orenstein WA, Bart KJ, Schonberger LB, Hinman AR, Kew OM. Vaccine-ass ociated paralytic poliomyelitis: United States, 1973 through 1984. JAMA 1987; 257: 1335-1340
21. a, b, cBottiger M. The elimination of polio in the Scandinavian countries Public Health Rev 1993-94; 21 (1,2): 27-33.
22. ^John TJ. Vaccine-associated paralytic polio in India. Bull WHO 2002; 80(11): 917.
23. ^Ghosh S, Kumari S, Balaya S, Bhargava SK. Antibody response to oral polio vaccine in infancy. Indian P ediatr 1970; 7: 78-81.
24. a, bJohn TJ. Problems with oral polio vaccine in India. Indian Pediatr 1972; 9: 252-256.
25. ^John TJ, Jayabal P. Oral polio vaccination of children in the tropics 1.The poor seroconversion rates and the absence of viral interference. Amer J Epidemiol 1972; 96: 263-269.
26. a, bMetzelaar D, Mcdonald K, Gemert W, Nottay B, Muli JM. Poliomyelitis epidemiology and prophylaxis. 4. Serological and virological surveys conducted after a mass vaccination campaign for the control of a t hreatening poliomyelitis epidemic. Bull WHO 1977; 55: 747-754.
27. ^Oduntan SO, Lucas AO, Wennen EM. The immunological response of Nigerian infants to attenuated an d inactivated poliovaccines. Ann Trop Med Parasitol 1978; 72: 111-115.
28. ^Oduntan AO, Familusi JB. An appraisal of polio immunization in Nigeria and other tropical African cou ntries. Nigerian Med J 1979; 9: 645-649.
29. ^Keja K, Chan C, Heyden G, Henderson RH. Expanded Programme on Immunisation. World Health Stat Q 1988; 41: 59-63.
30. a, b, c, d, eGrassly NC, Fraser C, Wenger J, Deshpande JM, Sutter RW, Heymann DL, et al. New strategies f or the elimination of polio from India. Science 2006;314:1150–3

31. ^a, ^b, ^c*John TJ. Immunisation against polioviruses in developing countries. Rev Med Virol 1993; 3: 149-16 0.*

32. ^*Baicus A. History of polio vaccination. World J Virol. 2012 Aug 12;1(4):108-14. doi: 10.5501/wjv.v1.i4.10 8. PMID: 24175215; PMCID: PMC3782271.*

33. ^a, ^b, ^c, ^d, ^e*Melnick JL. Chapter 7. Live attenuated poliovaccines. In: Plotkin S and Mortimer EA, editors. Va ccines. 1st ed. Philadelphia: W.B. Saunders; 1988. p.115-157.*

34. ^a, ^b*N Carleton HA. Putting together the pieces of polio: how Dorothy Horstmann helped solve the puzzle. Yale J Biol Med. 2011 Jun;84(2):83-9. PMID: 21698038; PMCID: PMC3117421*

35. ^*University of Cincinnati. The Albert B. Sabin Archives. Available from: https://digital.libraries.uc.edu/co llections/sabin/*

36. ^a, ^b*World Health Organisation. Polio vaccines: WHO position paper – March 2016.. Available from: Week ly Epidemiological Record, 2016, vol. 91, 12 https://www.who.int/publications/i/item/WHO-WER9112*

37. ^a, ^b, ^c, ^d, ^e, ^f, ^g, ^h*John TJ, Dharmapalan D. Polio: The Eradication Imbroglio. The Malady and its Remedy. Chennai: Notion Press, 2022.*

38. ^*John TJ, Dharmapalan D. Lessons from Vaccine-Related Poliovirus in Israel, UK and USA. Vaccines (Ba sel). 2022 Nov 20;10(11):1969. doi: 10.3390/vaccines10111969. PMID: 36423064; PMCID: PMC9695509.*

39. ^a, ^b, ^c*World Health Organisation Expert Committee on Poliomyelitis. The relation between acute persisti ng spinal paralysis and poliomyelitis vaccine (oral): results of a WHO enquiry. Bull World Health Organ. 1976; 53(4):319-31.*

40. ^a, ^b, ^c*World Health Organisation Expert Committee on Poliomyelitis. The relation between acute persisti ng spinal paralysis and poliomyelitis vaccine-results of a ten-year enquiry. Bulletin of the World Health Organization;1982 (60):231-24.*

41. ^a, ^b, ^c*Esteves K. Safety of oral poliomyelitis vaccine: results of a WHO enquiry. Bull World Health Organ. 1 988;66(6):739-46.*

42. ^a, ^b, ^c, ^d*World Health Assembly, 46. (1993). Forty-sixth World Health Assembly, Geneva, 3-14 May 1993: resolutions and decisions, annexes. World Health Organization. https://apps.who.int/iris/handle/10665/ 176262.*

43. ^*Wikipedia. Texas sharpshooter fallacy. Available from https://en.wikipedia.org/wiki/Texas_sharpshoo ter_fallacy. Accessed 20 Feb 2022.*

44. ^a, ^b*Global Commission for the Certification of the Eradication of Poliomyelitis. Meeting (1st: 1995: Genev a, Switzerland) & WHO Expanded Programme on Immunization. (1995). Report of the 1st Meeting of th*

e Global Commission for the Certification of the Eradication of Poliomyelitis, Geneva, Switzerland, 16-17 February 1995. World Health Organization. https://apps.who.int/iris/handle/10665/59821

45. ^a, ^b*John TJ. Vaccine-associated paralytic polio in India. Bull WHO 2002; 80: 917.*

46. ^*John TJ, Dharmapalan D. Consequences of Neglecting Epidemiology by Global Polio Eradication Initiative [preprint]. Qeios 2022. doi:10.32388/Q07COA.*

47. ^a, ^b, ^c, ^d, ^e*John TJ. Two good reasons to drop type 2 virus from oral polio vaccine Lancet 2004; 364: 1666.*

48. ^a, ^b, ^c, ^d*John TJ and Dharmapalan D. Challenges en route to polio eradication. Lancet. 2022; 400: 428-429.*

49. ^a, ^b*WHO. Polio eradication strategy 2022–2026: delivering on a promise. Available from https://www.who.int/publications/i/item/9789240031937.*

50. ^*Novel Oral Polio Vaccine type 2 (nOPV2) granted EUL recommendation. Available from: https://polioeradication.org/news-post/novel-oral-polio-vaccine-type-2-nopv2-granted-interim-emergency-use-listing-recommendation/ Accessed on 20th Feb 2023.*

51. ^*Jorba J, Diop OM, Iber J, et al. Update on vaccine derived polioviruses—worldwide, January 2016–June 2017. MMWR Morb Mortal Wkly Rep 2017; 66: 1185–91.*

52. ^*Andrus JK, Strebel PM, de Quadros CA, Olivé JM. Risk of vaccine-associated paralytic poliomyelitis in Latin America, 1989-91. Bull World Health Organ. 1995;73(1):33-40. PMID: 7704923; PMCID: PMC2486585.*

53. ^a, ^b*Kew O, Morris-Glasgow V, Landaverde M, Burns C, Shaw J, Garib Z et al. Outbreak of poliomyelitis in Hispaniola associated with circulating type 1 vaccine-derived poliovirus. Science. 2002 Apr 12;296(5566):356-9. doi: 10.1126/science.1068284. Epub 2002 Mar 14. PMID: 11896235.*

54. ^*Global Polio Eradication Initiative. Classification and Reporting of Vaccine-Derived Polioviruses (VDPV), August 2016. Available from: https://polioeradication.org/wp-content/uploads/2016/09/Reporting-and-Classification-of-VDPVs_Aug2016_EN.pdf. Accessed on 15th Jan 2023.*

55. ^*Lai YA, Chen X, Kunasekaran M, Rahman B, MacIntyre CR. Global epidemiology of vaccine-derived poliovirus 2016-2021: A descriptive analysis and retrospective case-control study. E Clinical Medicine. 2022 Jun 25;50:101508. doi: 10.1016/j.eclinm.2022.101508. PMID: 35784443; PMCID: PMC9240990.*

56. ^*Global Polio Eradication Initiative. Post-Certification Strategic Plan. 2017. Available from: https://terrance.who.int/mediacentre/data/sage/SAGE_Docs_Ppt_Oct2017/5_session_polio/Oct2019_session5_Post-Certification.pdf. Accessed on 10th Jan 2023.*

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