

## Editorial

### Polio eradication & India - Bringing science into public health

The world's most vaccinated under-five children, with oral polio vaccine (OPV), are in Uttar Pradesh (UP) and Bihar. Coverage with 4-10 doses is near 100 per cent for a decade; average 15 doses per child since 2003. Yet, wild poliovirus types 1 and 3 transmission continues there. Nearly all polio is in children given more than 3 doses; almost half in those given more than 10 doses. To investigate this paradox, in 2006 the Global Polio Eradication Initiative (GPEI) commissioned studies on the effectiveness of trivalent (t-) and monovalent (m-) OPVs<sup>1,2</sup>. The per-dose vaccine efficacy (VE) against type 1 was only 9-11 per cent for tOPV but 3 times higher (30%) for mOPV-1<sup>1,2</sup>. In USA they were more than 70 per cent with either vaccine<sup>3</sup>.

For OPV, seroconversion rate (SCR) is a surrogate of VE. In 1976 in Vellore mOPVs induced 2 to 2½ times higher SCR for types 1 and 3, than tOPV<sup>4</sup>. In 1970 in New Delhi, SCR after 3 doses of tOPV was 39 per cent to type 1 and 49 per cent to type 3<sup>5</sup>. OPV does not "prime" and "boost"<sup>6</sup>. Responses to sequential doses lie along the path of 'arithmetic proportional increments', allowing extrapolation of SCR for any dose<sup>6</sup>. Calculated backwards, in Delhi, per-dose SCR was 15 per cent for type 1 and 20 per cent for type 3<sup>5,6</sup>. More recently in UP the SCR after 8 doses of tOPV was 54 per cent for type 1 and 65 per cent for type 3, derived from antibody prevalence in the vaccinated minus that in unvaccinated<sup>7</sup>. Extrapolated, per-dose SCRs were 10 and 12 per cent for types 1 and 3, respectively<sup>6,7</sup>. These are the world's lowest recorded SCR/VE. Apparently GPEI was unaware of these reports<sup>4-7</sup> as none was cited<sup>1,2</sup>. Type 2 virus, against which the VE of tOPV is much higher, was eliminated in 1999. In States with higher VE against types 1 and 3, they too were eliminated in 1999-2000, as predicted<sup>6</sup>, when the average reached 8-10 doses per child<sup>1</sup>. Persisting types 1 and 3 virus transmission despite high OPV coverage is associated with extremely low VE<sup>1-6</sup>.

India's Ministry of Health (MoH) decided on polio eradication in 1988, without a dedicated "war room" with trained professionals and a chain of command, unlike programmes against tuberculosis, malaria, leprosy and human immunodeficiency virus. The MoH did not ask the Indian Council of Medical Research (ICMR) or National Institute of Communicable Diseases (NICD), both wings under its control, to verify conclusions of earlier Indian studies or provide scientific basis for strategy-design and mid-course corrections. Science was neglected due to blind faith in the prescriptions of GPEI, which had always disregarded Indian research. The World Health Organization (WHO) rejected our recommendation of 5 doses of OPV in infancy based on evidence of the inadequacy of 3 doses, documented before the Expanded Programme on Immunization (EPI) was launched<sup>6,8</sup>. Given inexpensive OPV and 5 EPI contacts for other vaccines, its rejection was inexplicable. Moreover, WHO disallowed introduction of the alternate inactivated poliovirus vaccine (IPV), which has far superior VE and "herd effect"<sup>6,8</sup>.

The GPEI now confirms that 3-dose OPV schedule in EPI was indeed unethical<sup>1,2</sup>. The majority of vaccinated children remained unprotected; over half polio cases during 1980s had received 3 doses<sup>8</sup>. Had polio incidence been reduced in UP/Bihar with "routine" vaccination before applying "supplementary" campaigns, this problem could have been exposed and remedied. Even now EPI coverage remains very low in UP/Bihar<sup>9</sup>. High coverage, even with 3 doses of OPV in the first 3-4 months of age, would have built an immunity platform<sup>6,8</sup>. Without high coverage with other vaccines under-served communities were reluctant to co-operate for polio eradication. Low routine OPV coverage below 4-6 months of age is another reason for persisting poliovirus transmission<sup>6</sup>, despite extremely high "supplementary" coverage in older children.

Yet another reason is the extremely high “force of transmission” (basic reproduction number,  $R_0$ ) of wild types 1 and 3 viruses in UP/Bihar, necessitating very high “herd effect” for interrupting transmission - setting the bar extremely high<sup>6,8,10</sup>. The GPEI tactic to protect 100 per cent children to close “immunity gap” is inefficient against the highly contagious infection. Instead, “herd effect” had to be established<sup>6,8,10</sup>, either by “pulse vaccination” with OPV or >80 per cent coverage with IPV<sup>6,8,10</sup>. The two are not mutually exclusive, with EPI-compliant IPV and campaign-friendly OPV. Pilot-testing of these old concepts in the present context would have been ideal. The enormous investment for eradication should have included a small proportion, such as 5 per cent, for research on intervention tactics. Currently India spends more on polio eradication than all other disease control programmes<sup>11</sup>, even though cases are only <0.5 per cent compared to 1980s. A fraction spent in scientifically validated ways would have avoided delay, embarrassment and enormous expenditure of the continuing struggle for eradication. Bringing science into public health is welcome<sup>1,2</sup>, but too little has come too late. GPEI has not measured the speed of wild virus transmission, immunity gaps by age and SCRs of sequential doses of tOPV, mOPV or IPV. New research explains past errors<sup>1,2</sup>, but what about innovative tactics?

With strong seasonality of poliovirus transmission, during “low season” (currently February-April, previously November-February) the force of transmission is the lowest ( $R_0 < 1$ ). “Pulse vaccination”, as defined earlier, is with 3 doses of OPV 4 wk apart, annually once, in the low season, to exploit natural fragility of virus transmission<sup>6,8</sup>. Its purpose is to suddenly shrink the size of the “susceptible pool” of infants and young children, to pull  $R_0$  towards zero, just for a short period (8 wk). Pulse vaccination exaggerates herd effect when transmission is weakest<sup>6,8,10</sup>. Vaccination campaigns during “high season” (when  $R_0 > 1$ ) are wasteful of resources, just as in any outbreak. Since 1999 UP/Bihar saw 50 campaigns, mostly during high season, illustrating this lesson. Due to fear of frequent feeding of OPV, parents have been “protecting” very young infants from the campaigns - undermining the prospects of shrinking the susceptible pool. Pulse vaccination leaves 10 months of the year for strengthening EPI; multiple campaigns leave little time or energy to improve EPI.

The speed of type 1 virus circulation is fastest in UP/Bihar than elsewhere, as seen from the age profile

of polio<sup>1,2</sup>. The battle is unequal - for victory the speed of infection must be overtaken by vaccine-induced immunity, by a large margin. The virus is highly contagious, infecting infants beginning from soon after birth. Its “amplification” efficiency is maximum in the first 6 months of life, followed by second 6 months, then next 6 months and so on until the under-five population is saturated<sup>1,2,6,8</sup>. As 15-18 doses of tOPV or 5-6 doses of mOPV-1 or 3 were needed to immunize near 100 per cent children, its speed necessarily lagged behind that of wild virus transmission<sup>1,2,6,8</sup>. The low routine coverage delayed the build-up of immunity in the critical age of under-six months; repetitive campaigns also missed many of them<sup>1,2,6,8</sup>. In summary, the synergy between extremely high force and speed of wild virus transmission, extremely low vaccine efficacy, low routine vaccination coverage and lack of strategic interventions due to poor grasp of epidemiology of wild viruses has resulted in the failure, so far, to interrupt transmission of types 1 and 3 viruses. The GPEI approach of increasing the number of campaigns year after year compounded these problems. Exclusive use of mOPVs will accelerate immunization, but the very young must be reached<sup>1,2</sup>. New stratagem of intelligent interventions can be designed from these observations.

The GPEI papers missed an intriguing phenomenon- the contrast between very high infection efficiency of wild and very low infection efficiency of vaccine viruses in the same children<sup>1,2</sup>. Although vaccine viruses are less infectious than wild viruses, both belong to one species, use identical cell surface receptors, and ought to move together in the same direction of infection efficiency. If vaccine virus is less efficient here than elsewhere, wild virus also should be less efficient. Here vaccine viruses are inefficient to infect but wild viruses spread faster than elsewhere. This paradox can be explained only by different routes of exposure. Highly contagious wild virus infects every child irrespective of standards of sanitation or hygiene. In rich nations improved sanitation did not reduce polio incidence. The absence of food-or water-borne outbreaks and cyclical surges (in 1998, 2002 and 2006) are typical of respiratory transmission and unlike pathogens transmitted by faecal-oral route. All highly contagious infections spread via respiratory transmission. For wild viruses the source is pharyngeal shedding by infected children. This was the accepted teaching before the advent of OPV. As intestines are only secondarily infected, OPV-induced mucosal immunity seems irrelevant for wild

virus transmission. This critical epidemiological question was not explored by GPEI<sup>1,2,6,8</sup>. Epidemiology must not be neglected; it is the foundation science of public health.

Polio eradication is the most ambitious and expensive public health programme ever undertaken by the MoH. Inadequate scientific scrutiny of the intervention tools, lack of application of research findings in designing vaccination tactics<sup>4-8</sup>, failure to monitor epidemiology and transmission dynamics of wild polioviruses<sup>6,8</sup> and absence of management superstructure, together have caused the present embarrassing situation. The MoH must bring science back into polio eradication with full involvement of ICMR, NICD, and independent scientists.

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Note added in proof: The author and Editors are happy to note that serious attempts are now being made to reach infants below 6 months with several doses of polio vaccine.

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