12. WHO Consultative Group. The relation between acute persisiting paralysis and poliomyelitis vaccine (oral): results of a WHO enquiry. *Bulletin of the World Health Organization* 1976;53:319-31.
13. WHO Consultative Group. The relation between acute persisiting spinal paralysis and poliomyelitis vaccine. Results of a ten-year enquiry. *Bulletin of the World Health Organization* 1982;60:231-42.
14. Andrus JK, Strebel PM, de Quadros CA, Olive JM. Risk of vaccine-associated paralytic poliomyelitis in Latin America, 1989–91. *Bulletin of the World Health Organization* 1995;73:33-40.
15. Kohler KA, Banerjee K, Hlady WG, Andrus JK, Sutter RW. Vaccine-associated paralytic poliomyelitis in India during 1999: decreased risk despite massive use of oral polio vaccine. *Bulletin of the World Health Organization* 2002;80:210-16.
16. John TJ. Vaccine-associated paralytic poliomyelitis in India. *Bulletin of the World Health Organization* 2002;80:917.
17. Technical Consultative Group to the World Health Organization on the Global Eradication of Poliomyelitis. "Endgame" issues for the global polio eradication initiative. *Clinical Infectious Diseases* 2002;34:72-7.
18. Poliovirus infections. In: Pickering LK, editor. *2000 red book. Report of the Committee on Infectious Diseases,* 25th edition. Elk Grove Village (IL): American Academy of Pediatrics; 2000:465-70.
19. Schmidt HJ. Implications of and experience with the combined DTPa-IPV/Hib and DTPa-Hep.B vaccines. *InPharma Weekly* 1999 Suppl.1:28-9. Cited by: Capian C, Poolman J, Hoet B, Bogaert H, Andre F. Development and clinical testing of multivalent vaccines based on a diphtheria-tetanus-acellular pertussis vaccine: difficulties encountered and lessons learned. *Vaccine* 2003;21:2173-87.
20. Oral poliomyelitis vaccines. Report of Special Advisory Committee on Oral Poliomyelitis Vaccines to the Surgeon General of the Public Health Service. *JAMA* 1964;190:161-4.
21. Stratton KR, Howe CJ, Johnston Jr RB. Adverse events associated with childhood vaccines other than pertussis and rubella. *JAMA* 1994;271:1602-5.
22. Basu RN. Magnitude of problem of poliomyelitis in India. *Indian Pediatrics* 1981;18:507-11.
23. Prabhakar N, Srilatha V, Mukerji D, John A, Rajarathnam A, John TJ. The epidemiology and prevention of poliomyelitis in a rural community in south India. *Indian Pediatrics* 1981;18:527-32.
24. John TJ, Pandian R, Gadomski A, Steinhoff M. Control of poliomyelitis by pulse immunization in Vellore, India. *BMJ* 1983;286:31-2.
25. John TJ. Poliomyelitis in India: problems and prospects of control. *Reviews of Infectious Diseases* 1984;6:S438-41.
26. John TJ. Poliovirus neurovirulence and attenuation, a conceptual framework. *Developments in Biological Standardization* 1993;78:117-9.
27. John TJ. Immunization in India with trivalent and monovalent oral poliovirus vaccines of enhanced potency. *Bulletin of the World Health Organization* 1976;54:115-7.
28. Minor PD. The molecular biology of poliovaccines. *Journal of General Virology* 1992;73:3065-77.
29. Chumakov KM, Norwood LP, Parker ML, Dragunsky EM, Ran Y, Levenbook IS. RNA sequence variants in live poliovirus vaccine and their relation to neurovirulence. *Journal of Virology* 1992;66:966-70.
30. Kew O, Maurice-Glasgow V, Landaverdo M, Burns C, Shaw J, Garib Z, et al. Outbreak of poliomyelitis in Hispaniola associated with circulating type 1 vaccine-derived poliovirus. *Science* 2002;296:356-9.
31. Centers for Disease Control and Prevention. Circulation of a type 2 vaccine-derived poliovirus – Egypt 1982–1993. *Morbidity and Mortality Weekly Report* 2001;50:41.
32. Centers for Disease Control and Prevention. Acute flaccid paralysis associated with circulating vaccine-derived poliovirus – Philippines 2001. *Morbidity and Mortality Weekly Report* 2001;50:874.
33. Bart KJ, Foulds J, Patriarca P. Global eradication of poliomyelitis: benefit-cost analysis. *Bulletin of the World Health Organization* 1996;74:35-45.
34. Nathanson N, Fine P. Poliomyelitis eradication – a dangerous endgame. *Science* 2002;296:269-70.
35. Andre FE. Strengths and weaknesses of current polio vaccines – a view from industry. *Developments in Biologicals* 2001;105:61-3.
36. Krishnan R, John TJ. Efficacy of inactivated poliovirus vaccine in India. *Bulletin of the World Health Organization* 1983;61:689-92.
37. Simoes EAF, Padmini B, Steinhoff MC, Jadhav M, John TJ. Antibody response of infants to two doses of inactivated poliovaccine of enhanced potency. *American Journal of Diseases of Children* 1985;139:977-80.
38. WHO Collaborative Study Group on Oral and Inactivated Poliovirus Vaccines. Combined immunization of infants with oral and inactivated poliovirus vaccines: results of a randomized trial in the Gambia, Oman and Thailand. *Bulletin of the World Health Organization* 1996;74:253-68.
39. Moriniere BJ, van Loon FP, Rhodes PH, Klein-Zabban ML, Frank-Senat B, Herrington JE, et al. Immunogenicity of a supplemental dose of oral versus inactivated poliovirus vaccine. *Lancet* 1993;341:1545-50.
40. Sutter RW, Suleiman AJ, Malankar P, Al-Khusaiby S, Mehta F, Clements GB et al. Trial of a supplemental dose of four poliovirus vaccines. *New England Journal of Medicine* 2000;343:767-73.
41. John TJ. The final stages of the global eradication of polio. *New England Journal of Medicine* 2000;343:806-7.

Commentary

A developing country perspective on vaccine-associated paralytic poliomyelitis

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I started to read the abstract to Jacob John's review on vaccine-associated paralytic polio (VAPP) in full agreement with his observation that wherever oral poliovirus vaccine (OPV) is used, there are risks of VAPP to vaccinees and their contacts. Indeed, where polio immunization programmes are poorly implemented, there are risks of circulating vaccine-derived polioviruses (cVDPV). However, by the time I reached the end of the abstract, I found myself seriously disagreeing with much of what Jacob John had to say, and even more so by the end of the article.

Jacob John raises the spectre of cVDPV to give credibility to the potential seriousness of revertent vaccine strains. We have known for many years that VAPP is a rare but measurable consequence of the use of OPV, and until relatively recently there had been no concern that outbreaks of polio followed VAPP cases. The greatest risks of cVDPV are when immunization coverage is low, but VAPP is more likely to occur the higher the coverage in any population.

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I was seriously worried when I read the proposition that developing countries should shift to inactivated polio vaccine (IPV), and that once IPV coverage reached high levels, the withdrawal of OPV could begin. Did this mean that developing countries should introduce IPV as well as using OPV and discontinue the latter only when the IPV coverage was high? How would that impact on the costs of polio eradication? How would high IPV coverage be achieved? What does this say about inequalities when some children who will receive OPV are denied the benefits given to others, who receive IPV, within the same country? And how could a mixed programme be implemented in a developing country?

Many of Jacob John's arguments are based on the belief that many more doses of OPV are needed per child to protect against polio in developing countries than would be needed if IPV were used in the routine programme, and he advocates a switch to IPV to prevent the high cost of supplementary campaigns with OPV. This argument could be justified only if there was convincing evidence that IPV is as effective as or more effective than OPV in interrupting polio transmission in a developing country setting. Also, routine coverage would need to be sufficient to prevent the accumulation of enough children who are susceptible to polio and who might, therefore, sustain the transmission of wild polioviruses should they occur — or even cVDPV should there be any OPV being used in the population. Given that the countries currently posing the final barriers to polio eradication are those with the lowest immunization coverage through routine services, this seems to be a high-risk approach. He suggests that primary immunization with diphtheria–tetanus–pertussis (DTP)-IPV plus a dose of DTP-IPV in the second year would be as effective as — and safer than — primary OPV immunization followed by annual doses in campaigns, until a child reached 5 years of age. Although this may be valid for individual protection, it brings high risks on a population basis, most especially in countries where routine primary coverage is low and routine fourth doses do not even exist.

It is true that many countries are switching to IPV, and it is also true that VAPP is as much a tragedy for the individual as the natural disease itself. Jacob John fails to identify how routine coverage can be brought up to levels at which IPV can be substituted for OPV, or even convinces that it needs to be used universally once polio transmission has been interrupted. In Cuba, where there is no routine provision of OPV outside of annual campaigns, cVDPV has not been documented in the face of excellent surveillance.

Finally, I was concerned by the statement that "developing countries … should have been warned about VAPP". Polio eradication represents a phenomenal global partnership in health, between countries and international organizations. Nevertheless, there are responsibilities on all of the partners to be properly informed, especially those who accept responsibilities on behalf of their populations. ■

Conflicts of interest: none declared.