

ANTI-MEASLES IMMUNITY ASSESSMENT IN UKRAINIAN HEALTH WORKERS AND SCHOOL TEACHERS

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Introduction

The global measles (and rubella) initiative, launched around the world in 2001 (the partnership led by the American Red Cross, the United Nations, the US Centers for Disease Control and Prevention, UNICEF and WHO) envisaged a 95% reduction in measles death by 2015 and measles elimination in 5 WHO regions by 2020. Immunization activities reduced measles mortality in the world by 80% by 2015, but the targets planned for 2015 have not been achieved and vice versa - since 2017 measles epidemic in the world has worsened [1]. The WHO Regional Committee for Europe back in 1998 adopted the Health 21 program, which provided for the measles elimination from the region until 2007, and by 2010, measles elimination was to be registered and certified in every country in Europe. However, these targets were not reached - the WHO Strategic Advisory Group of Experts on Immunization concluded that the interim goals and the goal of measles elimination were not achieved due to gaps in vaccination coverage. In 40 European countries (Great Britain, Germany, Italy, France, Finland, Bulgaria, Albania, Serbia, Romania and others) from 2011 to 2017, more than 26 thousand cases of measles were recorded. Almost the entire huge rise in measles incidence since 2017 by the next moment (2019) arose in several countries (Bulgaria, Serbia, Albania, Ukraine) [1, 2]. In 2019 almost two-thirds of all world's reported measles cases are in only two countries - Ukraine and Madagascar. According to the Public Health Center of the Ministry of Health of Ukraine during the last outbreak (from summer 2017 to July 2019), nearly 115 thousand people fell ill with measles, 39 of them died; from the beginning of the year (from December 28, 2018 to July 26, 2019), 56594 people fell ill with measles - 26602 adults and 29992 children (under 17 years old), and 18 people died from measles complications. The last outbreak of measles in Europe and Ukraine has its own characteristics: high percentage of vaccinated among measles patients, a large number of complications in the form of severe primary (viral) pneumonia in adults, an increase in measles in children under 1 year old [3]. It is known that adults suffer from measles harder than children and more often have complications. In the case of measles, medical workers can infect a large number of patients in contact with them with another pathology, causing possible serious consequences. Measles is a highly contagious acute viral infection (like smallpox) that can be eradicated on a planetary scale by vaccination. The theoretical possibility of eliminating measles is due to the presence of the only one single serotype of the virus; the absence of other than human reservoirs of the virus in nature; lifelong immunity after infection; the

availability of effective vaccines. In the pre-vaccination period, almost the entire population of children had measles (the contagiousness index was 95–96%), the incidence was observed at the level of 1000–2000 cases of measles per 100 thousand inhabitants, and the mortality rate was from 0.02 to 0.1%. So, before the introduction of immunization in the USA in 1963, from 300 to 400 thousand people a year suffered from measles, about 500 reported lethal cases per year. Widespread use of the vaccine led to a reduction in measles cases by the end of the 20th century in the United States by more than 99% - the incidence rate decreased by 1000 times, deaths occurred every few years [4]. In Ukraine, measles vaccination began 50 years ago (in 1968 - 1969) and after 20 years the incidence decreased by 50-100 times. In 1986, revaccination of children at the age of 6 was implemented into the national vaccination calendar. Over the past 20 years in Ukraine there has been a rise in the incidence of measles every 5-7 years. Since 2008, the level of vaccination coverage in Ukraine has sharply decreased due to the intensification of anti-vaccine moods [5]. In 2015-2016 coverage declined again due to the fact that vaccines were not imported because of procurement transition through international organizations. Thus, the critical epidemiological situation of measles in Ukraine has developed over a long period due to the low coverage of regular vaccination of the child population and the emergence of a large layer of measles-susceptible people in all age groups. Order of the Ministry of Health of Ukraine No. 958 of 04/23/2019 changed the order of measles vaccination in the outbreak: if there are epidemiological indications, vaccination of children over 6 months of age is allowed and vaccination of adults with no age restrictions is recommended (if they have not had measles and / or have no documented confirm the introduction of two doses of the vaccine, or have negative results from studies of specific IgG levels) [6]. For measles, it would be wise for adults to administer anti-measles mono-vaccine. To date, Ukraine has registered four 3-valent vaccines produced in Belgium (Priorix), USA (MMRII) and India, and one 4-valent vaccine made in Belgium (Priorix - tetra), but not a measles mono-vaccine has been registered. Vaccination against mumps is required only for adults unprotected from this infection. There is no need to vaccinate men against rubella, and women need rubella vaccination only when planning a pregnancy in the absence of a protective level of antibodies. The use of vaccines containing rubella for women carries a high risk of post-vaccination reactive arthritis. It is rational before vaccination to determine the concentration of anti-measles, anti-rubella and anti-mumps antibodies for women, anti-measles and anti-mumps - for men. It is advisable to renew registration of measles mono-vaccines for vaccination of adults.

The purpose

Determination of the intensity of anti-measles immunity in Ukrainian health workers and teachers of schools in the context of an epidemic increase in the incidence of measles in the country to identify susceptible individuals for further immunization.

Materials and methods

In February and March 2019, the levels of specific anti-measles IgG in blood serum in 981 health workers from 17 medical institutions in Kharkov and 308 school teachers from more than 100 different Ukrainian secondary schools aged 18 to 85 were analyzed. The concentration of anti-measles IgG was determined by ELISA using Ridascreen enzyme-linked immunosorbent assays produced by r-Biopharm (Germany) using the Lisa Scan EM microbiological enzyme-linked immunosorbent analyzer (Czech Republic). In accordance with the instructions for the test system, anti-measles IgG levels of 150 mIU/ml or less were considered a negative result, from 151 to 200 mIU/ml inclusive - a dubious result, above 200 mIU/ml - a positive result. Statistical processing of the obtained data was carried out using non-parametric statistics methods with Atte Stat 12.0.5 statistical software package integrated into Microsoft Excel 2013. The average values of IgG concentration by age groups are equal to sample medians, since sample distributions do not fit the normal distribution criteria according to Kolmogorov-Smirnov confidence criterion estimates.

Results and discussion

The studies revealed the absence of protective concentrations of anti-measles IgG in 3.3% of the tested; doubtful results were observed in 2.8%. In the age group older than 57 years (born in 1961 and earlier), there were no individuals with a lack of a protective level of anti-measles IgG and only 1 person (0.5%) had doubtful antibodies concentration. Since measles vaccination in Ukraine began in 1968, all representatives of this group were ill with measles and developed natural lifelong immunity, which was fortified in subsequent meetings with the virus. Among medics and teachers of this group, the highest average concentrations of measles IgG (2442 ± 410 mIU/ml) are noted. This age group does not need measles revaccination. In persons aged 48 to 57 years old (born from 1962 to 1971), less than 1% were found to have negative and doubtful results. The average levels of measles IgG in this group are high (1667 ± 213 mIU/ml). Most people of this age suffered from measles in

childhood, and the rest (born after 1968) were vaccinated once and all repeatedly received natural booster immunization during their lifespan in periods of increasing incidence of measles. This age group, in our opinion, also does not need measles revaccination, but it is recommended to check the level of protection to identify selective susceptible people. Among medical workers and teachers aged 38 to 47 years old (born from 1972 to 1981), 4.6% of negative and 3.7% of doubtful results of the intensity of anti-measles immunity are noted. Most of this group was vaccinated once, and those born after 1979 were vaccinated twice. The average concentration of measles IgG in them is high (1083 ± 146 mIU/ml), but lower than in older age groups. It is known that vaccination causes a less intense immune response than a natural infection itself. In our opinion, health workers and teachers of this age category need to be screened for measles-susceptible individuals and then vaccinated according to the level of antibodies. In persons aged 28 to 37 years (born from 1982 to 1991), about 5.3% of negative and 5.0% of doubtful results were revealed. This age group should be already 2 times vaccinated according to the schedule of vaccination in Ukraine. The levels of anti-measles IgG in representatives of this group are also quite high (867 ± 117 mIU/ml). Medics and teachers of this age also need to be examined to determine the levels of anti-measles IgG and those who do not have protective concentrations of antibodies has to be revaccinated. The largest number of health workers and teachers unprotected against measles was found in the age group of 18 to 27 years old (born from 1992 to 2001): 7.5% had negative and 5.6% had dubious results of the intensity of measles immunity. In our opinion, this is due to the insufficient coverage of measles vaccination for children in Ukraine for a long period of time, as well as to the lower number of natural repeated contacts with measles virus (enhancing immunity) of people of this age than representatives of older age groups. The average concentration of anti-measles IgG in this group was the lowest. Persons of this age group must be fully examined to determine the levels of measles IgG, since among them there is the greatest number of measles susceptible people (Table).

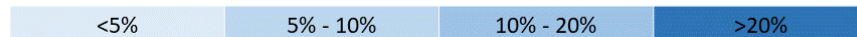
Table. Levels of specific anti-measles IgG in health workers and teachers in Ukraine (February – March, 2019)

| Age groups | Number of persons | Average IgG (mIU/ml) | Level of the immune response | | | | | |
|------------------|-------------------|---------------------------------------|------------------------------|-----------------------------------|-----------|-----------------------------------|-------------|------------------------------------|
| | | | Negative | | Doubtful | | Positive | |
| | | | n | % | n | % | n | % |
| 18-27 y/o | 107 | $753 \pm 143^{**}$ | 8 | $7,5 \pm 2,5^*$ | 6 | $5,6 \pm 2,2^*$ | 93 | $86,9 \pm 3,3^*$ |
| 28-37 y/o | 262 | $867 \pm 117^{**}$ | 14 | $5,3 \pm 1,4^*$ | 13 | $5,0 \pm 1,3^*$ | 235 | $89,7 \pm 1,9^*$ |
| 38-47 y/o | 410 | $1083 \pm 146^{**}$ | 19 | $4,6 \pm 1,0^*$ | 15 | $3,7 \pm 0,9^*$ | 376 | $91,7 \pm 1,4^*$ |
| 48-57 y/o | 313 | $1667 \pm 213^{**}$ | 2 | $0,6 \pm 0,4^*$ | 1 | $0,3 \pm 0,3^*$ | 310 | $99,0 \pm 0,6^*$ |
| 58 y/o and above | 197 | $2442 \pm 410^{**}$ | 0 | 0,0 | 1 | $0,5 \pm 0,5^*$ | 196 | $99,5 \pm 0,5^*$ |
| Total | 1289 | $1321 \pm 122^{**}$ | 43 | $3,3 \pm 0,5^*$ | 36 | $2,8 \pm 0,5^*$ | 1210 | $93,9 \pm 0,7^*$ |

Note: * standard error for the fraction ($p < 0.05$); ** confidence interval for median ($p < 0.05$)

Most often, among all age groups of health workers and teachers, anti-measles IgG concentrations from 500 to 1000 mIU/ml are detected (Pic.).

| Interval (mIU/ml) | Interval frequency | | | | | Total |
|-------------------|--------------------|-----------|-----------|-----------|------------------|-------|
| | 18-27 y/o | 28-37 y/o | 38-47 y/o | 48-57 y/o | 58 y/o and above | |
| 0 - 150 | 7,5% | 6,1% | 5,4% | 1,0% | 0,0% | 3,8% |
| 150-200 | 7,5% | 6,5% | 4,6% | 0,6% | 0,5% | 3,6% |
| 200-300 | 6,5% | 10,3% | 5,9% | 3,8% | 2,5% | 5,8% |
| 300-500 | 11,2% | 6,1% | 5,1% | 5,8% | 1,5% | 5,4% |
| 500-1000 | 32,7% | 26,7% | 26,6% | 21,7% | 14,7% | 24,1% |
| 1000-1500 | 9,3% | 9,5% | 13,2% | 11,8% | 11,2% | 11,5% |
| 1500-2000 | 4,7% | 6,9% | 8,0% | 13,4% | 12,2% | 9,5% |
| 2000-2500 | 3,7% | 5,7% | 6,3% | 7,7% | 10,2% | 6,9% |
| 2500-3000 | 4,7% | 6,5% | 5,6% | 6,4% | 7,6% | 6,2% |
| 3000-3500 | 3,7% | 5,3% | 4,9% | 8,0% | 13,2% | 6,9% |
| 3500-4000 | 3,7% | 3,4% | 5,4% | 7,3% | 8,6% | 5,8% |
| 4000-4500 | 2,8% | 3,4% | 4,1% | 5,1% | 11,2% | 5,2% |
| 4500-5000 | 1,9% | 1,9% | 2,0% | 4,5% | 4,6% | 2,9% |
| 5000-5500 | 0,0% | 0,4% | 2,0% | 2,2% | 2,0% | 1,6% |
| 5500-6000 | 0,0% | 1,1% | 0,7% | 0,6% | 0,0% | 0,6% |



Pic. Scatter of levels of specific anti-measles IgG in different age groups among health workers and teachers of Ukraine (February - March, 2019)

High levels of anti-measles antibodies (from 4,000 to 4,500 mIU/ml) exposure reports 4 times more frequent in medics and teachers over 57 than in the youngest age group. A low level of anti-measles antibodies (from 200 to 500 mIU/ml) in the older age group are 2.6 times less frequent than in the group from 38 to 57 years old and 4.3 times less frequent than in the group of people from 18 to 37 years old. In order for vaccination to be effective, the vaccine virus must enter the lymphoid tissue and vegetate in the body for a certain time in order to strengthen the humoral and cellular immunity. Vaccination of individuals with high levels of anti-measles IgG does not make sense, as it will neutralize the vaccine virus antigens with antibodies. In addition, it is possible to get the side effect of the complex vaccine hence vaccination of people who do not need it carries additional risks and is not justified. Therefore, we recommend that all medics and teachers determine the level of anti-measles IgG before vaccination.

Conclusion

1. At 3.3% of 1289 examined health workers and school teachers of Ukraine exposed the absence of protective levels for anti-measles IgG; doubtful results were observed in 2.8%.
2. In the age group over 57, there were no individuals with a lack of protective level of anti-measles IgG and only 0.5% of the tested showed low protective antibodies concentration (150 - 200 mIU/ml). This group needs neither measles revaccination, nor determination of the strength of anti-measles immunity.
3. The largest number of unprotected medics and teachers were found in the age group from 18 to 27 years. This may be due to both low coverage of regular

vaccinations and a decrease in the dynamics of post-vaccination antibodies.

4. All medics and teachers who were born in 1961 and later need to determine the anti-measles IgG concentration level. Measles susceptible must be revaccinated regardless of the number of doses received previously. After one and a half months, it is desirable to monitor the level of immunity.

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Introduction Adults suffer from measles harder than children and more frequently have complications. Medics and school teachers are at increased risk of measles disease. In the case of measles, medics and teachers can infect a large number of people in contact with them with possible serious consequences. The study of anti-measles humoral immunity in doctors and teachers of Ukraine during the measles epidemic in the country is to identify and vaccinate susceptible individuals. **Materials and methods** In February-March 2019, the levels of specific anti-measles IgG in blood serum of 981 medics and 308 teachers aged 18 to 85 were analyzed. The concentration of anti-measles IgG was determined by ELISA using Ridascreen enzyme-linked immunosorbent assays produced by r-Biopharm (Germany) using the Lisa Scan EM enzyme-linked immunosorbent analyzer (Czech Republic). In accordance with the instructions measles IgG levels of 150 mIU/ml or less were considered a negative result, from 151 to 200 mIU/ml inclusive - a dubious result, above 200 mIU/ml - a positive result. Statistical processing of the obtained data was carried out using

non-parametric statistics methods with the Atte Stat 12.0.5 statistical software package integrated into Microsoft Excel 2013. The average values of IgG concentration by age groups are equal to sample medians, since sample distributions do not fit the normal distribution criteria according to Kolmogorov-Smirnov confidence criterion estimates. **Results and discussion.** It was shown that the largest number of measles-susceptible medics and teachers was observed in the age group of 18 to 27 years (7.5% did not have a protective level of specific anti-measles IgG, and 5.6% showed a dubious level of protection). In the age groups from 28 to 37 years old and from 38 to 47 years old, a rather large number of measles-susceptible individuals were also detected (5.3% and 4.6% with no protective level of anti-measles IgG and 5.0% and 3.7% - with a dubious level of protection, respectively). The minimum number of medics and teachers unprotected from measles was determined in the group aged 48 to 57 years (0.6% of negative and 0.3% of doubtful results), and among the group over 57 years of age, there were no individuals with a lack of protective levels of antibodies to measles virus. The possible reasons for the predominance of teachers and health workers unprotected from measles in the age groups from 18 to 47 years and the absence of unprotected people over 57 years of age are discussed. **Conclusion** The authors of the article concludes that there is no need for vaccination against measles in medics and teachers over 57 years of age and recommends vaccination of representatives of other age groups only after determining of the anti-measles immunity level, since more than 90% of the tested population have protective IgG levels.

Key words: vaccination, measles, specific anti-measles IgG, health workers, school teachers

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