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SURVEILLANCE OF ACUTE FLACCID PARALYSIS AND POLIOMYELITIS ON SOME TERRITORIES OF RUSSIA AND SOUTH VIETNAM. PART 1. POLIOVIRUSES AND PARALYSIS

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Abstract. The epidemiological and etiological aspects of poliomyelitis and acute flaccid paralysis (AFP) in Russia and Vietnam were analysed and compared. The polio-free status is maintained on 14 territories of Russia and 29 provinces of South Vietnam. The quality of epidemiological and virological surveillance for acute flaccid paralysis is in accordance with the requirements of the national and international polio surveillance systems. All AFP cases were revealed, registered, reported and investigated in both countries. The percentage of poliovirus isolation from 2492 samples collected from patients with acute flaccid paralysis and contact persons in different years in Russia ranged from 1.3±0.89 to 9.8±0.79. In South Vietnam, 2143 samples from patients with acute flaccid paralysis were investigated. In Russia and Vietnam, we isolated vaccine polioviruses of all three types with predominance of type 3 polioviruses (63% and 50%, respectively) in both countries. From AFP patients in Russia and Vietnam, polioviruses were isolated in 4.9% and 1.0% studied samples, respectively. Some VDPV strains were revealed on the territories of Russia and South Vietnam. Here, we describe five cases of vaccine-associated paralytic poliomyelitis registered in Russia and two cases of AFP caused by VDPV type 2 reported in Vietnam. To prevent the risk of developing vaccine-associated paralytic poliomyelitis, it is indispensable to ensure high-quality surveillance for acute flaccid paralysis, maintain 95% polio vaccine pediatric coverage and strictly comply with sanitary legislation, including the National Vaccination Schedule when vaccinating children, to improve virological surveillance of polioviruses using classical and new virological and molecular methods and to continue research on poliomyelitis, including development of new safe and effective poliovirus vaccines able to induce both humoral and mucosal immunity. The systematic control of adequate polio vaccination is indispensable in order to prevent transmission of imported wild polioviruses into polio free countries as well as circulation of vaccine-derived polioviruses worldwide.

Key words: *acute flaccid paralysis, vaccine-associated paralytic poliomyelitis, polioviruses, circulation, surveillance, vaccination schedule, poliovirus vaccines.*

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НАДЗОР ЗА ОСТРЫМ ВЯЛЫМ ПАРАЛИЧОМ И ПОЛИОМИЕЛИТОМ НА НЕКОТОРЫХ ТЕРРИТОРИЯХ РОССИИ И ЮЖНОГО ВЬЕТНАМА. ЧАСТЬ 1. ПОЛИОВИРУСЫ И ПАРАЛИЧ

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Резюме. Проведен сравнительный анализ эпидемиологического и этиологического аспектов полиомиелита и острых вялых параличей (ОВП) в России и Вьетнаме. Свободный от полиомиелита статус поддерживается на 14 территориях России и в 29 провинциях Южного Вьетнама. Качество эпидемиологического и вирусологического надзора соответствует требованиям национальных и международной систем надзора. Все больные ОВП выявлены, зарегистрированы и обследованы в обеих странах. В России процент выделения полиовирусов из проб от 2492 больных ОВП и контактных лиц в разные годы колебался от 1,3±0,89 до 9,8±0,79. В Южном Вьетнаме было исследовано 2143 пробы от больных с острыми вялыми параличами. В России и Вьетнаме мы выделили полиовирусы всех трех типов с преобладанием полиовирусов типа 3 (63 и 50% соответственно). В России полиовирусы были изолированы из 4,9% проб, во Вьетнаме в 1% проб содержались полиовирусы. Штаммы полиовирусов вакцинного происхождения (VDPV) были обнаружены в России и Вьетнаме. В статье дано описание пяти случаев вакциноассоциированного паралитического полиомиелита в России и двух случаев ОВП, вызванных VDPV типа 2, во Вьетнаме. Для предотвращения риска развития вакциноассоциированного паралитического полиомиелита необходимо обеспечивать высококачественный надзор за ОВП, поддерживать 95% охват детей вакцинацией, строго соблюдать санитарное законодательство и Национальный календарь прививок при иммунизации детей, совершенствовать вирусологический надзор с использованием классических и новых вирусологических и молекулярных методов и продолжать научные исследования по полиомиелиту, в том числе разработку новых безопасных и эффективных полиовирусных вакцин, индуцирующих гуморальный и мукозальный иммунитет. Необходимо контролировать качество вакцинации, чтобы предотвратить импортирование диких и циркуляцию производных от вакцины полиовирусов в свободных от полиомиелита странах и во всем мире.

Ключевые слова: *острый вялый паралич, вакциноассоциированный паралитический полиомиелит, полиовирусы, циркуляция, надзор, календарь вакцинации, полиовирусные вакцины.*

Introduction

Since the General Health Assembly set the ambitious goal of global eradication of poliomyelitis, impressive progress has been made in reducing the incidence of polio [1, 2, 5, 21]. In 1988, 350 000 cases of poliomyelitis were reported in 125 countries; in 2003, there were only 784 cases in 15 countries. But in the same year, wild poliovirus was imported from Nigeria into neighboring African countries, and then the international spread of wild polioviruses from endemic countries to countries free of poliomyelitis was recorded. To date five WHO regions from six are certified as polio free regions [5]. Wild type 1 poliovirus now circulates only in two countries — Afghanistan and Pakistan.

To achieve the goal of eradicating poliomyelitis, WHO has recommended maintaining polio vaccination coverage of children at a level of at least 95%. The effective triple oral poliovirus vaccine (tOPV), inducing both humoral and mucosal immunity in vaccine recipient, served as the main tool for routine and mass immunization [14, 15]. Since 2016, only two-component oral poliovirus vaccine (bOPV) containing virus types 1 and 3 has been used. Vaccine-derived polioviruses — VDPV. can be formed after vaccination of children with tOVP or bOPV during the persistence and replication of polioviruses in the cells of small intestine due to two mechanisms of virus evolution — recombination and mutation [9, 11, 13]. Subsequent circulation of VDPV of different types in the population is possible, which has become another problem of the Polio Eradication Programme.

The main concept of Polio Eradication Programme is the creation of surveillance system based on the data from epidemiological investigations of cases with acute flaccid paralysis (AFP) and on the results of clinical and laboratory diagnostics [1, 2, 21]. Laboratory diagnostics implies a mandatory virological study of two adequate samples of biological material from each patient within the decreed timeframe and in strict accordance with the recommendations of the World Health Organization [1, 20, 21].

In some cases the initial diagnosis is changed to vaccine-associated paralytic poliomyelitis (VAPP) [3, 10]. Based on WHO criteria in such cases the development of paralysis occurs from 4 to 60 days after vaccination with oral polio vaccine in vaccine recipients [19]. The same process occurs in nonvaccinated children as the result of contact with recently vaccinated children. VAPP is characterized by a typical clinical picture of poliomyelitis with an acute onset, rapid development of paralysis, mainly proximal and asymmetric, in the first three days from the onset of the disease, the appearance of atrophy by the 7th day of illness and the presence of residual paralysis after the sixtieth day after onset of paralysis. The diagnosis is made by isolat-

ing polioviruses, either wild, vaccine or vaccine-derived viruses, from the faeces of patients.

The Subnational polio laboratory in Saint Petersburg was created in the scientific laboratory of the Pasteur Institute in St. Petersburg. The laboratory is part of the World Health Organization network of polio laboratories. The laboratory constantly collaborates with virologists and epidemiologists of 14 administrative territories of Russia with the population of 25 million people, including 3 million (12%) children under 15.

The virological laboratory of the Pasteur Institute in Ho Chi Minh City is one of the National polio laboratories in Vietnam and covers 29 provinces of South Vietnam with the population of 45 million people, including 12 million (26,7%) children under 15.

Materials and methods

The analysis was carried out on the basis of information on the primary registration of patients (cards of the epidemiological investigation of cases of acute flaccid paralysis and poliomyelitis, including vaccine-associated) and state statistical reporting data.

During the observation period from 2002 to 2021, 2492 fecal samples were examined from patients with acute flaccid paralysis syndrome and contact persons sent from 14 administrative territories of the Russian Federation. Also, 2143 samples from children with acute flaccid paralysis collected in 29 provinces of South Vietnam were examined.

Isolation of polioviruses was carried out using standard procedures recommended by WHO manual on three cell lines RD, L20B and Hep-2 [20]. Identification of polioviruses was carried out using a neutralization test with specific diagnostic sera on the cell culture on which poliovirus was isolated in accordance with WHO recommendations [17, 20]. Intratypic differentiation (ITD) of polioviruses was performed using ELISA with polyclonal cross-adsorbed sera and PCR with primers specific to vaccine strains of polioviruses [17, 24]. A neutralization reaction was also carried out with monoclonal antibodies to wild and vaccine polioviruses [8]. Molecular studies were performed by partial sequencing of the VP1 region of poliovirus genome [16].

The average errors were determined, and the significance of statistical differences was evaluated using Student's t-test. Differences were considered statistically significant at 95% confidence interval (values of $p < 0.05$).

Results

During the study of 2492 fecal samples from children with acute flaccid paralysis syndrome and people who were in close contact with them from 14 territories of Russia, 60 polioviruses (4.5%) were isolated. According to the results of intratypic differentiation, the majority of polioviruses were vaccine (some polioviruses were classified as VDPV). Identification of polioviruses showed that 15 polioviruses belonged to type 1, seven polioviruses belonged to type 2, and 38 strains belonged to type 3. The percentage of poliovirus isolation fluctuated over the years (Table 1).

In 2002–2007, 58 polioviruses were isolated from patients with AFP (6.2% of cases). In 2008–2009, the percentage of poliovirus isolation decreased to 1.3% that was statistically significant ($p < 0.05$). In 2009, when vaccination of infants with inactivated poliovirus vaccine (IPV) was introduced in the country, not a single poliovirus was isolated [25].

In 2010, when wild type 1 poliovirus was imported into Russia from Tajikistan, 13 vaccine polioviruses were isolated from the AFP cases [22]. In such difficult epidemic situation, the percentage of detection of polioviruses significantly increased to 9.8% ($p < 0.05$). This can be explained by supplementary immunization in order to protect children [1, 3, 9]. It should be noted that in 2010 we also isolated 4 wild type 1 polioviruses in three healthy children who arrived in St. Petersburg from Tajikistan. It is extremely important to state that not a single case of AFP or VAPP caused by wild type 1 poliovirus was record-

Table 1. Isolation of polioviruses and nonpolio enteroviruses from AFP cases and contact persons on 14 territories of Russia

Years	Number of samples	Number of isolated enteroviruses (PV and NPEV)				
		PV (%)	PV1	PV2	PV3	NPEV (%)
2002–2003	378	30 (7.9)	9	11	10	15
2004–2005	256	17 (6.6)	1	7	9	19
2006–2007	300	11 (3.7)	4	6	1	9
2008–2009	232	3 (1.3)	0	1	2	11
2010	133	13 (9.8)	4	4	5	4
2011–2012	230	5 (2.2)	0	1	4	13
2013–2014	216	11 (5.1)	0	0	11	6
2015–2016	245	18 (7.3)	8	2	8	11
2017–2019	325	9 (2.8)	1	0	8	14
2020–2021	178	4 (2.2)	2	0	2	4
Total	2492	121 (4.9)	29	32	60	106 (4.3)

ed in 14 administrative territories of the Russian Federation located in the area of responsibility of the SNL in St. Petersburg.

In 2011–2012, the detection rate of polioviruses in patients with AFP decreased to 2.2% ($p < 0.05$). In 2013, seven patients with AFP living in 5 administrative territories of St. Petersburg RC were found to have type 3 polioviruses. All these children received 4–5 vaccinations against poliomyelitis — 2 doses of inactivated and 2–3 doses of oral vaccine. Acute flaccid paralysis events occurred 4th to 36th days after the last oral polio vaccine vaccination, with different vaccine series. It is important that all nine polioviruses of type 3 were vaccine according to the results of intratypic differentiation. The reason for this situation, most likely, can be associated with the state of the immune system of children. In 2014, only two polioviruses were isolated, both of them belonged to type 3. Most of polioviruses found in samples from patients with AFP in 2014–2015 belonged to type 3, samples from two patients contained mixtures of polioviruses of types 1 and 3, in samples from one patient in 2015 polioviruses of all three types were detected. All polioviruses, according to the results of the ITD, were vaccine viruses. During the next six years from 2016 to 2021, vaccine polioviruses of type 2 were not isolated from patients. This is due to the global switch from a three-component to a two-component oral poliovirus vaccine. During this period, 17 polioviruses (5 type 1 and 12 type 3) were isolated from samples of patients with AFP syndrome, the percentage of poliovirus isolation in 2016–2021 was 2.8% and all polioviruses were vaccine.

It is important to note that during the analyzed period, in some cases, the primary diagnosis "acute flaccid paralysis" was finally changed by the Federal Commission to "vaccine-associated paralytic poliomyelitis" [3, 10, 19].

VAPP can appear after receiving the first dose of oral polio vaccine, usually in recipients with primary or secondary immunodeficiencies. The main reasons for the occurrence of VAPP are the lack of vaccinations in children who should have been vaccinated against polio in accordance with the National Vaccination Schedule. This circumstance contributes to the development of VAPP in unvaccinated children who have been in contact with recently vaccinated children, who can excrete vaccine polioviruses within two months after immunization. In addition, the development of VAPP in vaccinated recipients is possible due to ignoration of the requirements of sanitary legislation by medical personnel during immunization against poliomyelitis in the case when previously unvaccinated children more than 12 months old are vaccinated with an oral vaccine (OPV) instead of an inactivated vaccine (IPV). In Russia in accordance with the National Vaccination Schedule, to protect children against the development of VAPP, an inactivated poliovirus vaccine must be used for the first two vaccinations, regardless of the age of the child.

The following is a description of five cases of acute flaccid paralysis which were classified as vaccine-associated paralytic poliomyelitis.

VAPP case 1: Acute flaccid paralysis was registered on June 14, 2002 in a non-vaccinated girl aged 20 months. It happened during her stay in a noninfectious hospital, that's why she was transferred to hospital for infectious diseases. The girl was immunodeficient (hypogammaglobulinemia). Vaccine type 2 polioviruses were isolated from fecal samples taken from the second to the 78th day from the onset of paralysis. In the blood serum taken on the 2nd day after the detection of paralysis, there were no antibodies to PV1 and PV3, the titer of antibodies to PV2 was 1:16. The antibodies titers to PV2 increased four-fold (1:64) on the 21st day after the onset of paralysis. When examining four children without paralysis who had contact with the sick child in hospital, poliovirus type 2 was also detected, three of them were not vaccinated. On the 60th day from the onset of paralysis, the child had residual paralysis. The final diagnosis was Vaccine-associated Paralytic poliomyelitis in a contact person.

VAPP case 2: Acute flaccid paralysis was registered in a boy on February 7, 2005 at the age of 20 months after receiving the fourth dose of oral polio vaccine. Paralysis developed on the 60th day after revaccination. Vaccine poliovirus type 2 was isolated from fecal samples taken on days 1, 2, 30, 45 from the onset of paralysis. Poliovirus excretion continued for 4 months after vaccination. In blood sera taken on the first and 30 days from the onset of paralysis, there were no antibodies to poliovirus types 1, 2 and 3. The immunological study show the Bruton's disease (agammaglobulinemia). On the 60th day of the onset of paralysis, residual paralysis was recorded. Final diagnosis: Vaccine-associated paralytic poliomyelitis in the vaccine recipient.

VAPP case 3: Acute flaccid paralysis was registered in a boy on July 20, 2016 at the age of 21 months after the first in his life vaccination with bivalent oral poliovirus vaccine. When choosing the vaccine, the medical staff was guided by the age of the boy, and not by his actual vaccination status. In Russia, in accordance with the National Vaccination Schedule, the inactivated poliovirus vaccine must be used for the first two vaccinations, regardless of the age of the child. Acute flaccid paralysis developed in the course of 12 days after immunization. Vaccine polioviruses types 1 and 3 were isolated from two fecal samples. In blood serum taken late from the onset of paralysis, antibodies to two polioviruses were found in titers: PV1 — 1:256, PV3 — 1:32. On the 60th day of the onset of paralysis, residual paralysis was recorded. Final diagnosis: Vaccine-associated paralytic poliomyelitis in the vaccine recipient.

VAPP case 4: Acute flaccid paralysis in a nonvaccinated child was registered on September 26, 2017 at

Table 2. Isolation of polioviruses and nonpolio enteroviruses from AFP cases and contact persons in 20 provinces of South Vietnam

Years	Number of samples	Number of isolated enteroviruses (PV and NPEV)				
		PV (%)	PV1	PV2	PV3	NPEV (%)
2010	109	1	0	0	1	12
2011–2012	480	7	3	3	1	54
2013–2014	363	2	1	0	1	38
2015–2016	340	8	1	2	5	31
2017–2019	544	4	1	0	3	70
2020–2021	307	0	0	0	0	44
Total	2143	22 (1.0)	6	5	11	249 (11.6)

the age of 11 weeks. The boy was hospitalized in the intensive care unit with tetra paresis and paresis of the muscles of the diaphragm, and was on artificial lung ventilation for a month. Vaccine poliovirus type 3 was isolated from two fecal samples. The antibodies titers against PV3 increased four-fold on the 21st day after the onset of paralysis. We isolated the same poliovirus from the patient's elder sister who received 3 doses of IPV and had high antibodies titer to this poliovirus (1:512). The girl could be the only possible source of poliovirus for this VAPP patient, the source of poliovirus for the girl could not be established. During examination on the 60th day after the onset of paralysis residual paralysis was revealed. Final diagnosis: Vaccine-associated paralytic poliomyelitis in the contact person.

VAPP case 5: The child was vaccinated with the first in his life dose of inactivated vaccine "Polimilex" at the age of 10 months. Acute flaccid paralysis was registered in a boy on December 7, 2018 during his stay in hospital of the Far East. From two fecal samples dated December 7 and 8, 2018 vaccine poliovirus type 3 was isolated. In the blood serum antibodies only to two polioviruses (PV1 — 1:256, PV3 — 1:64) were found. On December 27, 2018 the child was transferred to central hospital for infectious diseases in St. Petersburg. In blood serum taken on the next day, antibodies to three polioviruses were found in titers: PV1 — 1:512, PV2 — 1:64, PV3 — 1:512. The antibodies titers against PV3 increased eight-fold on the 21st day after the onset of paralysis. On the 60th day, the patient had residual paralysis. Final diagnosis: Vaccine-associated paralytic poliomyelitis in the vaccine recipient or in the contact person.

During the surveillance of acute flaccid paralysis in South Vietnam, 2143 fecal samples from children with AFP syndrome from 29 southern provinces of Vietnam were examined and 22 polioviruses (1.0%) were isolated. Most of them, according to the results of intratypic differentiation, were vaccine. Type 2 poliovirus strains isolated from two children in 2012 were classified as vaccine-derived polioviruses based on intratypic differentiation results. Six of the 22 isolated polioviruses were classified as type 1, five as type 2, and eleven viruses (50%) were type 3 polioviruses (Table 2).

It is extremely important that two cases of acute flaccid paralysis registered in 2012 were caused by vaccine-derived polioviruses of type 2. Below you can see the description of these cases:

Case of AFP 1: A child, 19 months old, was not vaccinated against polio. Acute flaccid paralysis in a girl was registered on February 14, 2012 in the district close to the sea with humid tropical climate, poor sanitary conditions and more than 80% of the population of ethnic minorities origin. The girl was sent to hospital. From two patient's samples there were isolated two polioviruses which were classified as VDPV of type 2 according to intratypic differentiation. The results of poliovirus search on the 30th day after the onset of paralysis were negative. On the 60th day, the patient had not residual paralysis. Final diagnosis: Acute flaccid paralysis in the non-vaccinated person.

Case of AFP 2: A child, 5 years old, received two doses of tOPV, the last dose was given more than 30 days before the onset of paralysis. Acute flaccid paralysis was registered on April 17, 2012, in the mountainous district hard to reach for the provision of vaccines. The population of the district consists of 11 ethnic groups. The boy was sent to hospital. From two samples two polioviruses classified as VDPV type 2 were isolated, on the 30th day after the onset of paralysis polioviruses were not found. On examination of the boy on the 60th day after the onset of paralysis, the residual paralysis was not found. Final diagnosis: Acute flaccid paralysis in the not completely vaccinated child.

The number of poliovirus strains isolated from AFP cases in Russia was 60, and it was more than in South Vietnam which was 22 (Fig.).

Discussion and conclusion

The number of registered and completely studied cases of AFP was large in both countries. In Russia in the course of 20 years (from 2002 to 2021) 2492 samples from patients with acute flaccid paralysis syndrome and their close contacts from 14 territories were examined. In Vietnam during 12 years 2143 samples from patients having acute flaccid paralysis from 29 provinces of South Vietnam were investigat-

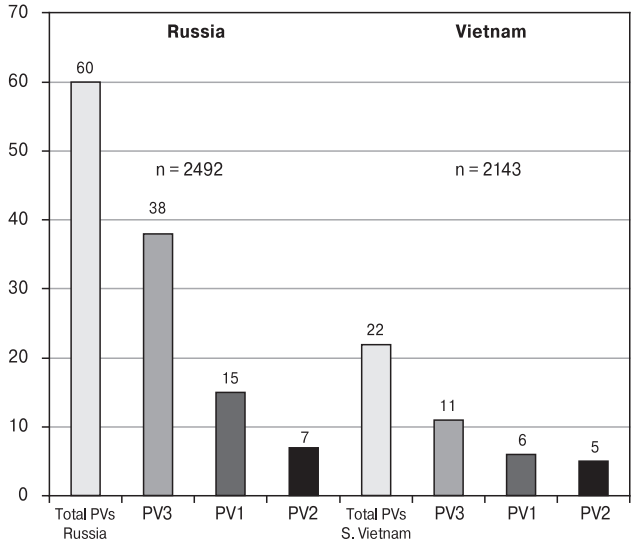

Figure. Polioviruses isolated from AFP cases on 14 territories of Russia and in 29 provinces of South Vietnam

ed. The samples from contact persons were not examined in accordance with the National surveillance system.

In Russia and Vietnam, in the course of surveillance for acute flaccid paralysis during the analyzed periods we isolated vaccine polioviruses of three types with predominance of type 3 polioviruses (63% and 50%, respectively) in both countries. From patients with AFP from Russia, polioviruses were isolated in 4.9% of samples; in Vietnam, only 1.0% of samples contained polioviruses. If we compare the total poliovirus isolation in the two countries over the same period of time from 2010 to 2021, then the ratio of positive for polioviruses samples will remain the same. The percentage of polioviruses isolated in Russia in 2002–2021 (4.9%) or in 2010–2021 (4.5%) statistically exceeded the percentage (1.0%) of poliovirus isolation in 2910–2021 in Vietnam ($p < 0.001$). In Russia four wild type 1 polioviruses were isolated in 2010 from healthy children, who arrived in Saint Petersburg from Tajikistan, as well as various types of VDPV. In Vietnam no wild polioviruses have been identified during 12 years since 2010. From the middle of 2016 in Russia and in Vietnam polioviruses of type 2 have not been isolated. On the contrary the percentage of isolation of nonpoliomyelitis enteroviruses from patients with AFP syndrome in South Vietnam was higher than in Russia (11.6% and 4.3%, respectively) because of extremely high level of enterovirus circulation in South Vietnam, the details will be discussed in the article "Surveillance of acute flaccid paralysis and poliomyelitis in some territories of Russia and in South Vietnam. Part 2. Non-polio enteroviruses and paralysis".

The higher percentage of poliovirus isolation from AFP patients in Russia can be explained by the difference in the National Vaccination Schedules in the two countries. In Russia now each child should receive six polio vaccinations against polio during their lifetime — 2 doses of the inactivated vaccine — at 3 and 4 and a half months, and 4 doses of the oral vaccine — at 6, 18 and 20 months, and then at 6 years. Earlier the 6th dose of OPV was given at the age of 14 [4, 18]. Until May 2016, a three-component OPV was used. Since the global switch to bivalent oral poliovirus vaccine in 2016, all the countries use only bivalent OPV for vaccination. The Vietnamese National Vaccination Schedule earlier provided three doses of OPV at the age of two, three and four months. In September 2018, the additional dose with inactivated vaccine IPV at five months was introduced into the Vaccination schedule of Vietnam, currently the children in Vietnam should receive four vaccinations against poliomyelitis.

There exists the risk for the polio eradication programme, such as the development of AFP and VAPP caused by VDPV in the context of continued use of oral poliovirus vaccine. In Russia in 2002–2021 several cases of VAPP were diagnosed in 14 territories. In 29 provinces of South Vietnam, VAPP cases have not been reported. But two provinces in South Vietnam in 2012 reported one case each of acute flaccid paralysis caused by vaccine-derived polioviruses, VDPV type 2, isolated from sick children.

In order to analyse the causes of VAPP development we choose five cases of VAPP. The cases 1 and 2 demonstrate the contribution of immunodeficiencies to VAPP development. The case 3 shows the consequence of ignoring requirements of the Russian Vaccination Schedule and the lack of alertness of medical personnel. The case 4 gives the example of poliovirus transmission to nonvaccinated child by recipient of IPV without mucosal immunity. The reason for VAPP in the case 5 is unclear, maybe it was not complete vaccination or the use of not adequate vaccine for the immunisation of this child.

It should be noted that in Russia over the 25-year period, cases of VAPP have been repeatedly recorded, they were caused by both vaccine polioviruses and vaccine-derived polioviruses of different types [1, 2, 3, 10]. In the SNL of St. Petersburg, nucleotide substitutions were detected in more than 40 polioviruses isolated from patients with AFP and VAPP since 1998 [13]. In three strains isolated from patients with VAPP, the percentage of nucleotide divergence with vaccine strains in the VP3–2A genome region ranged from 0.7% to 1.4%, and in the VP1 genome region it was 0.9–1.1%, the percentage of amino acid substitutions (0.8–1.4%) was also high [13]. In one child with immunodeficiency (our VAPP case 2) from the 2nd to the 78th days from the onset of paralysis, type 2 polioviruses were isolated. These strains had only 0.2% of nucleotide substitutions, including one neurovirulent mutation (T→C), in the genome region encoding the VP1 protein [6, 7]. The poliovirus, that caused VAPP in the child with paralysis, was a recombinant

strain (S2/S1), it could be formed in a vaccinated child during the replication of polioviruses of different types in intestinal epithelial cells [9, 11, 13]. Just one neurovirulent mutation gave poliovirus an increased possibility to be transmitted to other children [3, 7]. Type 2 polioviruses with the same characteristics were found in four other non-paralyzed children in an adjacent hospital ward. As five children shed such polioviruses, they were detected in sewage samples from the hospital sewer [3, 7]. These results showed that among children' population, with very good vaccination coverage, long-term persistence and circulation of vaccine-derived polioviruses had been possible. Since the number of children receiving OPV in Russia is high, each unvaccinated child is likely to contact with recently vaccinated children who can shed vaccine polioviruses or even VDPV which can become the cause of paralytic disease. The number of VAPP among the recipients of polio vaccine dramatically decreased after the introduction of two IPV doses into the National Vaccination Schedule [4, 18, 25], the risk of VAPP in unvaccinated children still exists.

In 2012 Vietnam also reported two cases of AFP caused by VDPV type 2 in two provinces. Barriers to vaccine delivery as well as inadequate epidemiological and sanitary situation have created the prerequisites for the spread of VDPV type 2, which was isolated from healthy contact children and from sewage water samples in 13 other countries between April 2011 and June 2012 (Update of vaccine-derived polioviruses — worldwide, April 2011 — June 2012).

Another risk for the polio eradication is the decreased mucosal and humoral immunity in vaccinated children. The circulation of VDPV type 3 in an orphanage led to the case of paralytic poliomyelitis caused by this virus in one child was described [12]. The complete genome sequencing was performed for five polioviruses isolated from the patient and three contact children. The level of divergence of the isolates' genomes corresponded to approximately 9–10 months of evolution. The possibility of VDPV3 transmission from poliovirus excretor to susceptible recipients (unvaccinated against polio or vaccinated with inactivated poliovirus vaccine) and circulation in the closed children's group was demonstrated. The study of the blood sera of orphanage residents at least twice vaccinated with IPV revealed the absence of neutralizing antibodies against two poliovirus serotypes in almost 20% of children. Thus the authors of the article [12] showed that the rejection of OPV vaccination can lead to a critical decrease in collective immunity.

When studying the levels of immunity to polioviruses in vaccinated with bOPV vaccine we fixed the decrease of humoral immunity to poliovirus type 2 in children of two age groups (3–4 and 15–17 years old) from one territory of Russia. Below there are the data showing the absence of antibodies to type 2 polioviruses in some children after vaccination with a bivalent poliovirus vaccine (Table 3).

Table 3. The percentage of children vaccinated by bOPV having no anti-PV2 antibodies in the two age groups

Year	Number of children	Children aged 3–4 years	Children aged 15–17 years
2017	204	0	0
2018	202	1%	2%
2019	200	2%	6%
2022	206	8%	3%

Our data also prove that the complete rejection of OPV for vaccination of children may lead to a significant decrease in collective immunity.

Russia and Vietnam are situated in two WHO Regions — European Region and South-East Asia Region. Both regions were certified as polio free regions — EURO in 2002 [5] and SEAR in 2014. Throughout the post-certification period, the polio-free status was maintained on 14 territories of Russia and 29 provinces of South Vietnam. The quality of epidemiological and virological surveillance for acute flaccid paralysis was in accordance with the requirements regulated by the national and international polio surveillance systems. All cases of AFP were revealed, registered, virologically studied and timely reported in both countries.

To prevent the risk of developing vaccine-associated paralytic poliomyelitis, it is indispensable to maintain 95% polio vaccine coverage of children; to comply with sanitary legislation, including the National Vaccination Schedule when vaccinating children and minimize the number of refusals to vaccinate children against poliomyelitis counteracting anti-vaccination propaganda in every way.

Poliomyelitis and AFP surveillance must be continued because the risk of wild poliovirus importation into polio free countries exists till the complete eradication of WPV circulation in the world. It is necessary to strengthen the epidemiological surveillance of poliomyelitis and acute flaccid paralysis, to improve the virological surveillance of polioviruses [23], to continue researches on poliomyelitis, including the development of new safe and effective poliovirus vaccines that can create both humoral and mucosal immunity. The goal of surveillance is to evaluate the circulation of imported wild polioviruses and vaccine-derived polioviruses with nucleotide substitutions. The detection of these pathogenic strains is based on the analysis of poliovirus strains isolated during polio surveillance with the help of classical and new virological and molecular methods. The systematic control of adequate polio vaccination is indispensable in order to prevent transmission of imported wild polioviruses into polio free countries and circulation of vaccine-derived polioviruses all over the world.

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