POST-VACCINATION IMMUNITY: FORMATION AND ASSESSMENT OF EFFECTIVENESS IN THE POPULATION OF THE KHARKIV REGION

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Summary

A complex mosaic of immune responses was identified among the population of the Kharkiv region during the administration of combination vaccines designed to prevent multiple infectious diseases. The majority of vaccinated individuals respond adequately to several components of combined vaccines simultaneously; however, groups of individuals can invariably be identified who exhibit either weak or strong responses to one, two, or several vaccine antigens included in the formulation. Assessment of immune system status is most appropriately conducted both upon completion of the primary immunisation schedule and thereafter. This makes it possible to decide whether further booster vaccinations may be unnecessary or, conversely, to determine the need for enhancement of the immune response. The implementation of serological monitoring would enable a more accurate determination of the true levels of herd immunity across different social groups and regions, facilitate the management of vaccination schedules, assess the effectiveness of vaccines and vaccination programmes, and allow the estimation of the quantities of vaccines, diagnostic tools, medicinal products, and public health efforts required to ensure comprehensive population protection.

Key words: effectiveness of specific prophylaxis against vaccine-preventable infectious diseases, serological monitoring.

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1. Introduction

Until recently, medical practice in the field of vaccinology was based on the principle that all individuals within a population should be immunised according to a universal vaccination schedule using the same set of vaccines, provided that no contraindications existed. Several assumptions underlie this approach. One such assumption is that every individual will produce similar levels of protective antibodies, with an almost negligible incidence of associated adverse effects. It is also assumed that all individuals have approximately the same level of protection against disease and that the vaccine doses and the number of doses required to induce robust immunity are identical across the entire population. The primary objective of

this approach was the paradigm of population-level immunity, which has enabled the control of many infectious diseases to a certain extent. The main limitation of this approach is that it ignores individual variability in immune responses to different types of vaccines, as well as any genetic predisposition to reactogenicity, and differences in the doses and immunisation schedules required to establish strong and long-lasting immunity *(Smilianska, 2022).*

At present, advances in immunology, genetics, molecular biology, and bioinformatics demonstrate the value of a personalised approach to vaccine selection and dosing. Consequently, a new paradigm in vaccinology is emerging between the traditional population-based public health perspective and a new individual-level approach that recognises unique interindividual variations in responses to biological agents *(Montero, 2024; Poland, 2018).* Mass-specific prophylaxis of vaccine-preventable infectious diseases is aimed at establishing herd immunity. Its effectiveness is assessed through serological monitoring. The results of such monitoring indicate that, even in the presence of herd immunity, there are always groups of individuals who do not possess protective antibody levels *(Pollard, 2020).* This highlights the need to identify such individuals and to correct or optimise their immune responses to vaccines. In other words, this involves the individualisation (personalisation) of vaccination strategies *(Kennedy, 2020).*

2. Characteristics of Post-Vaccination Immunity to Hepatitis B

At present, among all known parenterally transmitted hepatitis infections, only hepatitis B (HBV) can be prevented through vaccination. One of the criteria for assessing the immunological effectiveness of hepatitis B vaccine prophylaxis is the level of humoral immune response, characterised by the frequency of detection of specific antibodies (anti-HBs) at protective concentrations against the vaccine antigen.

We analysed the effectiveness of hepatitis B vaccination and the actual level of protection among vaccinated children, adolescents, and healthcare workers, depending on the time elapsed since the last hepatitis B vaccination, age, and the immunisation schedule used. As the interval since the last hepatitis B vaccination increased, the level of post-vaccination immunity among vaccinated individuals declined. Thus, 12–36 months after completion of the vaccination course, the proportion of seropositive individuals was 93.9%; after 3–6 years, it decreased to 89.2%; and after 7 years or more, it fell to 77.5% (Table 1).

The obtained results were consistent with published data indicating that, within 5–7 years following completion of the recommended vaccination course, 30–50% of individuals lose detectable antibodies. Among vaccinated children and adolescents, seroconversion was observed in 92.7–100% of cases within 3–84 months after the last vaccine dose. However, with increasing time since vaccination (more than 7 years after the last dose), the proportion of seropositive individuals decreased substantially, reaching 65%. Overall, regardless of the time elapsed since the last vaccination, the proportion of children and adolescents with specific antibodies to HBsAg detected in blood serum was 90.8%.

Indicators of the immunological effectiveness of vaccination among healthcare workers who had completed the full course of hepatitis B immunisation did not reach the normative level (82.1% versus a required minimum of 90%), irrespective of the time elapsed since immunisation. In children and adolescents, these indicators significantly decreased after the end of a seven-year period (65%, compared with the group average across time intervals of 90.8%). An important factor influencing the immune response is the age of vaccinated individuals. The maximal immune response is observed between 2 and 19 years of age, as well as in young adults. Newborns demonstrate a comparatively weaker immune response. The weakest immune

response is observed in elderly individuals from the age of 60 onwards, where seroconversion is detected in only 65–70% of vaccinated persons *(WHO, 2019)*. However, according to other studies, hepatitis B vaccination provides protection against infection for at least 15 years across all age groups. Antibody titres decline more rapidly in individuals vaccinated before the age of four *(Batra, 2015)*. A meta-analysis published in *Clinical Infectious Diseases* reported that the risk of vaccine failure increases with age *(Van Damme, 2016)*. It was found that the risk of vaccination failure in elderly patients is 1.76 times higher than in younger individuals, with half of the studies demonstrating a significant reduction in immune response in older populations. The association between age and vaccine failure remained relatively consistent even when the upper age threshold was set at 30 years.

Table 1

Dynamics of anti-HBsAg seroconversion rates (%) in different population groups according to the duration of the post-vaccination period

Population group		Post-vaccination period					Total
		2 mths	4 mths	1 yr – 2 yrs 11 mths 29 days	3 yrs – 6 yrs 11 mths 29 days	7 yrs and more	
Children and adolescents	Seropositive individuals (% [CI])	100	100	97,4 [95,2–99,6]	92,7 [89,7–95,7]	65 [55,8–74,2]	90,8 [88,6 – 93]
Healthcare workers	Seropositive individuals (% [CI])	–	84,7 [74,3–95,1]	84,2 [75,7–92,7]	80,7 [73,6 – 87,8]	81,8 [77,4 – 86,2]	82,1 [78,8 – 85,4]
Total	Seropositive individuals (% [CI])	100	93,6 [89 – 98,2]	93,9 [91–96,8]	89,2 [86,2 – 92,2]	77,5 [73,4 – 81,6]	87 [85,1 – 88,9]

In our study, the proportion of seronegative individuals among vaccinated healthcare workers in the age group 18–30 years (10.8%) and 30–40 years (8.2%) was two times lower than in the 40–50 years group (20%), and three times lower than in those aged 50 years and older (32.2%, $p < 0.05$). Thus, among healthcare workers, an age-related decline in the proportion of individuals with a protective antibody level was observed: from 90.8% in the 18–40 years age group to 67.8% ($p < 0.05$) among individuals aged 50 years and older. The criterion of epidemiological safety for hepatitis B (no more than 10% seronegative individuals and those with antibody concentrations below 10 IU/L) was achieved among children and adolescents, as well as healthcare workers under the age of 40, irrespective of the time elapsed since the last vaccination.

The strength and persistence of post-vaccination immunity depend on the time since the last vaccination, age, and even the immunisation schedule used. The conducted studies showed that the proportion of individuals with a protective anti-HBs antibody titre among vaccinated healthcare workers reached 82.1% (standardised benchmark: not less than 90%), while 17.9% were seronegative. Among the staff, individuals with antibody concentrations of 11–100 IU/L constituted 51.1%, whereas those with high antibody concentrations (101–500 IU/L) accounted for 48.9%. The geometric mean titre among the examined healthcare workers was 79.6 IU/L.

In the context of mass vaccination programmes, the strategy of annual preventive screening of healthcare workers for hepatitis B markers should be reconsidered, and a booster vaccination strategy should be introduced according to the following scheme:

- implement screening of vaccinated individuals from high-risk groups with occupational exposure to biological fluids, as well as those with a high risk of skin or mucosal barrier disruption, for anti-HBs antibodies one year after vaccination and annually thereafter. Seronegative individuals should be tested for HBsAg to exclude hepatitis B infection;
- seronegative healthcare workers should receive a single booster dose, followed by serological control after three months. If the result remains negative, a second booster dose should be administered. If such individuals remain negative during subsequent annual anti-HBs screening, further immunisation should be discontinued, and they should be reassigned to work not associated with risk of hepatitis B virus exposure;
- vaccinated individuals not belonging to risk groups should be tested for anti-HBs after five to seven years; seronegative individuals should be tested for HBsAg to exclude infection. Booster vaccination should be administered to seronegative vaccinated healthcare workers, with subsequent serological control after three months;
- unvaccinated individuals against hepatitis B should be tested for anti-HBs and HBsAg in the first year of employment, followed by annual testing throughout their professional activity.

3. Serological Assessment of Population Susceptibility to Measles, Rubella and Mumps Viruses

The increase in measles incidence has raised concerns within the medical community regarding the reliability of key indicators used to assess the effectiveness of vaccination programmes. A number of hidden factors of different origins have been identified that negatively affect vaccination quality, including breaches in the cold chain, unjustified medical exemptions from vaccination, an increasing number of parental refusals to vaccinate children, and deviations from recommended vaccination schedules *(GBD, 2023).*

According to many authors, the main cause of the worsening epidemiological situation with regard to measles is the accumulation of susceptible individuals within the population, i.e. a decline in population immunity. The only and most effective method for its assessment is serological monitoring *(Karadeniz, 2020).*

Within such monitoring, based on laboratory analysis of serum samples, the proportion of susceptible (seronegative) individuals to vaccine-preventable infections is calculated. The criterion of epidemiological safety for measles and rubella is the presence of no more than 7% seronegative individuals in the examined group, while for mumps this threshold is 15%.

The results of the study on the level of population immunity to vaccine-preventable infections among different population groups are presented in Table 2.

As can be seen, with regard to rubella, all examined population groups are sufficiently protected: the proportion of seronegative individuals does not exceed the epidemiological safety threshold of 7%.

A substantial proportion of susceptible individuals to measles infection was identified among the examined groups. The most susceptible group was military personnel, where the proportion of seronegative individuals was maximal and amounted to 25.8%, which is 3.6 times higher than the epidemiological safety criterion. Among healthcare workers, on average 7.6% of individuals were susceptible.

Among healthy individuals, a considerable proportion (21.6%) consists of persons who, under certain conditions (in the event of introduction of the infection into the region), may contribute to measles transmission and the formation of outbreak clusters, including within closed

settings such as military collectives. Thus, the current epidemiological situation regarding measles may be characterised as unstable.

Table 2

Population immunity levels to measles, rubella and mumps among selected population groups in Kharkiv city and region

Population group	Seronegative proportion for measles virus, % [95% CI]	Seronegative proportion for rubella virus, % [95% CI]	Seronegative proportion for mumps virus, % [95% CI]
Healthcare workers (n = 66)	7, 6 * [3,6; 14,1]	5, 3 [1,9; 10,8]	20, 7 [13,6; 29,0]
Military personnel (n=70)	25, 8 [19,8; 31,8]	4, 7 [2,2; 8,2]	29, 8 [23,6; 36,1]
Healthy individuals (n=100)	21, 6 [16,2; 27,0]	8, 8 * [5,6; 13,3]	32, 5 [26,3; 38,6]
Total (n=236)	**19, 5 [16,2; 22,9]**	**6, 6 [4,6; 8,8]**	**28, 8 [25,1; 32,7]**

Note. * – differences compared with the epidemiological safety criterion (7%) are statistically non-significant ($p > 0.05$).

In all examined population groups, a substantial proportion of individuals susceptible to mumps was identified (29.8% among military personnel and 32.5% among other groups), which is on average twice as high as the epidemiological safety criterion for this infection (no more than 15%) and creates conditions conducive to disease spread.

Based on the obtained data, it may be stated that susceptibility to rubella in sentinel groups and in the population as a whole is low and meets the epidemiological safety criterion for this infection (the average proportion of seronegative individuals was 6.5%). These findings are consistent with official statistical data indicating sporadic rubella incidence. It is important to note that over the past five years, the proportion of seronegative individuals to rubella in sentinel groups has remained unchanged, which is also a favourable prognostic indicator.

There is a likelihood of measles spread in the event of its introduction into the country, as in all examined groups the proportion of susceptible individuals does not meet the epidemiological safety criterion (on average 19.5%). Military personnel were found to be the most vulnerable group, with 25.8% seronegative individuals. Regarding mumps, the obtained results indicate a substantial "immunological potential" for the spread of this infection within the population, as the highest proportion of susceptible individuals was observed among healthy persons (32.5%), with an overall average of 28.8% across all examined groups. According to official statistics, mumps incidence demonstrates a clear increasing trend, although it is still characterised by sporadic occurrence.

Measles, rubella, and mumps are generally considered viral infections with a similar epidemic process, for which live attenuated vaccines are administered according to the same schedule (vaccination at 12 months of age and revaccination at 6 years). However, the differences observed by us and other researchers in the proportion of susceptible individuals to these infections may be attributed to the varying immunological effectiveness of the measles, rubella,

and mumps components of the vaccine. According to international researchers *(Coppeta, 2020),* the effectiveness of MMR vaccine components is 97% (range 67–100%), 97% (94–100%), and 88% (66–95%), respectively.

Although insufficient vaccine coverage is a clear and primary cause of many outbreaks, primary and secondary vaccine failure also plays a significant role *(Lubanda, 2024).* A decline in population immunity, regardless of its explanation, inevitably leads to an increase in incidence and the occurrence of outbreaks, as observed in Ukraine, Europe, and the United States. In outbreaks in developed countries, previously vaccinated individuals have been involved in many cases *(Liang, 2025).* Thus, within the system of epidemiological surveillance of MMR infections, under conditions of high vaccination coverage at scheduled time points, serological monitoring of population immunity is of primary importance.

Monitoring the state of population immunity over time through seroepidemiological studies allows not only the assessment of vaccination effectiveness but also the prediction of future epidemiological trends and the planning of preventive measures. Our results indicate the need to organise additional immunisation campaigns targeting unvaccinated populations, particularly military personnel. The presence of a large number of individuals susceptible to mumps across different population groups suggests a potential deterioration of the epidemiological situation in the near future, and preventive measures to avert mumps outbreaks can already be planned. The epidemiological situation regarding rubella is favourable, indicating the potential for disease elimination in the future.

4. Serological Monitoring of Immunity to Diphtheria, Tetanus and Pertussis

Morbidity and mortality associated with infectious and non-infectious chronic somatic diseases necessitate continuous improvement of vaccination strategies. This is driven by a steady increase in the number of cases among vaccinated individuals, a higher incidence of childhood infections in persons over 18 years of age, an increased frequency of post-infectious complications, rapid waning of vaccine-induced immunity with age, high lethality and the development of complications leading to disability, as well as the challenges associated with inducing strong immunity in elderly individuals *(WHO, 2025).* Effective control of infectious diseases requires achieving a population protection level exceeding 95%. Weak immune responses and lack of protection against infectious diseases create a niche for pathogen circulation and serve as a source for the development of epidemics and pandemics *(WHO, 2025).*

An important step towards addressing these challenges is the comprehensive study of the post-vaccination process, which involves all regulatory systems of the organism, as well as the nature of immunological changes depending on the overall physiological condition of the body *(Mantel, 2020).*

It is well established that the immune response to vaccine administration is not monospecific. The response to combination vaccines is considerably more complex, and following administration of such preparations, specific antibodies are produced against multiple antigenic determinants. The development of sustained immunity to infections depends not only on the quality of the vaccine preparations used, but to a greater extent on the immunoreactivity of the vaccinated individuals *(Boey, 2021).* The resistance of the organism to infectious agents is known to depend on both innate and acquired (adaptive) immune responses *(Liang, 2018).*

The aim of the study was to investigate, using the ELISA method, the immunological structure of the population of Kharkiv city and region with regard to specific immunity to diphtheria, tetanus and pertussis.

In examining the effect of vaccination on the level of population immunity, it was found that in children aged 7 and 14 years the level of anti-pertussis immunity decreased, and the proportion of individuals lacking immunity amounted to 33.3% and 27.3%, respectively, whereas at the ages of 8 and 15 years this indicator was 5.6–7.7% (Sommer's d = –0.224, p = 0.004). With regard to the adult population, as shown in Table 1, from the age of 20 years onwards the proportion of individuals without immunity to pertussis increased, indicating a significant negative correlation between age and the level of immunity to pertussis (Sommer's d = –0.371, p < 0.000). According to our data, the proportion of immune individuals to pertussis in the overall population was 82.0% (Table 3).

Table 3

Distribution of examined individuals by age and level of immunity to Bordetella pertussis, Corynebacterium diphtheriae and Clostridium tetani

Age group, *years*	**Number of individuals,** *n*	**Level of immunity (%) pertussis /diphtheria /tetanus**								
		absent			**weak**			**sufficient**		
< 1 year	66	7,6	4,5	1,5	27,3	6,0	7,2	65,1	89,5	91,3
1–4	96	12,7	0,0	6,4	27,1	10,2	6,6	60,2	89,8	87,0
5–9	72	18,5	0,0	6,8	42,4	17,4	6,1	39,1	82,6	87,1
10–14	65	12,3	0,0	13,1	35,4	4,6	12,3	52,3	95,4	74,6
15–19	48	4,2	0,0	8,6	43,8	4,2	10,2	52,0	95,8	81,2
20–29	53	17,8	1,4	1,7	38,4	4,1	2,3	43,8	94,5	96,0
30–39	58	19,0	1,7	2,4	39,7	13,8	2,1	41,3	84,5	95,5
40–60	77	54,5	0,0	1,8	28,6	11,7	1,9	16,9	88,3	96,3
Total	**535**	**18,0**	**0,7**	**5,3**	**33,0**	**9,6**	**6,1**	**49,0**	**89,7**	**88,6**

The proportion of the population with weak immunity against diphtheria aged 1–9 years is 10.2–17.4%, then decreases to 4.6–4.1%, and rises again in individuals aged 30 years and older. Overall, the higher level of immunity against diphtheria compared to tetanus is probably associated with the mass vaccination against diphtheria carried out in 1995, which covered over 1.5 million people aged 3–40 years (vaccination coverage reached 94.4–95.9% of the population).

An analysis of the data presented in the table shows that the proportion of individuals non-immune to tetanus is low among infants in their first year of life who received the DTP (diphtheria, tetanus, and pertussis) vaccine. Subsequently, the proportion of non-immune individuals in the population increases to 13.1% in the 10–14 age group and then begins to decline, presumably as a result of natural immunisation. Overall, specific immunity to tetanus toxin was 94.7%.

The majority of the adults we examined possessed protective antibody titres against diphtheria and tetanus. A significant proportion of them had high antibody titres, indicating the presence of robust immunity. The results obtained demonstrate a high level of anti-diphtheria and anti-tetanus immunity, which can be considered a result of the revaccination of the adult population against these infections. Conversely, the majority of the adults we examined had low anti-pertussis antibody titres. Mean anti-pertussis antibody titres in adults were significantly lower than those in the vaccinated young children we examined, indicating the need to develop vaccination programmes for adolescents and adults.

5. Conclusions

The effectiveness of specific prophylaxis against vaccine-preventable infectious diseases is typically assessed through serological monitoring, which is currently not implemented on a systematic basis. Results of such monitoring over the past year have shown that, even under conditions of established herd immunity, certain population groups remain without protective levels of antibodies. The immune response to vaccination is highly individual. Individuals who respond poorly to one vaccine may respond adequately to another. A weak immune response is manifested by low antibody levels that do not ensure sufficient protection against infections, thereby creating conditions for the circulation of bacterial and viral pathogens.

Another aspect of the problem is over-immunisation. Continuous circulation of certain pathogens within the population may contribute to the natural development of immunity even in the absence of vaccination. In some individuals, a high baseline level of antibodies is observed, rendering even primary vaccination unnecessary. In certain cases, after the first vaccine dose, antibody levels increase significantly, eliminating the need for further revaccination. At the same time, there are situations in which, following booster vaccination, antibody levels do not increase and may even decline to minimal values. This highlights the importance of identifying such individuals and correcting their immune response to vaccination. Thus, there is a clear need for a personalised approach to immunisation.

Adjustment of immune status based on antibody titres in individuals at increased risk is a feasible and practical task. An individualised approach to vaccination may involve the selection of specific vaccines from among similar preparations, optimisation of dosage, selection of the most appropriate administration schedules, and the use of adjuvants or other immunomodulatory agents. At the same time, each vaccine has its own specific properties, which determine a distinct approach to immunological correction.

Current methods for assessing population-level protection against infections (based on vaccination coverage and morbidity data, which do not ensure relevance to the overall population) do not, either individually or collectively, provide an accurate representation of true population immunity and cannot serve as reliable predictive tools. Moreover, existing serological studies are often fragmentary and local, and therefore contradict the principles of global coverage, continuity, and data uniformity.

The ongoing state of war, the increasing complexity of modern vaccination schedules, population migration and ageing, and vaccine hesitancy driven by various factors necessitate the implementation in Ukraine of a dedicated system for monitoring the population's specific serological profile. Such a system would enable assessment of the current landscape of population protection against infections in modern society and identification of susceptible groups. Its implementation would allow for more accurate estimation of true herd immunity levels across different social groups and regions, improved management of vaccination schedules, assessment of vaccine and immunisation programme effectiveness, and calculation of the required volumes of vaccines, diagnostic and medicinal resources, and operational efforts necessary to ensure comprehensive population protection.

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