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## **Age characteristics of the hepatitis A epidemic process in federal districts of Russia in the modern period. Justifications of the introduction of a children's routine hepatitis A vaccination**

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*In recent years, there were published several epidemiological observations concerning the maximum incidence of hepatitis A (HA) shifting into the older age groups, including adolescents aged 15-19 and young adults 20-39 years old, and the reduction of the role of children as a significant risk group. These phenomena have not been sufficiently studied yet and have not received an adequate explanation. The aim of this study is to investigate the age characteristics of the epidemic process of the HA in Russian Federation and federal districts in the modern period to assess the need for routine vaccination of children against the infection, as well as to determine the optimal age for its implementation.*

*There was conducted a comparative analysis of age-related morbidity of Hepatitis A (the proportion of children and adults, the ratio of adults and children's rates, the intensity of the population) in the federal districts of the Russian Federation in 1999, 2001 and 2010.*

*It was discovered that Hepatitis A remains a significant child problem in Russian Federation. The proportion of children aged 0-14 years among Hepatitis A cases in 2010 (28%) was not significantly different from that in 1999 (40%). In the Far East, Siberia and the North Caucasus the incidence of children is continuously increasing 4-6 times faster than those of adults. These characteristics of the epidemic process of Hepatitis A indicate the need for the introduction of a routine vaccination of children.*

**Key words:** *hepatitis A epidemic process, disease, age characteristics, immunizations.*

### **Introduction**

The most important characteristic of the epidemic process of hepatitis A (HA) allowing to set risk groups and to predict the development of the epidemic process, as well as to justify preventive measures, is surely the incidence in different age of the population [1]. A classic expression of the HA is the epidemiological spread of intensive infection among children. This is mentioned in almost all textbooks on epidemiology and guidelines for infectious diseases [2, 3]. However, in recent years both domestic and foreign experts tell in their publications about HA "becoming an adult problem" and about reallocation of the maximum incidence to the older age groups, including adolescents aged 15-19 and young adults 20-29 years [4 - 7]. A decreased circulation of the virus HA in many countries around the world is largely due to the significant

increase in health and hygiene standards of living, demographic change (fertility decline) and reduced proportion of individuals, possessing immunity to the virus HA, among adolescents and young adults [8, 9]. All this allows some experts to argue that there is no need to vaccinate children against HA in Russia.

The purpose of this study was to clarify age-related characteristics of the epidemic process of the HA in Russian Federation and federal districts in the modern period to assess the need for routine vaccination of children against the infection, as well as to determine the optimal age for its infiltration.

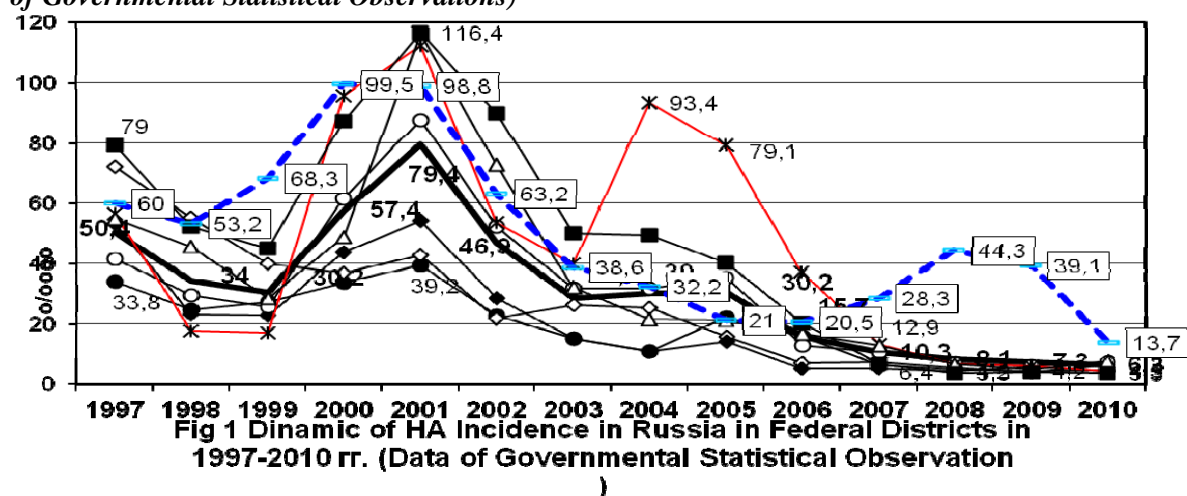
## Patients and Methods

Incidence of HA of 1997-2010 period has been calculated on the basis of federal statistical observation, which included information about 630 292 reported cases of this disease in several federal districts of the country. Age-related characteristics of incidence (the proportion of children aged 0-14 years among the cases the HA, the ratio of incidence rates in children and adults, the incidence in different age groups) have been studied in details for 2010 and compared with similar data for 1999 and 2001. These years were chosen for the following reasons: 1999 was a year with minimal long-term morbidity in the previous cycle of the epidemic process of HA; 2001 was the year of the last significant morbidity rise in Russia. Age-related indicators of the epidemic process were evaluated for the country in whole and for individual federal district. Area districts matched their boundaries on January 1, 2011. Age-related incidence rates were calculated per 100 thousand of population in each age group: up to 1 year, 1-2, 3-6, 7-10, 11-14, 15-19, 20-29, 30-39, 40-49, 50-59, 60 years and older. 44 286 cases of HA, registered in 1999, 115,222 cases - in 2001 and 8944 cases - in 2010 served as a basis for rates determination.

## Results

Long-term dynamics of the HA epidemic process from 1997 to 2010 as a whole in the Russian Federation is characterized by the incidence increase in 2001 (79.4 0/0000) and further decrease to 6.3 0/0000- indicators in 2010 (Fig. 1). Previous incidence rise was recorded in 1999, and the lowest level of the HA was 30.2 0/0000. In some federal districts during the study period there could be seen a very significant rise of incidence. For example, in North-West Federal District (North-West), there was an activation of the epidemic process in 2004-2005 with the incidence 79,1-93,4 0/0000. A very significant rise of HA incidence was observed in the North Caucasus Federal District (North Caucasus Federal District) in 2008-2009. (39,1-44,3 0/0000).

**Fig. 1. The incidence of hepatitis A Incidence in Russia and in the federal districts in 1997-2010. (data of Governmental Statistical Observations)**



*Note:* The North-West - North-West Federal District, Volga Federal District - Volga Federal District, Urals Federal District - Urals Federal District, Federal District - Southern FD, CFD - Central Federal District, Far Eastern Federal District - Far Eastern Federal District, Siberian Federal District - Siberian Federal District, North Caucasus Federal District - North Caucasus federal district.

Despite significant differences in incidence rates in 1999 and 2001 the proportion of children aged 0-14 years among patients, registered in Russian Civil Aviation, was the same - 40-41% (Table 1). During this period, the largest proportion of affected children was observed in North Caucasus Federal District (71-72%), Far East Federal District (FEFD) - 49-51%, and Siberian Federal District (SFD) - 47-53%. In other federal districts, the proportion of children among HA cases ranged around 30%.

In 2010, given a significant reduction of the epidemic process intensity, a portion of children with HA reduced up to 28% in the whole country. In three districts of FEFD, the NFD and North Caucasus Federal District numbers have not changed and amounted to 43-59%. In the Southern, Volga and Ural Federal District (SFD, PFD and MSS), the proportion of children in the incidence decreased to 23-25% compared to 1999 - 32-37%. The biggest change in the proportion of children among the cases had place in HA Central Federal District (CFD) and at North-West, resulting in a two-fold decrease in rate - 14% in 2010 compared to 27-28% in 1999

The above description of the epidemic process is reflected in the ratio of incidence rates in children aged 0-14 years and persons over 15 years (see Table. 1). A significant excess of children's incidence over that of adolescents and adults had places during all years of statistical observations in FEFD, NFD and North Caucasus Federal District. In FEFD this ratio of 3.8 remained unchanged in 1999 and 2010; in SFD it has increased from 3.4 to 5.2 in the same period, and in North Caucasus Federal District it fell to 5.8 in 2010 in comparison with 7.3 in 1999. In 2010 SFD, PFD and MSS higher rates of children morbidity remained comparable with that of 15-year-olds and older (approximately two-fold excess). This pattern was observed in 1999 in CFA and the North-West. HA for children and adults did not differ in 2010, while the ratio of incidence in these groups was 1:1.

**Table 1. The proportion of children aged 0-14 years and the ratio of the incidence of hepatitis A in children and adults in the federal districts of Russia in 1999, 2001 and 2010**

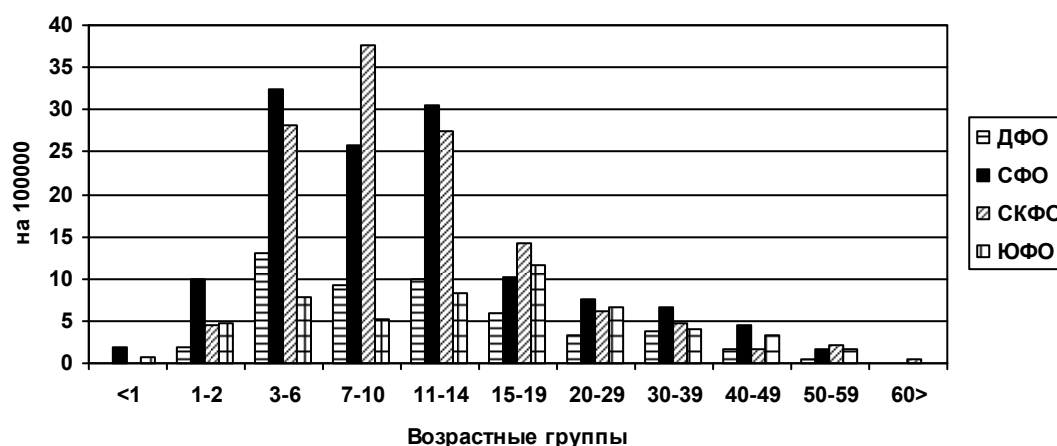
Federal District	The proportion of children aged 0-14 years in the incidence of hepatitis A (%)			Ratio of the incidence of children aged 0-14 years and persons 15 years and older		
	1999	2001	2010	1999	2001	2010
Far East	49	51	43	3,8:1	4,5:1	3,8:1
Siberian	47	53	50	3,4:1	4,8:1	5,2:1
North-Caucasian	71	72	59	7,3:1	7,9:1	5,8:1
South	32	36	23	2:1	2,6:1	2:1
Volga	30	35	23	1,8:1	2,5:1	1,7:1
Ural	37	35	25	1,9:1	2,5:1	1,7:1
Central	28	31	14	1,9:1	2,4:1	1:1

*Notice.* \* - Federal districts as of January 1, 2011, the calculation of rates in 1999 and 2001, made on the basis of territorial jurisdiction in 2011

Depending on the multiplicity of the incidence excess of children's HA in 2010 compared with those aged 15 and over, all the federal districts were combined into two groups. In these groups more detailed analysis of the incidence according to age was carried out. Fig. 2 shows the four districts - FEFD, NFD, the North Caucasus Federal District and South Federal District, in which the incidence of child with HA significantly exceeded the performance of adult population. In the FEFD and the NFD's leading group of diseases were children aged 3-6 years, with rates 13.0 and 32.5 0/0000, respectively. In the North Caucasus Federal District greatest

exponent of the HA could be seen for schoolchildren aged 7-10 years - 37.7 0/0000. In these districts only South Federal District demonstrated greater involvement in the epidemic process of adolescents aged 15-19 years, the incidence of whom was 11.5 0/0000 and only slightly increased the rates for under-school children of 3-6 years and pupils of 11-14 years old (about 8 0/0000).

**Fig 2. Dynamic of HA Incidence of different age groups in Russia in Federal Districts in 2010**



*Note:* На 100 000 населения – per 100 000 of population; Возрастные группы, годы – Age groups, year; ДВФО - Far Eastern Federal District, СФО - Siberian Federal District, СКФО- North Caucasus federal district, ЮФО - Southern FD

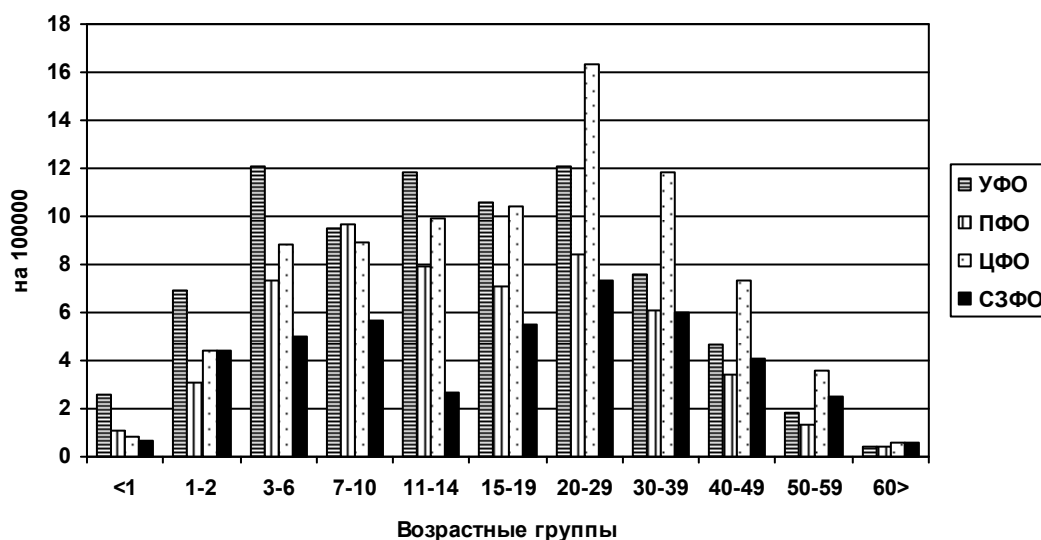
Another distribution of HA incidence by age occurred in the territories of four remaining federal districts - UFD, PPD, CFA, and North-West (Fig. 3). Here, along with children's age groups, relatively high levels of HA were recorded in age groups of 20-29 and even of 30-39 years. In UFD and PFD the incidence of 20-29-year-olds (12.1 and 8.4 0/0000, respectively) was similar to that of children in the age groups 3-6, 7-10 and 11-14 years living in those areas. At the same time, CFA and North-West figures on those aged 20-29 years (16.3 and 7.3 0/0000) clearly exceeded the incidence in children.

### Discussion

In our previous study [10], we compared the incidence of HA for two model age groups - 3-6 and 20-29 years in Russia - and concluded that the infection often affects both children and adults in these groups. One of the main reasons for this phenomenon lies in the extremely low herd immunity to the virus HA of the population aged 40 years. This was shown at the example of St. Petersburg [9], where only 32.5% of the population had antibodies to HA (anti-HAV) in 2009; seroepidemiological studies of different parts of Russia revealed that the country belongs to the areas with intermediate endemicity of HA; that is, the majority of the child and the adult population does not have protective antibodies [11].

The results of this study show that half of Russian federal districts (FEFD, NFD, the North Caucasus Federal District and South Federal District) are still at the most significant risk on children aged 0-14 years, because the incidence among them is significantly higher than for the adult population. In two districts – UFO and PFD - the incidence of children is not inferior to that of adults. Only in the Central and Northwest districts in 2010 there was a clear excess of incidence for people over 15 years; the age group 20-39 dominated. The latter confirms the presence of low herd immunity to the virus HA.

**Fig 3. Dinamic of HA Incidence of different age groups in Russia in Federal Districts in 2010**



*Note:* На 100 000 населения – per 100 000 of population; Возрастные группы, годы – Age groups, year; УФО - Urals Federal District, ПФО - Volga Federal District, ЦФО - Central Federal District, СЗФО - North-West Federal District

Special studies of HA molecular epidemiology demonstrated, that isolates, related to the subtype IA, are the main circulating HA viruses in Russia, being a leading causative agent, ensuring its continued circulation in the low and high endemicity [12, 13]. It was shown that viruses of this subtype have a high reproductive activity [14] and can be effectively distributed in every way as typical for infections with the fecal-oral transmission. It is important to emphasize that all the major food outbreaks of HA have recently been associated with this subtype IA [15, 16]. Long-term monitoring of circulating genetic variants of the virus HA in St. Petersburg revealed the introduction of new, previously not encountered types of pathogen [12], which gives reason to believe that covert circulation of the pathogen takes place among low-manifestation of the epidemic process. Probably the same conclusion can be drawn for other areas of the country.

### Conclusion

Classic epidemiological understanding of hepatitis A as an important issue of childhood Infectology is supported by evidence in the modern period. This is justified by indicators of the intensity of the epidemic process of HA among children. According to the research in 2010, in six out of the eight federal districts HA incidence for children was higher or not different from that of adults. Analysis of information about low herd immunity and the ongoing intensive covert circulation of the virus suggests a high probability of an unfavorable development of the epidemic process in the country where there are factors spreading the pathogen.

The natural and logical measure of preventing the spread of HA virus among children is to increase an immune layer by vaccination. Recently there came into effect sanitary regulations for the prevention of hepatitis A [17] providing vaccinations GA in the amount, which depends on the "epidemiological situation of this infection, as well as the features of the dynamics and trends of the epidemic process in a particular area." Age structure of incidence persuades of the need for the introduction of routine children vaccination against Hepatitis A before their going to the social environment-kindergartens, which has place at the age of up to 3 years.

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