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Maximising the impact of inactivated polio vaccines

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With the globally coordinated switch from the trivalent oral polio vaccine (OPV) to the bivalent OPV in April, 2016, the international public health community entered a new chapter in the endgame of polio. Although OPV has served as the cornerstone of polio eradication efforts over the past 30 years, trivalent inactivated polio vaccine (IPV) has re-ascended to prominence in the past year, now acting as the sole source of protective immunity against type 2 poliovirus in routine immunisation programmes. Despite its immense public health value, the global supply of IPV is failing to meet demand. The October, 2016, meeting of the Strategic Advisory Group of Experts on Immunization cautioned that, "the IPV supply situation is further deteriorating; 50 countries are experiencing delays in supply or stock-outs, a situation which is likely to persist until 2018".[1]

Given the existing resource constraints, pragmatic solutions are urgently needed to maximise the impact of IPVs during the transitional and post-OPV immunisation era. In *The Lancet Infectious Diseases*, Birgit Thierry-Carstensen and colleagues[2] report one such novel strategy in the form of reduced-dose IPVs administered intramuscularly with an aluminium hydroxide (Al) adjuvant. The three IPV-Al candidates were formulated at one-third, one-fifth, and one-tenth the concentration of standard IPV and administered to healthy children living in the Dominican Republic at 6, 10, and 14 weeks of age. The results of the well conducted phase 2 trial indicate that the antigen-sparing IPV-Als were able to achieve substantial (ie, ≥75%) seroconversion against the three serotypes of polio after only two vaccine doses. Promisingly, after three doses, all three formulations of IPV-Als achieved more than 94% seroconversion to poliovirus types 1, 2, and 3, and the seroresponses were non-inferior to those of the standard IPV, which was administered unadjuvanted, but at up to ten-fold higher concentrations.

Enhancing the immunogenicity of IPVs is an important achievement in view of the ongoing shortfalls in IPV production by global pharmaceutical firms. Moving forward, an antigen-sparing IPV with adjuvant would be a welcome addition to the expanding portfolio of alternative IPV approaches under development, which also includes fractional (ie, reduced-volume) intradermal IPVs[3,4] and enhanced potency high dose IPVs[5] that might limit the number of serial doses required to uniformly induce immunity. Overall, dose-sparing IPV strategies have the potential to reduce costs of immunisation activities,[6] facilitate the protection of individuals during outbreaks by enabling both prompt responses and high levels of coverage,[7] and stretch dwindling vaccine supplies. However, selecting and then operationally optimising an IPV strategy for a specific context will be challenged by a number of logistical barriers (eg, scalability and costs of vaccine production and storage, availability of trained vaccinators, procurement of immunisation devices) and immunological considerations (eg, scheduling to mitigate interference by maternal antibodies, inducing seroprotection of an appropriate magnitude and duration).[8]

In preparing the global public health system to withstand shortages in IPV supply moving forward, it is also important to give due consideration to a limitation of all IPVs—namely, that inactivated vaccines appear to have a limited capacity to induce intestinal immunity against polio. There is no question that serum antibodies produced in response to IPVs are able to successfully protect vaccinees against paralytic polio by inhibiting viraemia and entry into the CNS. Perhaps less appreciated is that with polio—and probably many other pathogens replicating at mucosal surfaces—a vaccine's ability to induce mucosal immunity is tightly linked to the vaccine's capacity to block viral shedding and, thereby, potential onward transmission. Mounting evidence from OPV challenge trials[5,9,10] indicates that, when delivered in a primary vaccine series, IPV seems to have only limited effects on the duration and degree of viral shedding. By contrast, the intestinal immunity induced by live, oral vaccines is close to achieving the ideal of sterilising immunity.[10–12] Ultimately, blocking transmission (eg, via integrated OPV-IPV intestinal immune-boosting strategies[13,14] and the development of the more highly attenuated and genetically stable novel OPVs) and thus reducing IPV demand for outbreak control is also a paramount consideration for capitalising on the utility of IPVs under the reality of existing supply limitations.

Eradication of polio is tantalisingly close. In the final steps toward eradication and for the post-eradication era, there is a need for as many arrows in the quiver as possible, and it would be valuable to add aluminium hydroxide-enhanced IPV to that arsenal.

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Should we continue to monitor 4CMenB coverage with MATS?

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A long research process has led to development of a multicomponent vaccine indicated for prevention of invasive meningococcal disease associated with serogroup B *Neisseria meningitidis* (4CMenB; Bexsero, GlaxoSmithKline Vaccines, Siena, Italy).[1] The vaccine was licensed despite no clinical trial data for efficacy because of the very low prevalence of the disease. Similar to conjugate vaccines against other serogroups, the licensure process was based on data obtained through correlates of protection.[2] For polysaccharide conjugate