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The epidemiological situation in Ukraine in terms of the implementation of preventive vaccinations according to the Protective Vaccination Program

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ABSTRACT

The level of immunization of children and adolescents under the Protective Vaccination Program in Ukraine is lower than in Poland, and, due to the outbreak of the war in Ukraine, many people now live in conditions that are often unsanitary. Centers for refugees are also places of increased risk of outbreaks of infectious diseases. This risk is increased by the low percentage of the vaccinated, limited access to healthcare (including diagnostics) and overcrowding.

The paper presents the state of vaccination in Ukraine against poliomyelitis, measles, diphtheria, tetanus and pertussis, the most important problems in the field of infectious diseases, as well as the resulting risks and the need to prevent them.

INTRODUCTION

Even before the ongoing war, Ukraine was one of the least vaccinated countries in Europe. And the percentage of vaccinated children in Ukraine varied, depending on the age group and region of the country, from approximately 60% to 99% [1]. In Ukraine, vaccinations are undertaken according to the Protective Vaccination Program against 10 infectious diseases, i.e. tuberculosis, hepatitis B, diphtheria, tetanus, pertussis, *Haemophilus influenzae* type b, poliomyelitis, measles, mumps and rubella. These vaccinations are carried out for free by the age of 16 [2].

The vaccination contribution to the reduction in mortality from VPI (vaccine-preventable infections) is characterized by statistical and causal (epidemiological) accordance of indicators of incidence, mortality and lethality [3]. During the 1944-2015 period in Ukraine, the mortality reduction rate for VPI was very impressive. It ranged from 40.5 fold (tetanus) to 1,061.1 fold (measles). However, the incidence reduction rate was significantly lower in general and ranged from 42.4 fold (measles) to 471.1 fold (diphtheria). This is probably due to external factors unrelated to vaccines, including improved medical facilities, treatments and better health information collection, enhanced quality of life, the bettering of the environment, and so on. Importantly, the vaccination contribution to the reduction in infectious mortality was more significant for the pediatric population, among who the annual mortality from VPI is currently absent or very rare except for cases of tuberculosis.

According to WHO data, in 2020, in Ukraine, 81.9% of all children were vaccinated against measles, 84.2% against poliomyelitis, 81.3% against pertussis and 80.9% against hepatitis B. Moreover, there are large differences in the implementation of preventive vaccinations between large and small towns and in the countryside [4-6]. The state of vaccination in Ukraine in 2020 (according to the WHO) is lower than in Poland, and is:

- poliomyelitis: 84.2% (after administration of 3 doses of polio vaccine),
- measles: 81.9% (after 2 doses of MMR vaccine),
- tuberculosis: 92.7% (after administration of a dose of BCG vaccine),
- diphtheria/tetanus/pertussis: 81.3% (after three doses of DTP against diphtheria, tetanus and pertussis),
- *Haemophilus influenzae* type b (Hib): 85.2% (after 3 doses of vaccine against Hib),
- hepatitis B: 80.9% (after 3 doses of vaccine against hepatitis B),
- rubella: 84.9% (after administration of 1 dose of MMR vaccine against measles, mumps and rubella).

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The bad socio-political situation after 2010 has caused a few years of collapse of the preventive vaccination system. In 2008-2010, the proportion of the population of vaccinated children according to the compulsory vaccination schedule was very large (up to 90%), but it decreased significantly in subsequent years [7]. Between 2014 and 2016, only 20% of all children were vaccinated in accordance with the vaccination program, with the third dose of DTP against diphtheria, tetanus and pertussis [7]. The proportion of children vaccinated against measles also decreased and in 2010-2016 it was equal to only 31-57%, which means it was significantly below the threshold required to achieve population resistance (>95%), leading to an outbreak of measles epidemy in the years 2017-2019 (almost 100,000 cases were reported in Ukraine at that time). Although in recent years the implementation of compulsory vaccination in children in Ukraine has improved significantly (in 2019, the percentage of vaccinated children with a second dose of vaccine against measles was 92% and with the third dose of vaccine against poliomyelitis or DTP respectively 78% and 80%), vaccination against polio and measles in the population should be considered insufficient.

Poliomyelitis

Poliomyelitis is endemic in Pakistan and Afghanistan, but can be spread in every vulnerable population. In Ukraine, children are given both the inactivated poliomyelitis vaccine (IPV) and the oral, live OPV vaccine [4]. In Poland, in 2016, the oral OPV vaccine was replaced with the IPV vaccine [8]. The entire scheme of vaccination against poliomyelitis in Ukraine includes the administration of 6 doses of the vaccine: at 2 and 4 months of age (IPV vaccine doses), at 6 and 18 months of age, as well as at 6 and 14 years of age (OPV vaccine doses).

According to the WHO, the vaccination rate against poliomyelitis in Ukraine in 2020 was 84.2%. In children up to 1 year of age in the first 8 months of 2021, vaccination coverage was estimated at 53%. However, in 2021, disturbing information with regard to poliomyelitis has been reported. Two cases of paralysis of the limbs due to polio VDPV2 infection, i.e. type 2 of vaccine origin, have occurred. The infection was also detected in 19 people with no signs of paralysis. In Ukraine, there has been no infection with a wild strain of polio virus for many years.

In 2021, the risk of the disease spreading in Ukraine was assessed by the WHO as high due to historically low vaccination rates. The cases of polio in 2021 were the first since 2015. An educational campaign and supplementary vaccinations were planned with the participation of the WHO.

Measles

Measles is one of the first concerns in any humanitarian crisis. Ukraine had a large outbreak that started in 2017 and continued until 2020, with more than 115,000 cases [9]. By 2020, reported national coverage with two doses of measles-containing vaccine was up to 82%, according to the CDC.

In Ukraine, the MMR vaccine against measles, mumps and rubella is administered similarly to Poland in the form of 2 doses, at 12 months of age and at 6 years of age. The measles outbreak in Ukraine in 2017-2019 also had an impact on the state of immunization against this disease [6,10]. Most of the population is likely to have been exposed to the measles virus. Children of up to 2 years of age may not have been immunized, as they have not been yet vaccinated against measles.

A significant increase in the number of measles infections occurred in 2017, when a 47-fold increase in infection was recorded compared to the previous year. In 2019, the number of detected measles cases exceeded 57,000, as a result of a decline in childhood immunization coverage [6]. While in the first decade of the 2000s, the percentage of persons vaccinated with the first and second dose of the MMR vaccine fluctuated in Ukraine between 94% and 99%, in the second decade it dropped by several dozen percent. In 2016, only 43% of all children received one dose and only 37% received the second dose. In 2020, more than 80 percent were vaccinated with the second dose. However, this is not enough to establish population immunity, which in the case of measles must be at least 95%.

Pertussis

The pertussis morbidity cycle has 5 years intervals in Ukraine [11]. The prognosis is for increasing the pertussis morbidity from 4.91-5.54 to 5.48-7.06 per 100,000 people. The generalized coefficient was significantly higher in the western part (83.3%) than in the central (50.0%) and eastern (16.6%) parts of the nation. The study also showed that population reproduction rates, natural population increase, and the proportion of people against vaccination were higher in the western part than in other parts of the country.

The pertussis cyclicity depends on the internal mechanisms of interaction in the ecological system. There is a prognosis of worsening in the epidemic situation of pertussis spreading. The risk area is the western part of Ukraine, which is characterized by active demographic processes and a greater number of people who are negative about vaccination.

In 2015-2017, most Ukrainian children did not receive the third dose of this vaccine. Improvement came in the following years, but still needs to be optimized, especially as there are still many cases of pertussis in Europe.

Diphtheria

Diphtheria is a dangerous and life-threatening disease in humans with a high mortality and disability rate. Immunization is the only means of creating a favorable epidemic situation.

Diphtheria remains endemic in many parts of the world. In 2018, the WHO recorded 16,611 reported cases. Generally, diphtheria is under-reported from many regions, including Asian, African and the Eastern Mediterranean countries [5].

The WHO reports that epidemic situation in diphtheria morbidity has worsened in the world, particularly in Latin America, where a rise in incidence has been recorded since 1990s [10].

In Ukraine, Rubtsova *et al*. [12] carried out a retrospective analysis of the incidence of diphtheria, the carriage of infection, vaccination coverage and the severity of diphtheria immunity of the Transcarpathian region. The authors

concluded that in view of the low coverage of the population with vaccination against diphtheria, and the registration of an outbreak of diphtheria among international students of the region (and in other regions of Ukraine), and a situation of increased population migration, the possible development of another significant epidemic rise of diphtheria morbidity in Transcarpathia exists.

Acute respiratory tract infection

Detection of viral seasonality in Ukraine and estimating of clinical features in case of infection allows predicting the probable clinical course of disease, so as to provide medical care, to optimize the therapy and to develop preventive measures, vaccination, in particular.

The presence of potential pathogens of ARTIs in children in Ukraine was tested in 487 children in the MC "Eurolab", Kyiv, Ukraine between 2018-2020, by Khomenko *et al.* [13]. Seven respiratory viruses: Respiratory Syncytial virus (RSV), Parainfluenza virus (PIV), Adenovirus (AdV), human Metapneumovirus (MPV), Rhinovirus (RV), human Bocavirus (BoV), Coronavirus (CoV), were identified by PCR. Qualitative detection of Influenza type A, type B, Group A Streptococcal infection was also performed. In 487 nasal and throat swabs from children with ARVI, 400 (82.1%) samples were found to be positive. A total of 403 viruses were identified. RV (27.1%), ADV (13.4%), RSV (13.2 %), IVA (10.7 %) were the most commonly identified viruses.

Hepatitis A

In 2019, the age-standardized incidence rate of hepatitis A differed dramatically between countries or regions [14]. For example, Africa, South Asia, and several countries located in Latin showed the highest rates [15]. Considering the transmission route of HAV, increasing the availability of clean water and food resources can help minimize the burden of AHA in the low- and low-middle income economic areas of the world. The Sustainable Development Goals, which include increasing access to water and sanitation, may enhance the reduction of HAV infection. The war in Ukraine has caused many people to live in conditions that are usually unsanitary, which may increase the number of infections with hepatitis A virus, which spreads by the fecal oral route.

Hepatitis B

Before hepatitis B vaccine introduction, the level of endemicity of hepatitis B virus (HBV) in Ukraine was estimated as intermediate, but the prevalence of HBV infection markers has not been measured in population-based serosurveys [16]. Coverage with 3 doses of Hepatitis B, introduced in 2002, was 92%-98% during 2004-2007, but declined to 21%-48% during 2010-2016. HBV prevalence among children in surveyed regions of Ukraine in 2017 was low, including in Zakarpattya, the only site above the 0.5% European Regional target for HBsAg seroprevalence. However, Hepatitis B vaccination was suboptimal, particularly among children born after 2009, resulting in large numbers of unvaccinated or incompletely vaccinated children at risk of future HBV infection.

Tuberculosis

Ukraine has the fourth-highest TB incidence in the WHO European Region and the fifth-highest number of confirmed cases of extensively drug- resistant TB in the world [17]. Since the Russian invasion on Feb 24, Ukraine's health-care system has come under increasing pressure amid relentless bombardment of cities and targeting of hospitals and health-care workers by Russian forces. In Ukraine, the BCG vaccine against tuberculosis is administered similarly to Poland in the form of 1 dose in the first day after birth. According to the WHO, the vaccination rate with BCG vaccine in Ukraine in 2020 was 92.7%. Ukraine has one of the world's highest burdens of multidrug-resistant (MDR) TB [18]. An estimated 32.000 people there develop active TB each year, and about one-third of all new cases are drug resistant. Twenty-two percent of people in Ukraine with TB are infected with HIV, and TB is the leading cause of death among those living with HIV.

HIV

Eastern Europe and Central Asia (EECA) remains the region with the highest increases in HIV incidence and mortality, surpassing Southern and Eastern Africa [19]. Ukraine bears the second-largest HIV epidemic in Eastern Europe and Central Asia - with an estimated 240-750 registered cases in 2018, 3,448 AIDS related deaths and 15,787 newly diagnosed HIV cases [20]. Ukraine is seeing both increasing HIV incidence and mortality [21]. The Ukrainian Center for Public Health (UCPH) provides aggregate data on the annual number of new HIV diagnoses for three age groups, stratified by sex: 15-24 years; 25-49 years; and ≥50 years (i.e., older adults) for the years 2015 (N=12,893), 2016 (N=14,249), 2017 (N=15,580), and 2018 (N=15,671). Of 13,286 young people aged 10-24 years registered for HIV care nationally in Ukraine in January 2016, 1,675 were aged 10-18 years. In addition, released statistics indicate that 72% of all 20-24-year-olds had a sexually-acquired infection. Moreover, five regions accounted for two-thirds of all 10-18 year olds in paediatric and 85% of all 19-24 year olds in adult services [22]. Beyond the aforementioned, older adults comprise an increasing proportion of newly identified cases, clinically present with significantly more advanced HIV, and are at significantly increased risk of death within the first year of diagnosis [23].

COVID-19

According to Ukraine's Ministry of Health, as of February 24, 2022, confirmed cases of the disease include 4 809 624 persons, while 105 505 have died of the disease (February 24, 2022) [2]. Vaccination of adults against COVID-19 in Ukraine began in February 2021 and the estimated vaccination rate of adults is approximately 35% (data as of 02/23/2022). In terms of vaccination against the SARS-CoV-2 virus, Ukraine is in one of the last places in Europe. Six vaccines were used in the adult COVID-19 vaccination program in Ukraine: Spikevax (Moderna), Comirnaty (Pfizer-BioNTech), COVID-19 Vaccine Janssen, Vaxzevria (AstraZeneca), Covishield (the equivalent of AstraZeneca), CoronaVac (Sinovac) – the equivalent of Nuvaxovid

(Novavax). Vaccination against COVID-19 in children and adolescents aged 12-17 in Ukraine began in July 2021. The Comirnaty (Pfizer/BioNTech) vaccine was used. During this period (as of February 23, 2022), 193,380 vaccinations were performed in the age group of 12-17 years: 55,834 administered doses in the 12-15 years group and 137,546 administered doses in the 16-17-year-old group.

Preventing the spread of infectious diseases

Infectious diseases are likely to spread as Russia's invasion displaces people and disrupts health services. Since the escalation of aggression that began on 24 February 2022, many millions of people have fled Ukraine to Poland, Hungary, Moldova, Romania and Slovakia, according to the UN Refugee Agency (UNHCR). While the majority of those arriving are being dispersed into the community or are in transit to other countries, an increasing number of displaced people arriving in EU/EEA countries are also being hosted in reception centers, where there is a higher risk of communicable disease outbreaks [22]. Refugee centers are, therefore, places of increased risk of outbreaks of COVID 19 and other infectious diseases. This risk is enhanced by the low percentage of the vaccinated and limited access to healthcare (including diagnostics), as well as overcrowding.

With the outbreak of the war in Ukraine, over 2 million refugees have come to Poland, mainly children, young women and the elderly. People who work or stay with refugees on a daily basis are particularly vulnerable to infections – volunteers, people hosting Ukrainians, those working in aids centers [22-24]. The group of high risk of infections are people with reduced immunity, especially hemato-oncological patients, oncological patients, patients after transplantation, as well as people not responding to vaccinations, the so-called 'non respondents'. Another risk group includes children who have not yet received all vaccinations provided for in the immunization schedule. These people should be vaccinated and receive a booster dose of diphtheria, tetanus, pertussis (DTP) vaccine, as well as polio and MMR - rubella, measles, mumps - if they have not been vaccinated with 2 doses. Moreover, hepatitis A vaccination may be considered. Most refugees are not vaccinated against COVID-19. They also include people from high-risk groups, i.e. the elderly, obese, with chronic diseases and a weakened immune system. Considering the number of refugees arriving in neighboring countries, especially Poland, measures to promote vaccination against COVID-19, not only among refugees, but also Poles, are urgent. This is even more important, as restrictions have been lifted. SARS-CoV-2 is a virus that shows seasonality in temperate climates, which is why in autumn there may be an increase in the number of infections. For this reason, vaccinating as many Polish residents as possible, regardless of nationality, is important so that the growing number of infections does not mean another increase in hospitalization and deaths. The Team for Protective Vaccinations of the Ministry of Health recommends immunization of children up to 19 years of age who are not vaccinated against infectious diseases according to the Individual Vaccination Calendar established by the doctor qualifying for vaccination on the basis of the preventive vaccination program for 2022. Of note, compulsory vaccinations in accordance with the preventive vaccination program will cover all children from Ukraine who will stay in Poland for more than three months from the date of crossing the border.

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