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Current polio status in the world

Estado atual de poliomielite no mundo

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ABSTRACT

Poliomyelitis is still an endemic disease in Afghanistan, Nigeria, and Pakistan despite the efforts to eradicate the disease. Therefore, there is a potential risk of international spread. Since the start of the polio eradication program by the Global Polio Eradication Initiative in 1988, the incidence of polio has been reduced by 99%. In the last decade, wild poliovirus type 2 (WPV2) was eliminated and declared eradicated in 2015. Wild poliovirus type 3 (WPV3) was last reported in November 2012. These changes have allowed the removal of Sabin poliovirus type 2 from the oral poliovirus vaccine (OPV) in April 2016 and countries either introduced bivalent OPV (bOPV) containing Sabin types 1 + 3 poliovirus or added at least one dose of inactivated poliovirus vaccine (IPV) into their routine immunization schedule. Many efforts are needed to eradicate polio, and new strategies should be implemented such as the development and approval of new genetically stable OPV, and vaccines that do not require infectious processes for virus growth, such as virus-like particles (VLPs), or packing-cell technology. IPV will increasingly be produced from Sabin strains, and further attenuated or genetically modified strains. Furthermore, there is also a need for the development of antiviral drugs to treat immunodeficient patients who are long-term excretors infected with poliovirus, thus avoiding contamination of individuals susceptible to polioviruses, due to reversal of pathogenicity. If all these measures are successfully implemented, the world will be close to the global interruption of WPV transmission and polio eradication.

Key words: poliomyelitis; poliovirus; oral poliovirus vaccine.

RESUMO

*A poliomielite ainda é uma doença endêmica no Afeganistão, na Nigéria e no Paquistão, apesar dos esforços para erradicá-la. Portanto, há risco de propagação mundial. Desde o início do programa de erradicação da poliomielite pela Iniciativa de Erradicação Global da Pólio [Global Polio Eradication Initiative (GPEI)], em 1988, a incidência da doença foi reduzida em 99%. Na última década, o poliovírus selvagem do tipo 2 (WPV2) foi eliminado e declarado erradicado em 2015. O poliovírus selvagem do tipo 3 (WPV3) foi reportado pela última vez em novembro de 2012. Essas mudanças promoveram a remoção do poliovírus Sabin tipo 2 da vacina oral antipólio (VOP) em abril de 2016, e os países introduziram a vacina oral bivalente (VOPb), que contém os poliovírus Sabin tipos 1 + 3, ou adicionaram pelo menos uma dose da vacina inativada contra o poliovírus (VIP) no calendário de imunização. É necessário muito empenho para erradicar a poliomielite. Novas estratégias devem ser implementadas, como o desenvolvimento e a aprovação de novas VOPs geneticamente estáveis e vacinas que não requerem processos infecciosos para o crescimento do vírus, como partículas pseudovirais (VLP), ou tecnologia de células de empacotamento (*packing-cell*). A VIP será cada vez mais produzida a partir de cepas Sabin, de outras cepas atenuadas ou geneticamente modificadas. Além disso, é imprescindível o desenvolvimento de medicamentos antivirais para tratar os pacientes imunodeficientes que são excretores de longo prazo, evitando assim a contaminação de indivíduos suscetíveis aos poliovírus, devido à reversão da patogenicidade. Se todas essas medidas forem implementadas com sucesso, o mundo estará próximo da interrupção global de transmissão do WPV e da erradicação da poliomielite.*

Unitermos: *poliomielite; poliovírus; vacina oral contra a poliomielite.*

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RESUMEN

*La poliomielitis sigue siendo una enfermedad endémica en Afganistán, Nigeria y Pakistán a pesar de los esfuerzos por erradicar la enfermedad. Por lo tanto, existe un riesgo de propagación mundial. Desde el inicio del programa de erradicación de la poliomielitis por la Iniciativa de Erradicación Mundial de la Poliomielitis [Global Polio Eradication Initiative (GPEI)] en 1988, la incidencia de la poliomielitis se ha reducido en un 99%. En la última década, el poliovirus salvaje tipo 2 (WPV2) fue eliminado y declarado erradicado en 2015. El poliovirus salvaje tipo 3 (WPV3) se informó por última vez en noviembre de 2012. Estos cambios han permitido la eliminación del poliovirus Sabin tipo 2 de la vacuna antipoliomielítica oral (VPO) en abril de 2016, y los países introdujeron la VPO de tipo bivalente (bVPO), que contiene poliovirus Sabin tipos 1 y 3, o agregaron al menos una dosis de vacuna antipoliomielítica inactivada (VPI) al programa de inmunización de rutina. Se necesitan muchos esfuerzos para erradicar la poliomielitis y se deben implementar nuevas estrategias, como el desarrollo y aprobación de nuevas VPO genéticamente estables y vacunas que no requieren procesos infecciosos para el crecimiento del virus, como partículas pseudovirales (VLP) o tecnología de células empaquetadas (*packing-cell*). La VIP se producirá cada vez más a partir de cepas Sabin y otras cepas más atenuadas o modificadas genéticamente. Además, también es necesario desarrollar fármacos antivirales para tratar a pacientes inmunodeficientes que son excretores a largo plazo, evitando así la contaminación de individuos susceptibles a poliovirus, debido a la reversión de la patogenicidad. Si todas estas medidas se implementan con éxito, el mundo estará cerca de la interrupción global de la transmisión del WPV y la erradicación de la poliomielitis.*

Palabras clave: *poliomielitis; poliovirus; vacuna oral contra la poliomielitis.*

INTRODUCTION

Polio is a highly infectious, incurable viral disease[1] that mainly affects children under 5 years old[2]. It remains endemic in three countries: Afghanistan, Nigeria, and Pakistan[3]. One out of 200 infected people will have an irreversible paralysis (usually, but not always, of the lower limbs), 5% to 10% of these patients die from respiratory muscle paralysis[2]. Polio is a very old disease, found even in mummies in Egypt[4] and, only after the introduction of Sabin and Salk vaccines in the 1950s, the number of cases decreased[5, 6]. There are two types of polio vaccines: Salk, an injectable vaccine that contains inactivated viruses [inactivated polio vaccine (IPV)][5], and Sabin, an oral vaccine that contains attenuated viruses [oral polio vaccine (OPV)][6]. Oral polio vaccine can cause vaccine-associated paralysis [circulating vaccine-derived poliovirus (cVDPV)][7, 8] due to reversion of virulence, especially in patients with primary immunodeficiency, as it excretes the poliovirus vaccine for extremely prolonged periods, capable of causing infection in susceptible populations[9, 10]. Mass vaccination campaigns using Sabin and Salk vaccines have prevented the development of the million new cases, but even after a major reduction, the World Health Organization (WHO) keeps polio on the international health emergency list due to threats of global resurgence of the disease[11]. Thus, it is not possible to interrupt immunization, as there is still a risk of the disease returning on a worldwide scale.

Since the beginning of polio eradication by the Global Polio Eradication Initiative (GPEI) in 1988, which brought together several institutions, including the WHO, the Centers for Disease Control and Prevention (CDC), the United Nations International Children's Emergency Fund (Unicef), Rotary, and Bill & Melinda Gates Foundations; as a consequence, the incidence of polio has been reduced by 99%[12]. The eradication program could be divided into several distinct phases. The first phase began with the resolution of the World Health Assembly in 1988 and the definition of a goal for the end of the year 2000 as a target date for eradication[13]. This period was marked by efforts to implement a global program, including strategy of development, resource mobilization, field practice, and rapid progress[14]. Although substantial progress has been made, the goal of eradication was not achieved[15]. In 2000, there were 20 endemic countries, compared with 125 countries in 1988. The last diagnosis of polio in Brazil occurred in 1990[16]. WHO officially declared polio eradicated from the Americas in 1994[17]. The second phase of the eradication efforts started in 2001 and ended in early 2010s. This phase lasted about a decade and was characterized by focusing increasingly on difficult areas (particularly in areas with compromised security), and in general, the program's performance was lower than expected in implementing the field activities, especially vaccination campaigns. As the circulation of wild poliovirus had already been suppressed in many countries, even in the countries considered polio-endemic, the levels of immunity required to achieve interruption of transmission, now rely almost exclusively on vaccine-induced immunity, requiring frequent vaccination campaigns and mass vaccination[18]. Despite of the challenges, progress was made, and the number of endemic

countries decreased from 20 in 2000 to four in 2010[19]. WHO declared polio eradicated from the Western Pacific region and Europe in 2004[20, 21].

The third phase began in 2011 with the polio eradication in India[22]. Asia was certified as polio-free in 2014[15]. Despite the specific challenges in the different phases, GPEI is aggressively implementing the Polio Eradication and Endgame Strategic Plan 2013-2019, a comprehensive, long-term strategy that addresses what is needed to provide a polio-free world[23]. A major objective, the removal of Sabin poliovirus type 2 from the OPV, implemented in April 2016[24]. More than 150 countries developed national plans, carried out field activities, and closely monitored this effort[24]. At the same time, countries introduced bivalent OPV (bOPV), which contains types 1 + 3 Sabin poliovirus, and in countries where this has not been done previously, at least one dose of IPV was added into their routine immunization schedule to maintain an immunity base against poliovirus type 2[25]. In April 2016, therefore, GPEI has entered the post OPV2 cessation era. Although the withdrawal planning placed a high priority on the identification and destruction of the remaining trivalent OPV (tOPV) stocks, there is evidence that some of these vaccines continue to be used[18]. The emergence and possible circulation of vaccine-derived poliovirus type 2 is a growing concern in the presence of decreasing immunity against type 2. Besides, although appropriate IPV supply for a single-dose routine strategy has been agreed by the industry, the challenges faced with rapidly expansion of production have led to deliveries below expectations (currently < 50% of initial commitments). The shortages are affecting more than 30 countries that have not been able to introduce or could not be resupplied with IPV. These countries are on a holding path to access IPV, currently scheduled for 2018-2019[18]. Currently, in Brazil the immunization schedule is IPV at two, four, and six months of age and bOPV as a booster at the age of four years[26].

Major achievements were consolidated by GPEI during the third phase, such as the wild poliovirus type 2 (WPV2) that was declared eradicated in 2015, and wild poliovirus type 3 (WPV3) last reported in November 2012, building great confidence that global circulation has ceased. This was the greatest reduction in wild poliovirus (WPV) cases since 2014. There has been no WPV detection outside Afghanistan/Pakistan since 2016 and main circulating vaccine-derived poliovirus type 2 (cVDPV2) outbreak in the Syrian Arab Republic was controlled despite ongoing war[3], but currently, we still face a battle against poliovirus, according to the Global Polio Eradication Initiative, the numbers of case of wild virus and vaccine-derived polio worldwide in 2018-2019[27, 28] are shown in **Table**.

TABLE – Number of confirmed WPV and cVDPV infection in different countries in 2018-2019

Countries	2018				2019			
	WPV1	cVDPV1	cVDPV2	cVDPV3	WPV1	cVDPV1	cVDPV2	cVDPV3
Afghanistan	21				26			
Angola							88	
The Central African Republic							19	
Benin							7	
Chad							3	
China							1	
Democratic Republic of Congo			20				63	
Ethiopia							5	
Ghana							12	
Indonesia		1						
Malaysia								
Mozambique			1					
Myanmar						6		
Niger			10				1	
Nigeria			34				18	
Pakistan	12				117		22	
Papua New Guinea		26						
Philippines						1	11	
Somalia			6	7			3	
Togo							6	
Zambia							2	

WPV1: wild poliovirus type 1; cVDPV1: circulating vaccine-derived poliovirus type 1; cVDPV2: circulating vaccine-derived poliovirus type 2; cVDPV3: circulating vaccine-derived poliovirus type 3.

Currently, Afghanistan and Pakistan are the only two countries in which WPV transmission continues to be reported and both constitute a single epidemiological block[3]. Environmental surveillance and genetic sequencing have revealed that WPV1 has primarily persisted along the two countries[3]. They need to address their remaining challenges in a coordinated way to simultaneously interrupt the transmission[3]. In Afghanistan, 26 wild poliovirus type 1 (WPV1) cases were reported in 2019, and 21 cases in 2018[29]. In Pakistan, there were 117 WPV1 cases in 2019, despite 12 WPV1 cases reported in 2018[30]. Nigeria has seen no further cases of WPV1 since September 2016, however, circulation of wild poliovirus has never stopped and is currently affected by cVDPV2[31]. During the year 2019, 18 cVDPV2 cases were reported and 34 cVDPV2 cases were reported in 2018[31].

Between January and December 2019, the transmission of circulating vaccine-derived poliovirus type 1 (cVDPV1) was confirmed in three countries (Malaysia, Myanmar and Philippines) totalizing eight cases. During the same period, 251 cases of the cVDPV2 were confirmed in 15 countries (Angola, Central African Republic, Benin, Chad, China, Democratic Republic of Congo, Ethiopia, Ghana, Niger, Nigeria, Pakistan, Philippines, Somalia, Togo and Zambia). There are no cases of circulating vaccine-derived poliovirus type 3 (cVDPV3) so far[27, 28].

Throughout 2018, cVDPV transmission was confirmed in seven countries, totalizing 98 cases. One case of cVDPV1 were confirmed in Indonesia, and 26 cases in Papua New Guinea. In Democratic Republic of Congo, Mozambique, Niger, Nigeria, and Somalia 71 cases of cVDPV2 were confirmed. Somalia alone confirmed seven cases of cVDPV3[27, 28].

There is much to be done to reach the goal of eradication, and to continue this process and start the fourth phase. GPEI has published new Polio Endgame Strategy 2019-2023, which will face a dual emergency: interrupt WPV transmission and cVDPV outbreaks[3]. The main points of this new publication will be the implementation of improvements and the introduction of innovations in order to reach their three main goals, such as: to stop the transmission of all wild poliovirus through vaccination, stop all cVDPV outbreaks within 120 days of detection, and eliminate the risk of future vaccine-derived-poliovirus (VDPV)[3]. For this aim, regulations, and approvals of new OPV will be necessary so that they can significantly contribute to stopping or preventing VDPV outbreaks. These vaccines must be more genetically stable. The development of poliovirus vaccines will increasingly focus on IPV and vaccines that do not require infectious processes for the virus to growth. IPV will increasingly be produced from Sabin strains, and further other attenuated or genetically modified strains. Ultimately, polio vaccines will be produced by non-infectious processes, such as virus-like particles (VLPs), or packing-cell technology. Both can provide immunogenic non-infectious vaccines[32, 33]. However, although these vaccines are expected to prevent paralytic disease through humoral immunity following exposure to poliovirus, their ability to induce mucosal immunity is limited, and this may be the major limitation. Therefore, the efforts to develop mucosal adjuvants for these new generation vaccines are a high priority. The development of new oral vaccine against poliovirus type 2 is expected to respond to this critical need (induce mucosal immunity). Thus, the mOPV2 (monovalent) from stockpiles can be used[18]. There is also a need for the development of an antiviral drug to treat long-term immunodeficient excretors patients who are infected with poliovirus, thus avoiding contamination by poliovirus due to reversion of virulence in susceptible people[3].

The second goal is the integration of actions, which will help to build a polio-free world. This will increasingly depend on strong immunization, health and disease surveillance systems, as well as emergency response capabilities. This will require closer collaboration with other health programs in a new integrated way to protect the populations. The third goal is the eradication of WPV and poliovirus containment of all polioviruses. As the world approaches the global interruption of WPV transmission, the containment of all polioviruses will be especially important. The global number of poliovirus storage and handling will be reduced[21]. Appropriate poliovirus containment will be applied in laboratories, in vaccine manufacturing, and other safeguards facilities for the long-term containment of poliovirus[3]. Containment, as one of the main pillars for a polio-free world, will help to minimize risk associated of handling poliovirus after eradication, and then it will be necessary to discontinue the use of oral poliovirus vaccine[18]. This will be the ultimate goal for combating poliovirus. Polio eradication will continue to occupy another generation of public health professionals. Although the polio war has already been successful, for eradication, the final battle will be the complete removal of all polioviruses from communities (finding ways to detect and clear infection among immunodeficient individuals), and ensure that the contained polioviruses remain in appropriate facilities[18].

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