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Addressing the Re-emergence of Poliovirus

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Abstract

Eradicating polio is perhaps the largest worldwide public health initiative in history, and through extensive vaccination efforts, one of the three poliovirus types (poliovirus type 2) has nearly been exterminated while the incidence of polio has declined to the lowest levels ever. Unfortunately, poliovirus has begun to re-emerge in once polio-free countries and new vaccination and therapeutic strategies are being considered. Challenges are many but critical is maintaining good surveillance and sufficient supplies of Oral polio vaccine (OPV), as well as Inactivated polio vaccine (IPV) which ultimately will replace OPV when wild poliovirus transmission has been interrupted. There is a need to develop enhanced polio vaccine cell lines that can increase vaccine titers and production to provide the means lower the cost of vaccine manufacture, to meet worldwide demand, and to address vaccine efficacy by preventing vaccine losses due to 'cold chain' requirements implicit in delivering vaccines to third world nations. In addition, there is a need to develop safe and effective antivirals to address the incidence of OPV 'shedders' and in achieving and maintaining global eradication and containment of poliovirus.

Keywords: Polio; Poliovirus; Re-emergence; VAPP; Eradication; Antiviral

Introduction

To control disease, such as polio, there is the dilemma of vaccine-induced disease and the unvaccinated. Live vaccination against polio has effectively prevented disease in most developed countries and contained polio to only a few countries where outbreaks of poliomyelitis by the wild-type strain still remain. Over the last decade, largely through the efforts of the Global Polio Eradication Initiative that involves the Centers for Disease Control (CDC), World Health Organization (WHO), the Rotary Club, the Bill and Melinda Gates Foundation and others, there has been a significant reduction in polio in endemic and spill-over countries that suggested worldwide eradication could be eventually achieved through careful surveillance and a robust immunization effort [1-3]. Although the number of people worldwide with poliomyelitis caused by wild-type poliovirus infection has decreased to very low levels due to OPV vaccination, using live oral polio vaccine to control transmission is an issue because the vaccine is excreted, and because these vaccine-derived strains can cause pathogenicity [1,4,5]. It is important to eventually discontinue OPV vaccinations and switch to IPV vaccinations [6], or perhaps move to a polio immunization schedule that incorporates sequential doses of IPV and OPV that could improve both humoral and intestinal immunity [7].

Currently, the number of OPV carriers who are the primary source of neuro virulent viruses remains unknown. Excluding the immune suppressed, poliovirus has been shown to be excreted from humans for several months after OPV vaccination [4,5,8]. OPV vaccine-derived polioviruses are routinely isolated from river or sewage waters [9], and silent circulation of vaccine-derived strains is a risk. At issue are "chronic excreters," who are generally immune compromised and were vaccinated with OPV as children, who continue to shed live viruses from their intestines and upper respiratory tracts for years [10,11]. The issue of "chronic shedders" was recently highlighted in Israel, where despite very high polio vaccine compliancy rates recently identified wild poliovirus in sewage in several towns in southern Israel as well as in the West Bank and Gaza [12-14]. Despite mostly sanitary conditions in Israel, the appearance of wild type polio is nonetheless a high risk for transmission. The Israel epidemiology community rapidly identified >40 people shedding poliovirus, none of them had symptoms of paralysis, and all had been fully vaccinated with Inactivated poliovirus vaccine (IPV), which is used in routine immunizations and protects against all polio strains marking the first time that wild polio was detected without any clinical cases [12,13,15].

IPV is used my most developed countries, and if vaccines are exposed to imported polio, the findings from Israel suggest they could be at risk. It is well known that IPV provides robust humoral immunity, but poorer mucosal immunity in the gut suggesting that IPV-vaccines might still shed the virus in feces [16-19]. To stop silent polio transmission, Israel has since given nearly a million doses of OPV, and Syria administered >2 million doses. A consequence has been a rise in vaccine demand that is not being effectively addressed per worldwide needs. What is needed to bridge the poliovirus eradication program are effective antivirals. For example, once wild poliovirus transmission has been interrupted, OPV vaccination will end, leaving IPV as the only means to maintain worldwide polio eradication. Antivirals are needed to treat polio shedders and help bridge issues with vaccine manufacture and distribution, as well as outbreaks caused by accidental or deliberate release. It is clear that antiviral drugs are needed to treat the infected and protect the exposed. Unfortunately, development of a poliovirus antiviral drug will require commitment by a drug manufacturer, and this is unlikely as currently there is no commercial market and scant interest from pharmaceutical companies unless the antiviral reached across all picorna viruses, and in particular rhinoviruses, which cause substantial seasonal morbidity [20-22]. Funding is likely to come from

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philanthropic organizations, and government agencies that understand the public health benefits of an antiviral polio drug.

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