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## Poliomyelitis: new challenges on the way to eradication

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**Purpose.** To assess the poliomyelitis epidemic situation in Ukraine and determine ways to maintain the status of a country as free from poliomyelitis.**Materials and methods.** Findings of the epidemiological surveillance on acute flaccid paralyses (AFP)/ poliomyelitis, and statistical reports of the Ministry of Healthcare of Ukraine «Performance of Annual Immunization Plan» (Form 5) (from 2008 to 2015) were analyzed.

Findings and discussion. Since 2008 there has been a decrease of immunization coverage in Ukraine, as well as against poliomyelitis. Consequently, in 2012 pursuant to the conclusions of 7th Meeting of the Independent Monitoring Board of the Global Polio Eradication Initiative (October 29–31, 2012 London) Ukraine was listed as country at high risk of wild poliovirus transmission (alongside with the Horn of Africa, Kenya, Libya, Somalia, Uganda and Yemen). Despite the fact that polio immune prevention conditions in Ukraine were rated as critical and the fact that this issue has been raised by the scientific community and up to the government levels, immunization coverage rates still remain extremely low (2008 — >98%, 2008 — 90.9%, 2009 — 80.6%, 2010 — 57.3%, 2011 — 54.3%, 2012 — 73.7%, 2013 — 72.0 %). Considering the required rate of 95%, the situation became particularly critical in 2014 (44.7%) and in the following year (as at 01.08.2015 — 17.3%). This resulted in vaccine-derived poliovirus (VDPV). Three strains of VDPV-2 were discovered in 2014, and in 2015 two polio outbreaks (2 cases) caused by circulating VDPV-1 were registered. Responding to the outbreak from October 2015 to February 2016 three immunization rounds to vaccinate children with oral polio vaccine (2 rounds for age groups from 2 months to 6 years; 3rd round — from 2 months to 10 years) with the respective coverage rates of 64.4%, 71.7% and 80.7%. This was followed by mop-up immunization campaign till 17.04.2016. Measures taken enabled some improvement of the immunization coverage conditions, namely in children under the age of 1 year had 3 vaccinations (inactivated + oral vaccine) the rate was 90.1%. At the same time, these figures were below 90% in 10 administrative areas. If immunization covers less than 90% the main goal of prophylactic immunization will not be accomplished, namely the formation of specific population immunity.

**Conclusions.** The following conditions are necessary for the preservation and maintenance in Ukraine of status as a polio-free territory: the routine immunization coverage should remain at 95%; mop-up immunization should be provided for children till the age of 10 years that missed scheduled vaccinations; proper epidemiological surveillance of AFP/ poliomyelitis and other enteroviral infections should be conducted; virological control of wastewater should be enhanced.**Key words:** children, poliomyelitis, acute flaccid paralyses, eradication, immunization.

### Introduction

Problem of poliomyelitis as the contagious infection disease is known to mankind since the times of Egyptian Pharaohs. This medical problem hasn't been overcome over twenty centuries. Decisively successful separation of three main immunological types of viruses gave the grounds for American Yones Salk to patent killed injection vaccine in 1955 and the scientist A. Sebin patented live vaccine for oral administration. Further implementations of this vaccine into medical practice by the scientists M.P.Chumakov and O.O.Smorodintsev became fundamental in the battle against poliomyelitis [4].

In 1988 the World Health Assembly adopted a resolution on the implementation of the Global Initiative on Eradication of Poliomyelitis, namely circulation suspension of «wild» poliovirus in the global scale. Thus, at the time of Resolution adoption there were 125 endemic countries, 350 thousands cases of annual morbidity (approximately 1000 cases were registered daily) and 16–20 mln persons with the residual effects of poliomyelitis. An ambitious target has been defi-

ned to provide eradication of wild poliovirus till the end of 2000 [6].

The time has elapsed since the start of the Poliomyelitis Eradication Program, four out of six WHO regions have been certified as free from the «wild» poliovirus circulation — The American (1994), the Western Pacific (2000), European one starting from 2002, and the South-East Asia as of 2014 respectively [9,10,12–14].

Poliomyelitis (disease of Heine—Medine) is the acute infectious disease of humans caused by the polioviruses that is characterised by prevailing impairment of the nervous system followed by the development of the flaccid paralysis.

Polioviruses are the tiniest representative of the intestine viruses; science knows 3 their types: Serotype I Brunhilde (the widest spread and the most virulent), serotype II Lansing, serotype III Leon. However, the frequency of paralytic forms is negligible (1 case per 100–1000 asymptomatic forms). All pathogens remain for long period of time in the environment: in milk, water, patient's excrements. Poliovirus is highly resistant to low temperatures, endures freezing, impact of 70°

alcohol that's why it is assigned to the most resistant viruses.

Infection occurs through the faecal-oral route via the contaminated water, food, hands from the source of infection, i.e. a patient or a carrier. Incubation period makes from 3 to 35 days, most commonly 7–14 days. However, the symptoms signs develop only in 5% of cases, the majority of cases are free from symptoms. People fall ill suddenly, they suffer from nausea, vomiting, general weaknesses, muscle weakness in their limbs, headache. The most dangerous clinical forms are the ones accompanied by paralysis of limb muscles (pathogenically related to the impairment of motor neurons of the spinal cord), diaphragm muscles, breathing disorders and cardiovascular activity (paralytic and bulbar clinical forms).

All cases of acute (those that occurred suddenly) flaccid paralysis (AFP), which is the suspect of the poliomyelitis are liable to mandatory registration and immediate investigation during 48 hours [5].

Specific antiviral treatment, unfortunately, does not exist; timely clinical and laboratory examination and pathogen symptomatic treatment can help to avoid complications.

Vaccination is the main preventive method for poliomyelitis. Inactivated poliovirus vaccine (IPV) and oral poliovirus vaccine (OPV) are used. OPV is more reliable because it ensures both local (on the intestine mucous coat) and general immunity. Inactivated vaccine is used for the first two vaccinations (at the age of 3 and 4 months) in Ukraine. OPV vaccination is done at the age of 5 months and re-vaccination at the age of 18 months, 6 years and 14 years.

Global medical community considers as success the termination of global circulation of «wild» poliovirus Type 2 (since 1999 and in September 2015 it was declared about its eradication). It was reported about the termination of «wild» poliovirus circulation Type 3, the last «wild» P3 strain was isolated on November 10, 2012 [2,3]. Unfortunately, events of 2015 in Ukraine prove certain objective obstacles on this way.

**Objective of the study.** The objective of the study is to analyse current epidemic situation with regard to poliomyelitis viruses circulation in Ukraine (according to the data of own supervisions) and in the works (based on the data of scientific sources), morbidity of the disease and establishing the most effective ways of coping with the current epidemic situation.

### Materials and methods of studies

It was used the method of retrospective and operative epidemic analysis with the statistic data processing of basic reports, namely epidemic examinations of infectious disease, urgent case reports on acute infectious disease, food or professional poisoning or unusual reactions to vaccination; hospital patient cards of infectious departments of the city of Kyiv.

### Results of the studies

Nowadays morbidity in the world fell by more than 99% due to vaccination — from 350000 to 74 cases reported in 2015.

On June 21, 2002 Ukraine as the part of the WHO of European Region was certified as the territory free from circulation of «wild» poliovirus. This significant event was preceded by a long period of scientific researches, organizational and practical activities aimed at creating sufficient specific immune population, high-performance system of epidemiological surveillance and algorithms for operational actions in case of unforeseen situations. According to the definition of WHO experts, elimination (eradication) of infection involves morbidity reduction to zero and asymptomatic cases of infection caused by a specific agent, in a certain geographical area as a result of thoughtful efforts. This requires a further extension of measures to prevent the spread of infection in case the diseases occurrence due to their importation from other territories [3,7].

It's worth studying dynamics of circulation and isolation of «wild» poliovirus strains in the risk territories during last years (surveillance period 1980–2016). Thus, in 1980, India recorded 18 975 cases of polio caused by «wild» strain of poliovirus, in Pakistan — 2 980, Afghanistan and Nigeria — about 800. 12 years later after the active vaccination campaign, the numbers of cases in India have fallen to 265, and from 2012 up till now morbidity caused by «wild» poliomyelitis is absent altogether. Over the past 3 years, it was noted that «wild» strains were still circulating in Afghanistan and Pakistan, fluctuating at the level of 50–200 cases annually; while in the territories of Nigeria above mentioned strain was practically absent (it was not isolated in 2015 and 2 cases in the current year), indicating a successful eradication program in conjunction with anti-epidemic activities and vaccination of the population of this African country. Summing up we should mention that the world dynamics in isolation of «wild» poliovirus is positively directed

to the reduction of quantity of cases from 52 795 in 1980 up to 23 in 2016.

Since most clinical cases of acute poliomyelitis are asymptomatic in immunocompetent individuals, experts recommend to investigate thoroughly every case of manifestation in the form of acute flaccid paralysis (AFP) in terms of poliovirus laboratory studies. Based on the surveillance results, experts of WHO report on the annual statistical indicators of AFP morbidity among populations of major surveillance regions. As of September 9, 2016, 67,105 cases of acute flaccid paralysis have been registered, at this the index of cancelled non-poliomyelitis AFP constitutes 5.25; on African continent, in 2016 two strains of «wild» virus (wild poliovirus, wPV) were identified from poliomyelitis patients, at the same time in 2015 there were 18 strains of vaccine-derived poliomyelitis viruses (circulated vaccine poliovirus, cVDPV). In total during 2016, 23 WPV strains and 3 cVDPV strains were officially isolated; for comparison, in 2015 there were 74 WPV and 32 cVDPV strains. Thus, there is a positive dynamics towards circulation intensity reduction of «wild» as well as vaccine-derived strains of poliovirus in the world [8,12,13].

According to the weekly monitoring data, situation in Ukraine during the period from January 2015 till May 2016 is as follows: 124 cases of AFP, level of cancelled non-poliomyelitis cases makes 03.05, vaccine-derived strain is confirmed in two cases, «wild» poliovirus is not separated. For comparison, during the stated period AFP outbreak also occurred in Guinea, Myanmar and People's Democratic Republic of Laos.

On the recommendation of WHO experts (July, 2015) in order to increase the sensitivity of epidemiologic surveillance system in detecting circulating vaccine-related polioviruses (cVRPV) now it is needed to use the following new standard definition of the latter:

– Genetically related poliovirus strains separated from:

1) not less than two persons (not mandatory ill) who don't have family relations;

2) from one person out of one or more samples of the environment's objects within the limits of epidemiologic surveillance depending on his condition;

3) from two or more samples from environment if the sampling was carried out in more than one separately located sampling area (in the event of absence of partially overlapping areas covered by the epidemiologic area) or in the same area

**Characteristics of polioviruses monitoring in water samples in Ukraine for the period from 2010 to 2014 (By I.V. Demchyshyna)**

Year	AFP	VAPP	Isolation PV from VAPP patients
2010	130	1	PV2-1 case (2 samples)
2011	127	2	PV3-2 cases (4 samples)
2012	121	1	PV2-1 case (2 samples)
2013	121	0	—
2014	135	1	PV2-1 case (2 samples) DPV2!!!

if the sampling was carried out with the interval more than two months;

4) from one VRPV isolate with genetic characteristics that indicate the persistent circulation (i.e. when the quantity of nucleotide shuffling proves the autonomous circulation during 1.5 years and longer).

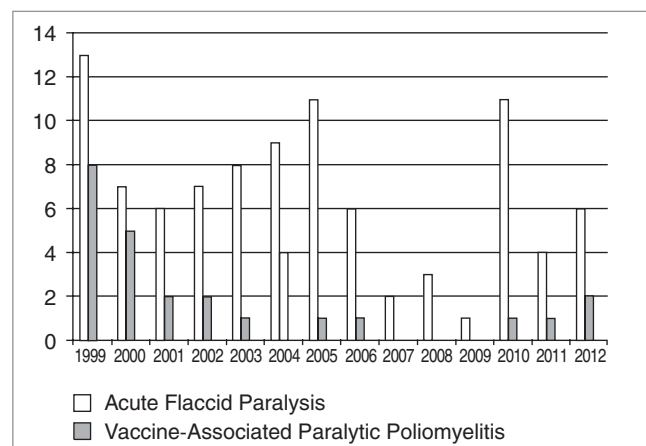
The materials of the 7th meeting of the Independent Monitoring Board, Ukraine is the only country in the European region having a high risk status along with the countries of the Horn of Africa, Kenya, Libya, Somalia, Uganda and Yemen.

It is recommended in the shortest possible term to rectify the situation regarding the level of coverage with three vaccinations and carry out «additional» immunization of those children in Ukraine who have not received age vaccination complex.

Monitoring of polio- and other entero viruses circulation in water samples was investigated in Ukraine by I.V. Demchyshyna for the period from 2010 to 2014 (Table 1).

Thus, only in 2012, 3 373 samples were examined and the share of enteroviruses was 2.1% and in 2013 – 3 063 samples with the enteroviruses share of 3.3%. Polioviruses circulation level in the water samples has increased from 18% in 2011 up to 35% in 2013.

Let's study three vaccination coverage of 1-year old children from 2007 to 2015: we noted a



**Fig. 1.** Dynamics of AFP cases related in time to OPV and VAPP (1999–2012)

strong tendency in decline of vaccination coverage level from 98% in 2007 to 57% in 2010, 42% in 2014 and critically low index – about 18% in the first 7 months of 2015. Thus, the of vaccination level in first year infants was gradually declining due to anti-vaccination campaign in the mass media, distrust in the health care system, reduction of social and economic welfare of population and others. It's necessary to establish the cause and effect relation between this and AFP morbidity (fig. 1).

In Ukraine the injection of the first IPV dose to children with counterindications to OPV correlates with the epidemic situation starting from year 2000; that is to say AFP morbidity decreased almost twice, and compulsory injection of two first doses of IPV for all children led to even bigger decrease of AFP up to level 5 (in extensive indices) during 2007–2009.

Thus, AFP related to the circulating vaccine-derived poliovirus according to the opinion of WHO experts [10] was of Ukrainian origin (Transcarpathian Region). The decision was made to abandon the trivalent vaccine and introduce a bivalent inactivated vaccine to a vaccination calendar that did not contain killed poliovirus component Type II, which could cause more frequent impairment of the nervous system. Ukraine came under special risk of poliovirus expansion due to the extremely low level of vaccination – only 50% of children were vaccinated in 2014.

Thus, the Ministry of Health of Ukraine initiated additional immunisation rounds on the request of the European Bureau of WHO as the response to the outbreak of cVRPV1 caused by tOPV. For the period from October 2015 to February 2016, 64.4% of children at the age from 2 months to 6 years were vaccinated; in the second round (11.30.15 – 19.12.15) – 71.7% of children of a similar age group, and the third round of additional immunization was conducted from 01.25.16 to 26.02.16 engaging 80.7% of children under the age of 10 years.

Epidemiological analysis of the situation at that time allowed formulation of certain conclusions on the fulfilled mass vaccination, i.e. Immunisation days (on WHO request) against poliomyelitis.

1. Only the principle of collective protection was taken into consideration. Individual protection was not considered.

2. Children aged from 2 months up to 10 years had to be the target population in the first round.

3. Autumn definitely decreased the effectiveness of the measures. It was initially planned to

finalise all three rounds till the end of the year but the third round had to be shifted till the end of January 2016.

4. The start of the third round coincided with the announcement of flu epidemic when all collective activities had to be cancelled. Earlier, during such period all even planned vaccinations were cancelled as the child could be in the flue incubation period or fell ill in post vaccination period. It can have negative effect on the individual protection level, the course of the flue, increase the risk of post vaccination complications, promote negative attitude to vaccination and decrease in the vaccine coverage level.

5. There were a lot of problems with mass media.

6. Agitation campaign did not work.

7. Loyalty of medical specialists was not enough.

8. A lot of issues occurred with regard to the outbreak classification caused by the vaccine-related viruses.

9. Recommendations of WHO representatives sometimes were insistent without taking into consideration certain aspects (legal, social, medical, etc.).

10. It was not always that scientifically substantiated point of view was taken into consideration.

Results of mass children immunisation in Ukraine in 1996 proved that during two vaccination rounds against poliomyelitis (during one week in September and one week in October) approximately 2 mln. children in the age up to 3 years 11 months and 29 days received two doses of OPV (in total 3 939 596 vaccinations) at the coverage level of almost 99%.

In 1998 there were two rounds of mop-up vaccination against poliomyelitis (during 1 week of April and one week of May) with vaccination of more than 500 thousand children in the age up to 2 years 11 months and 29 days in eight regions of Ukraine and they received 2 doses of OPV (in total 1 037 942 doses) also at the level of almost 99%.

As a result of studying the state of population immunity to 3 types of polioviruses effectiveness of Immunization Days was significantly lower than the mop-up immunization.

Among the most significant reasons we would like to emphasize the following: wrong choice of the season for Immunisation Days (the highest level of non-poliomyelitis enteroviruses circulation, formation of new children collectives, and morbidity increase of acute respiratory and intestine infections).

At the same time mop-up immunisation was carried out based on the scientific grounds: prior seasonal increase of enteroviruses circulation, which contributed to the widespread expansion of vaccine polioviruses among the population and increase in the indices of specific population immunity, it was postponed for one month later due to continued rise in influenza epidemic.

### Conclusions

1. Due to difficult epidemic situation in Ukraine Recommendations of European Certification Committee on Poliomyelitis Eradication as of June 2, 2016 contain following stipulations:

- Take the necessary actions to speed up delivery of bivalent OPV to the country and ensure high coverage with IPV bOPV as part of routine immunization.
- Consider fulfilment of mop-up immunisation (additional rounds) for the regions with low coverage of round immunisation.
- Continue trainings on OPV and surveillance on the poliomyelitis and ensure achievement of the target index non-polio AFP not less than 3 per 100 thousand of population by means of increasing surveillance sensitivity.
- Strengthen supervision over environment, standardize requirements for all regions and monitor supervision effectiveness, primarily with regard to polioviruses identification.

- Update the country plan and allocate funds from the State Budget for its execution.
  - Carry out 12 month evaluation (preparation of country report in September 2016) to determine the status of 6 month evaluation recommendations.
2. Risk of poliomyelitis caused by the vaccine-related poliovirus (VRPV) requires termination of OPV administration in several stages:
- First stage – the synchronous termination of tOPV administration (April 18 – May 1, 2016)
  - Second stage – the substitution of tOPV by bivalent OPV (bOPV) containing only polioviruses of Type 1 and 3; as of August 31, 2016 already 173 (89%) out of 194 member countries of WHO use IPV. However, 20 countries managed to postpone introduction of IPV till the time when more adequate deliveries will become available, most probably up to 4th quarter of 2017. Beside this, 29 countries that introduced IPV earlier will receive next IPV delivery only at the end of 2017.
3. Termination of tOPV administration is the important step for finalisation of global efforts in poliomyelitis eradication.
4. However, monitoring of poliovirus and response to outbreaks must be permanent, so that to create a world free from this disease.

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