

MODERN PERTUSSIS EPIDEMIC PROCESS IN UKRAINE AND SURVEILLANCE FOR PERTUSSIS

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Abstract. *The article is devoted to the investigation of the epidemic pertussis process in Ukraine at present time from the position of socially ecological conception and improvement of the epidemiological surveillance. Features of serotype-specific view of a causative agent, clinical course of the disease, immunological structure of the population and their influence on the epidemic pertussis process were defined. A reasonability of the use of modern laboratory methods of diagnostics (PCR and ELISA) was demonstrated and the criteria of their rational purpose have been established. The estimation of the system of diagnostics and predictive criteria of epidemic well-being and precursors of epidemic problems were suggested.*

Keywords: *pertussis infection, epidemiological surveillance, epidemic process, diagnostics, immune structure, vaccinal prevention.*

Introduction. In 1965 the WHO organized the headquarters of the epidemiological surveillance (ES) and recommended that National Health Services use the epidemiological surveillance as the only effective form of the epidemiological process management that enables to fight successfully against infectious diseases with the lowest expense of material resources[1]. Since then, the doctrine of the epidemiological surveillance develops as in the direction of improving the organizational and functional approaches, as in the direction of the development and the applied use of the epidemiological surveillance schemes to deal with definite nosological forms, including pertussis.

The prediction of the morbidity is possible with comparing and analyzing the various manifestations of the parasitic system. Quantitative and qualitative changes of the epidemic process at every functional and morphological level of interaction between the pathogen and the host (human) are displayed on the functioning of all other levels and on the whole epidemic process as on the single integrated system, which is consistent with the socioecological conception of the epidemic process by B.L. Cherkassky [2]. The systematic approach to the study of the epidemic process at all its subordinate levels leads to the necessity for the epidemiological surveillance of

pertussis infection at cyto-genetic, organismic, ecosystemic and socioecosystemic levels.

The standards of the epidemiological surveillance of pertussis infection, proposed by WHO, envisage the recommendations for the clinical disease definition and criteria for laboratory confirmation of it for the registration of each new case of pertussis [3, 4, 5].

The purpose of our study was to develop the ways of improving the epidemiological surveillance of pertussis on the basis of the study of epidemic manifestations of pertussis and system analysis of correlation between various levels of the epidemic process of pertussis infection under present conditions.

Materials and methods of the investigation. Comprehensive study of the relationship between social and biological subsystems in the development of pertussis epidemic process in present conditions was carried out by means of the systemic multivariate epidemiological analysis of pertussis in Ukraine for the last years of the vaccination period (1992-2013).

The analysis included studying the multiyear and annual dynamics of morbidity, its distribution in the social and age groups and certain groups among vaccinated and unvaccinated persons, and identifying indicators of the epidemiological vaccination efficiency on the socioecosystem level

At the ecosystem level the immune structure to pertussis in the population of 5 regions of Ukraine (Kyiv, Sumy, Donetsk, Kherson, Chernivtsi) and factors affecting the level of anti-pertussis immunity were studied. At the organismic level the clinical course of pertussis and condition of laboratory diagnostics were analyzed. In order to improve the laboratory diagnostics of pertussis ELISA was taken to identify anti-pertussis Ig M, A, G, and an agglutination test with pertussis liquid diagnosticum. At the cellular level the circulation of serological variants of *Bordetella* in the Donetsk region for the period of 1989-2013 was studied.

Epidemiological, serological (ELISA and AR) bacteriological, molecular-genetic (PCR), clinical, statistical methods were applied.

Results and discussion of investigation. With the purpose of the estimation of the accordance of the national system of epidemiological surveillance of pertussis with the WHO recommendations was conducted the analysis of the organization of measures against pertussis and directive documents operating in Ukraine. In our country the necessity of the improvement of epidemiological surveillance of pertussis is present.

The results of study of pertussis epidemic process in Ukraine are presented from the position of the systematic approach.

Epidemiological analysis of long time changes in the incidence of pertussis in the population of different ages and vaccination coverage against pertussis in Ukraine in 2000-2013 showed no trend of the incidence decrease and a low level of vaccination in recent years.

We have analysed the features of distributing of pertussis morbidity in persons of different age and formed «groups of risk» at a pertussis infection. Last years in a long-term dynamics a tendency is exposed to growth. The highest level of morbidity was registered at children under age 1. For the first time the high increase of morbidity of 5-6 years old children was shown, they are considered as a «risk group», formed in a modern period.

The epidemic process of whooping-cough at social-ecological level has a tendency to activation among the children of junior groups of ages.

The analysis of the completeness and timeliness of vaccination coverage against pertussis in Ukraine in 2000-2013 years was performed. The long-term stable high immunization coverage caused long-term stabilization in the dynamics of morbidity of pertussis with periodic increase with no clear dependence on the volume of routine immunization. In 2008-2009 vaccination coverage dropped to 92%. In 8 out of 27 regions timeliness of immunization children was less than 90,0%, which may lead to activation of epidemic process. In the system of epidemiological surveillance it is necessary to improve the monitoring of credible reporting.

Determination of epidemiology efficiency of immunoprophylaxy of whooping-cough in Donetsk region in 1997-2013 showed its high indexes among the children of

preschool age. The substantial decline of efficiency of antipertussis immunization is exposed among schoolboys 7-14 years as compared to the junior groups of ages and previous years. It specifies on multiplying the risk of disease of these persons. In the period of the long-term planned immunization against a whooping-cough it is necessary change the estimation of efficiency of immunoprofilaxy on immunological, clinical, microbiological indexes, it is for what necessary to extend methodical basis of laboratory researches.

High efficiency of long-term planned vaccinal prevention of pertussis was established. It promoted stabilization of morbidity on a low level, prolongation of the cyclic periods, decreasing the differences between the level of morbidity of urban and rural population, changes of levels of age-morbidity.

At ecological level the immunological structure of population is studied to the whooping-cough, the persons of junior school age are considered as a risk group.

The important role of immunological monitoring system for the epidemiological surveillance of pertussis was estimated. In the ELISA for detection of antibodies Ig G class to Bordetella pertussis toxin the state of population immunity against pertussis was studied in the five administrative regions of Ukraine (655 persons) in the north, east, south, west and center of the country. Representative indicator groups of persons aged 2 years, 6-7 years and 18-29 years were examined. The concentration of immunoglobulins expressed in DU / ml - international DRG units. Level of immunity was assessed as high, medium, low, vulnerable persons and seronegative individuals.

State of population immunity against pertussis was low. The total part of seronegative individuals to pertussis amounted to 44,7 % from the number of inspected patients in general in the country and ranged from 21,2 % in Chernivtsi region to 57,5 % in Donetsk region.

The level of immunity to pertussis was significantly different in different regions of Ukraine. The median concentration of pertussis immunoglobulin was 4,7 DU / ml in the Donetsk region, Kherson region – 8,5 DU / ml, Kiev region – 13,9 DU / ml, Sumy region – 17,3 DU / ml, Chernivtsi region – 19,2 DU / ml.

Children 2 years of age have higher rates of pertussis immunity in all areas in the immunological structure. The immunological efficiency of pertussis vaccine was confirmed. Children 6-7 years and adolescents were poorly protected. They are regarded as the age at risk, requiring additional preventive measures. The study of the immunological structure of pertussis in the population of 2, 6-7, 18-29 years age showed that the lowest rates immunity registered in the group of 6-7 years old children. 2-years children were better protected in all regions. Children of 6-7 years and adolescents regarded groups of risk in terms of immunological structure to pertussis. It is necessary to solve the problem of raising the level of immunity among them. The level of immunity adults of reproductive age was insufficient to protect infants.

The impotent value of immunomonitoring is confirmed in the system of epidemiology supervision after pertussis. The resulting data should be used for targeted improvements specific prevention of pertussis.

The study found no trend of the decrease of the incidence of pertussis in Ukraine in conditions of high vaccination coverage, low level of immunity against pertussis, the formation of risk grope among primary school children. The expediency of an implementing of second revaccination against pertussis among children aged 6 years was based upon epidemiological and immunological characteristics.

The influence of the organization of pertussis immunization and the intensity of its epidemic process on the population's pertussis immunity was assessed. A correlation between specific gravity of seronegative children aged 2 in five regions of Ukraine and the number of the vaccinated against pertussis children in 2008-2013 was established. The efficiency of determining the limits of fluctuations in the incidence of pertussis was showed, in cases when the circulation of the pathogen does not provide a "natural immunity increase" and does not affect the level of immunity.

The statistically significant influence factors on the level of antipertussis immunity were established. There are negative factors – a deviation from the regulated scheme, increasing of the period from the last vaccination, carried diseases

in anamnesis; there are positive factors – vaccination at autumn, using of AcellularDTP-vaccines.

An analysis and estimation of efficiency of antiepidemiologics measures in the epidemic focus of pertussis infection was conducted. There are an active exposure of patients by a pertussis, laboratory diagnostics, timeliness of isolation, establishment of reasons of disease's origin, medical looking after communicating in epidemic focus. Imperfect diagnostic possibilities of existent methods of laboratory diagnostic pertussis was shown.

Active detection of patients with pertussis among long coughing persons conducted bacteriological method and reaction of agglutination with paired sera. The small diagnostic capabilities of the methods for laboratory confirmation of pertussis was detected.

The comparative analysis of application of various methods of laboratory diagnostics of a whooping cough (bacteriological, RA) has shown, that at high level of coverage by bacteriological inspection sick of a whooping cough (78,6-85,2 %) and their inspections in agglutination reaction (64,8-88,6 %) frequency of positive results was low (8,6-43,6 %). For the introduction of PCR and ELISA for the detection of specific Ig M pertussis more research studies were performed.

We firstly in Ukraine summarized the experience of the use of polymerase chain reaction (PCR) for laboratory confirmation of pertussis infection in the Donetsk region for 2007-2009. Frequency of DNA isolation of the pertussis pathogen in PCR among the inspected persons of different age correlated with the level of morbidity a pertussis infection. The expedience of wide introduction of PCR for early diagnostics of pertussis infection is shown, because it is an informing and objective method of authentication of the pertussis pathogen.

The using PCR for identify *Bordetella pertussis* pathogen raises level of diagnostics a pertussis infection: 11,3-53,8 % registered cases in 2007-2009 are confirmed in PCR. By means of PCR *Bordetella pertussis* are revealed at 26,8 % of persons with long cough.

The modern conditions characterised by increase of frequency of easy and erased forms of a pertussis infection. Wide introduction in practice of health protection of ELISA for determination of specific IgA and/or IgM of antibodies to *Bordetella pertussis* will enable in good time to diagnose, it is correct to appoint treatment, conduct effective prophylactic measures, that will result in the decline of morbidity a pertussis infection in the and.

For the purpose of early diagnostics of a pertussis infection in the modern conditions the research of use of a method ELISA for revealing antipertussis antibodies Ig M were performed.

Research purpose: to estimate a presence and frequency of exposure of specific antipertussis antibodies of classes of IgM and IgA at persons with somatic pathology of respiratory tracts, showing up a long cough. In ELISA the wheys of 42 persons with different diagnoses were explored. Antibodies to the antigens of *Bordetella pertussis* (IgM and IgA) is exposed at 33,3 % these persons, including at 23,8 % there were antibodies of class of IgM, at 16,7 % – class of IgA, at 7,1 % both classes of antibodies were present simultaneous. Children in age 3-5 years more frequent than other groups of ages suffer pathology of respiratory tracts, at which differential diagnostics is required with a whooping-cough infection (62 % from all inspected persons). At 27 % from them specific antibodies, testifying to the flowing presently whooping-cough infection, were exposed.

Specific M-antibodies are revealed at 87,5 % of the hospitalised patients with the diagnosis "whooping cough". Use of this method raises possibility of diagnostics of a whooping cough in early terms of disease. Objectivity and informativity this method and expediency of its wide introduction in public health services practice is confirmed.

Analysis of the use of the bacteriological method and reaction of agglutination for laboratory diagnostics of whooping-cough has detected high level of scope of patients by them and insufficient informing of these methods (Table 1). The experience of application of PCR for *B. pertussis* determination and ELISA for the exposure of Ig M and Ig A testifies to possibility of improvement of epidemiology

supervision after whooping-cough by the improvement of laboratory diagnostics of this disease. The rational choice of the tactics of laboratory diagnostics of whooping-cough in a period, when the new perspective methods of researches become accessible, depends on age, term from the beginning of disease and inoculative status of diseased persons.

Table 1

Frequency of the confirmation of the diagnosis of pertussis using different laboratory methods (% of examined contingent)

Contingent examined	Bacteriological	PCR	ELISA	RA
Patients with pertussis	55,6 _{+8,7}	100,0	83,3 _{+8,8}	58,5 _{+4,9}
Persons with prolonged cough	3,0 _{+1,2}	22,6 _{+1,9}	26,3 _{+5,8}	2,0 _{+1,2}

At organism level a tendency is marked to the decline of weight of clinical displays of infection. To assess the factors affecting the severity of clinical course of pertussis 192 cases of pertussis that were registered in Donetsk region in 2008-2013 have been analyzed. The most influential factor according to mathematical model definition is vaccination against pertussis that the patient received earlier. The analysis of the infectious course of pertussis revealed the “risk groups” of severe clinical forms of infection, demonstrated that vaccineal prevention allows to make the clinical course of the disease easier, and confirmed the existing defects in the organization of vaccination.

At cellular level features of serotype-specific view of a causative agen were defined.

The analysis of *Bordetella* species circulation in the Donetsk region in 1989-2013 (Table 2) showed predomination of *B. pertussis* (83,2 %). Lately, frequency of *B. parapertussis* circulation grew to 14,6 %. Serotype 1.0.3 prevailed among pertussis agents (53,5 %), a tendency to reduction of its circulation and increase of all other serotypes of *B. pertussis* is exposed. On the second place by frequency of selection there was the variant 1.2.3. The tendency to the coincidence of his activation with epidemic morbidity rates of whooping-cough is revealed. Monitoring of the serotype landscape of *B. pertussis* is an important component of pertussis epidemiological supervision.

The prevalence of pathogens in the genus *Bordetella* in Donetsk region in 1989-2013 (% of identified microbial cultures)

Years	Allocated pathogens kind <i>Bordetella</i>	Including <i>Bordetella</i> species (% + m)						
		Total	<i>Bordetella pertussis</i>				<i>Bordetella parapertussis</i>	<i>Bordetella bronchi-septica</i>
			Including serotypes					
			1.0.3	1.2.3	1.2.0	1.0.0		
1989-1996	214	95,3±1,4	79,9±2,7	10,7±2,1	2,8±1,1	1,9±0,9	4,2±1,4	0,5±0,4
1997-2004	241	87,1±2,2	48,1±3,2	21,6±2,6	6,6±1,6	10,8±2,0	12,5±2,1	0,4±0,4
2005-2013	298	69,8±2,7	37,9±2,8	17,1±2,2	5,0±1,3	9,7±1,7	23,5±2,5	5,0±1,3
1989-2013	753	83,2±1,4	53,5±1,8	16,8±1,4	4,9±0,8	7,9±1,0	14,6±1,3	2,3±0,5

Spreading of the pertussis agents serological variants among persons of different ages had different. Relative density of the pertussis pathogen serological type 1.0.3 is the largest. The tendencies to reduce its circulation from 79,1% to 56,1% and to increase the relative density of the pertussis pathogen serological type 1.2.3 from 12,4% to 24,9% are exposed. The dependence is revealed in the dynamics of incidence and spreading of serotype B. pertussis, which was to change the dominant serotype in front of each subsequent epidemic rise.

Exploration of the prevalence of different types *Bordetella* and the incidence of whooping cough persons of all ages showed correlation of these processes. A mathematical model to predict trends of disease based on the assessment activity circulating serological variants of the pathogen made.

The control of pertussis epidemic process needs perfection. We have proposed the basic principles of organization of the surveillance system for pertussis infection. Developed a diagram showing the structural-functional model of the surveillance of pertussis infection. It includes measures for pertussis infection, based on the specifics of the infection and the principles of a systematic approach to the epidemic process. The essence of the model is to determine the relationships between the fragments of the functioning of medical and sanitary-epidemiological measures, the regulation of volume and content of information flows, diagnostic and management approaches to solving problems of prevention of pertussis.

Conclusions. Priority ways of improving the system of epidemiological surveillance were worked out; reasonability of the use of modern laboratory methods of diagnostics (PCR and ELISA) was demonstrated and the criteria of their rational purpose have been established. The estimation of mathematical prognosis of prediction the tendency of morbidity on basis of circulating serotypes of causative agents, the system of diagnostics and predictive criteria of epidemic well-being and precursors of epidemic problems were suggested.

On the basis of deep epidemiological analysis the system of diagnostically-prognostical criteria of estimation of pertussis epidemic processes tendency is offered by the purpose of increase of the functioning of epidemiology supervision after a whooping-cough. Criteria are grouped in the signs of epidemic prosperity and precursors of epidemic nonprosperity and engulf all functionally-morphological levels of epidemic process.

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Романенко Т.А.

Епідемічний процес кашлюку в Україні та епідеміологічний нагляд за ним в сучасних умовах

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Резюме. Стаття присвячена вивченню епідемічного процесу кашлюку в Україні в сучасних умовах з позиції соціально-екологічної концепції та удосконаленню епідеміологічного нагляду. Визначено особливості серотипового пейзажу збудника, клінічного перебігу хвороби, імуноструктури населення та їх вплив на епідемічний процес. Продемонстровано доцільність застосування сучасних лабораторних методів діагностики (ПЛР та ІФА) та визначено критерії їх раціонального призначення, запропоновано систему діагностично-прогностичних критеріїв епідемічного благополуччя та передвісників епідемічного неблагополуччя.

Ключові слова: кашлюкова інфекція, епідеміологічний нагляд, епідемічний процес, діагностика, імунологічна структура, вакцинопрофілактика.

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Эпидемический процесс коклюша в Украине и эпидемиологический надзор за ним в современных условиях

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Резюме. Статья посвящена изучению эпидемического процесса коклюша в Украине в современных условиях с позиции социально-экологической концепции и усовершенствованию эпидемиологического надзора. Определены особенности серотипового пейзажа возбудителя, клинического течения болезни, иммуноструктуры населения и их влияние на эпидемический процесс. Продемонстрирована целесообразность использования современных лабораторных методов диагностики (ПЦР и ИФА) и определены критерии их рационального назначения, предложена система диагностически-прогностических критериев эпидемического благополучия и предвестников эпидемического неблагополучия.

Ключевые слова: коклюшная инфекция, эпидемиологический надзор, эпидемический процесс, диагностика, иммунологическая структура, вакцинопрофилактика.

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