

MEASLES: MANIFESTATIONS AT THE STAGE OF ELIMINATION OF INFECTION AND DIRECTIONS FOR EFFECTIVE MANAGEMENT OF THE EPIDEMIC PROCESS

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MEASLES: MANIFESTATIONS AT THE STAGE OF ELIMINATION OF INFECTION AND DIRECTIONS FOR EFFECTIVE MANAGEMENT OF THE EPIDEMIC PROCESS

(Abstract): Controlling measles is still important despite the significant progress achieved through routine immunization. **Aim:** to identify the weak points of the infection control system and to determine the directions for effective management of the epidemic process using the example of the local epidemic situation. **Material and methods:** The materials for the study were data from the official registration of the incidence of measles among residents of a large industrial city in 1988-2016 and the results of serological screening for anti-measles IgG of health care workers during the outbreak of measles in 2016. The epidemiological, clinical, serological and statistical research methods have been used. **Results:** In conditions of a high level of vaccination against measles in the metropolitan population, significant quantitative and qualitative changes occurred in the epidemic process of this infection. Between 2001 and 2015, on the territory of the city, local cases of measles were not recorded, and its single penetration from endemic territories did not cause the spread of the infection. However, in 2016, a measles outbreak was registered, due to the spread of infection mainly in medical settings among patients and staff. Serological immunity tests for measles conducted among health care workers showed that up to 80% of those who underwent the tests had a protective level of anti-measles antibodies, with the highest proportion of people with seroprotection being detected in the age group over 50 years old. Up to 40% of workers with an interval of 10 years and more after the last vaccination were included in the cohort of persons with anti-measles IgG below 0.18 IU / ml, i.e. below protective level. **Conclusions:** Measles remains an important infection, which has a possibility to spread among children and adults who are not protected against it. To effectively control the epidemic situation for measles during the elimination stage of the infection, it is necessary to implement a system of continuous monitoring of the intensity of measles immunity in the indicator groups and to perform routine immunization against measles once every 10 years up to 50 years of age. In the outbreaks where the first patient was not previously vaccinated, it is necessary to carry out booster immunization with live measles vaccine for contact people without preliminary screening. **Keywords:** MEASLES, EPIDEMIC PROCESS, CONTROL.

Measles: manifestations at the stage of elimination of infection and directions for effective management of the epidemic process

Until the middle of the 20th century, the importance of measles was universally determined by the high incidence rate among young children, the ubiquitous spread of infection and high mortality (1, 2).

The introduction of live measles vaccine into the health care practice in 1967 made it possible to significantly change the situation: morbidity and mortality rate from this infection decreased, and the age distribution of the sufferers and the focality changed (3, 4).

Due to the constantly increasing coverage of the population with vaccinations, at the end of the 20th century and the beginning of the 21st century there was a pronounced tendency to reduce morbidity in most countries of the world and even to stop the circulation of the virus in separate time intervals (5, 6, 7).

However, since 2013, in many countries, the incidence of measles has been observed with the active involvement of adolescents and adults in the epidemic process, the emergence of measles outbreaks in community and the focality. Cases of measles were reported even in countries where measles had not occurred for a long time (USA, Canada, Australia and most European countries) (8, 9, 10, 11, 12, 13).

In several administrative territories of the Russian Federation, the cases of measles penetration and its spread with the formation of epidemic foci in families, medical settings and educational institutions began to be reported (14, 15).

The aim of the study is to identify the weak points of the infection control system and to determine the directions for effective management of the epidemic process using the example of the local epidemic situation.

MATERIAL AND METHODS

The study was conducted in 2016-2017

at the Department of Epidemiology of Ural State Medical University. The materials for the study were data from the official registration of the incidence of measles in a large industrial city for the period from 1988 to 2016: forms of federal state statistical surveillance № 1, 2; materials of the state report "On the state of sanitary and epidemiological welfare of the population in the Sverdlovsk region"; expedited reports, form 058 / y (1218).

To determine the main characteristics of the measles epidemic process, a more detailed analysis of the local epidemic situation which was formed in the megalopolis in 2016 was carried out. The analysis was based on reports on epidemic emergency situations (83), cards of epidemiological investigations of measles cases or suspected cases of this infection (72) and medical records of inpatients, form 003 / y (74).

Additionally, the results of serological tests for anti-measles IgG of health care workers were analyzed (369). Serological tests were performed at the accredited laboratories using the method of enzyme immunoassay (ELISA). The concentration of anti-measles antibodies of IgG class below 0.12 IU / ml was considered as the negative result of ELISA, 0.12-0.17 IU / ml was considered as doubtful and more than or equal to 0.18 IU / ml was positive. The analysis of the results was carried out considering age, position and vaccination history.

The epidemiological, clinical, serological and statistical research methods have been used. The study was retrospective. Generally accepted statistical techniques were used to assess the results obtained. The study of the trend of long-term morbidity pattern was carried out using the standardized range (estimated Hurst exponent) and the average growth / decline rate in morbidity. To evaluate the activity of epidemic foci of measles,

the indicators such as the index and the factor of focality, as well as the indicators of infection reproduction (reproductive indices) were calculated.

The calculations were made using the Microsoft Office 2007 application package. The statistical significance was assessed using the Student's test and the Fisher test. Differences were considered significant at $p < 0.05$.

RESULTS

With the high coverage of measles vaccinations in the city inhabitants of 95.0-97.0%, there have been significant changes in the epidemic process of this infection. Between 1988 and 2001 a steady downward trend in morbidity was reported in the city. The estimated Hurst exponent for the period studied was 0.6, which also allowed to determine the multi-year dynamics in measles as trend resistant, with an average decline rate of 10.87 per cent.

Between 2001 and 2015, on the territory of the city, local cases of measles were not recorded, and its single penetration from endemic territories did not cause the spread of the infection. The situation changed at the end of 2016 when the measles outbreak was recorded in the city. 72 clinically and laboratory confirmed cases of measles were identified within 11 weeks.

In the laboratory test using ELISA method, specific M antibodies were detected in all sufferers. In the PCR study, the antigen of the measles virus of genotype D8 was isolated, which circulated in previous seasons in the countries of South-East Asia, and in 2015 season it circulated in Europe and Russia.

In the age structure of the sufferers, children and adolescents up to the age of 18 (68.1%) predominated, and adults accounted for 31.9%.

The average age of the sick children was 3.8 years. Children of younger age groups, namely, up to 2 years old and 3-6 years old (46.9% and 40.9%, respectively) were mainly involved in the epidemic process, whereas children over 7 years old made up only 12.2%.

In adults, the average age was 33.2 years, and the greatest number of cases fell on the age group of 20-29 years (39.1%) and 30-39 years (30.4%). The proportion of people aged 18-19 was 4.4%, and over 40 years was 26.1%. There were no differences in the gender structure of measles cases.

According to the vaccination history, 68.1% of the cases had not previously been vaccinated against measles, including because of the refusal of vaccination (38.8%), medical exemption (34.7%), and age (16.3%). In 10.2% the reasons for the lack of vaccination were not documented. Among the measles sufferers, who were previously vaccinated, 30.4% were vaccinated once, 47.9% were vaccinated twice and 21.7% were vaccinated three times.

It should be noted that those who got measles among the previously vaccinated persons did not become active sources of infection for those who contacted them. The incidence rate in persons who contacted them was 0.53 ± 0.15 , whereas in foci in contact with previously unvaccinated sufferers it was 7.94 ± 0.56 ($t = 12.78$, $p < 0.05$).

According to clinical manifestations, in 90.3% of cases the typical measles is described with the presence of all classical symptoms and the stage of their appearance. Among the sufferers who were not previously immunized, typical manifestations of measles were observed in 98.1%, and they were observed among vaccinated sufferers only in 70%.

The change the rash (macular and roseous), the lack of staging of its appear-

Measles: manifestations at the stage of elimination of infection and directions for effective management of the epidemic process

ance and pigmentation were reported in atypical forms of measles, in the previously vaccinated sufferers. In the unvaccinated sufferers, the atypical forms of measles were characterized by the absence of symptoms of intoxication and unmarked catarrhal manifestations.

It should be noted that the clinical manifestations of measles in previously unvaccinated patients were more pronounced: hyperemia of the throat, rhinitis, cough and fever up to febrile figures were reported more often.

During the outbreak, 59 local foci were formed with a different number of sufferers, including 36 family-home, 14 in organized communities and 9 in medical settings. In 30.6% of family-home foci there was a spread of infection, including 8 - within the same apartment, in one - in the block and in two foci - both in the apartment and in the block to the higher floors. The index of focality in family-home foci was 1.33, the factor of focality was 30.6%, and the infection reproduction index was 1.1.

In 14 organized communities were involved in the epidemic process, including 7 preschool educational institutions, 5 schools and 2 higher educational institutions, including one with the spread of infection among students (3 people). The index of focality in organized communities was 1.14, the focal factor was 7.1%, the infection reproduction index was 3.0.

The most active spread of the infection occurred in medical settings, where the index of focality was 7.1, the factor of focality was 55.6 per cent, and the infection reproduction index reached 10.2.

DISCUSSION

Five multidisciplinary city hospitals, one of the departments of the children's anti-tuberculosis center, an ambulance

station, a private clinic and a medical and sanitary unit at the university were involved in the epidemic process. There was a spread of the infection in more than half of the hospitals. The total number of subsequent cases of measles was 51.

The spread of infection in the medical settings was due to the presence of children and adults who were not previously vaccinated against measles, late diagnosis of measles in the first and subsequent cases, and violations in the organization of anti-epidemic measures.

When analyzing the results of a serological test of the health care workers for anti-measles IgG, it was found that 79% of workers had sufficient seroprotection level.

In the 18-19 age group, the proportion of persons with and without seroprotection was approximately equal. However, for individual age groups, the proportion of persons with seroprotective antibody levels at the age over 50 was the largest and constituted 90.5% (fig. 1).

Among the different categories of health care workers, there were no significant differences in the proportion of persons with seroprotection (tab. I).

Considering the vaccination history, among those who were vaccinated once, the proportion of people with seroprotection was 82%, among those who were vaccinated twice and three times it was 76.6% and 77.8%, respectively. Among those who had had measles earlier, all examined persons showed a sufficient level of seroprotection, and in persons with a lack of data on measles vaccination the positive results in ELISA were about 80%

It should be noted that with an increase in the number of years elapsed since the date of the last application of the vaccine, the proportion of persons without seroprotection increased from 17 to 40% (fig. 2).

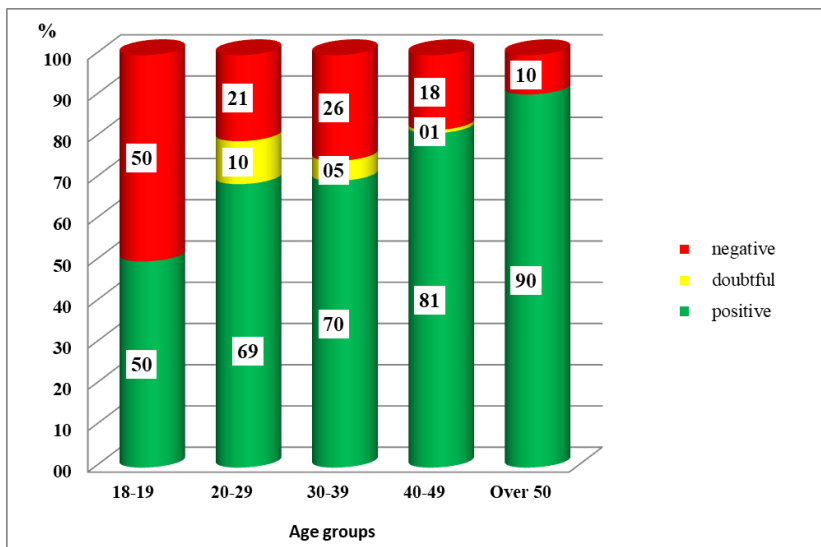


Fig. 1. Results of serological tests for anti-measles IgG in health-care workers in the selected age groups

TABLE I

Levels of protective concentrations of anti-measles IgG among health care workers

Position	Result of the study						Total	
	positive		doubtful		negative		No.	%
	No.	%	No.	%	No.	%		
Doctors	81	77.1	4	3.8	20	19.0	105	100.0
Nursing staff	98	78.4	6	4.8	21	16.8	125	100.0
Paramedical staff	42	85.7	0	0.0	7	14.3	49	100.0
Administrative staff	72	80.0	0	0.0	18	20.0	90	100.0

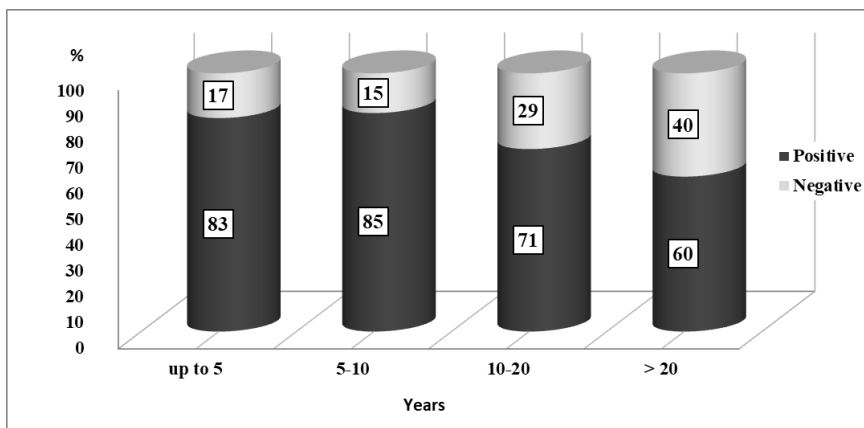


Fig. 2. Proportion of persons with seroprotection and interval from vaccination against measles

Measles: manifestations at the stage of elimination of infection and directions for effective management of the epidemic process

CONCLUSIONS

1. Despite positive changes towards the elimination of measles, it remains an important infection which can spread among children and adults who are not protected against measles.

2. The significance of measles cases in previously vaccinated sufferers as potential sources of infection in the foci is low, the spread of the infection upon exposure to them was 0.53 ± 0.15 , whereas it was $7.94 \pm 0, 56$ in contact with those who were not vaccinated and got measles.

3. A peculiarity of the outbreak of measles was its active spread in medical settings with the formation of secondary foci along the routes of sick children and adults.

4. According to the results of serological monitoring, it was established that up to 80% of health care workers had a protective level of specific antibodies, and the greatest number of persons with seropro-

tection was found in the age group over 50 years. In 30-40% of workers who do not have a protective level of antibodies, the interval from the last vaccination was more than 10 years.

To optimize the system of epidemiological surveillance of measles, it is necessary to:

- Carry out scheduled revaccination against measles at intervals of 10 years up to 50 years of age.
- Carry out booster immunization with live measles vaccine to the contact persons as soon as possible without prior screening as an infection control measure in the foci where the first sufferer was not vaccinated against measles.
- Implement a system for the continuous monitoring of the intensity of measles immunity in the indicator groups recommended for screening by WHO.

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NEWS

NEW DATA FOR TUBERCULOUS MENINGITIS IN HIV-POSITIVE PATIENTS

Tuberculous meningitis (TBM) ranks second in frequency in Africa, with a mortality of over 50% due to diagnostic difficulties. A recent study by Bahr et al. evaluated the diagnostic performance of the new Xpert MTB/RIF Ultra (Xpert Ultra) for TBM in the cerebrospinal fluid (CSF), comparing the Xpert MTB/RIF (Xpert) results with the results of cultures. The study group included 221 HIV-positive patients suspected of meningitis (headache, nuchal rigidity, altered mental status), of which 129 suspected of TBM were tested with Xpert, Xpert Ultra and culture. The results confirmed the diagnosis of TBM in 22 subjects (17%). Of the 21 cases positive by Xpert Ultra, 13 were positive by culture, Xpert or both, and 8 were only positive by Xpert Ultra. The study showed that Xpert Ultra had a 95% sensitivity for TBM, while the sensitivity of culture and Xpert was 45%. By using Xpert Ultra rifampicin resistance was undetected in 13 cases and undetermined in 9. In conclusion, this research demonstrated that Xpert Ultra detected more cases of MTB. The limitation of this paper is that the results cannot be extrapolated to the general HIV-negative population, as the study group consisted of a relatively small number of HIV-positive patients (Bahr NC, Nuwagira E, Evans EE et al. Diagnostic accuracy of Xpert MTB / RIF Ultra for tuberculous meningitis in HIV-infected adults: a prospective cohort study. *Lancet Infect Dis* 2017 Sept. 14 doi: 10.1016 / S1473-3099 (17) 30474-30477).

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