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PATTERNS OF RESISTANCE TO NOSOCOMIAL INFECTIONS AGENTS

Resume. *Nosocomial infections (NCI) are confounding the course of the disease among patient, make the treatment more difficult and expensive, prolong the period of hospitalization and can be life-threatening. This explains the relevance of the study of nosocomial infections, thei persistence, namely factors that make them resistant to biocides.*

Nosocomial infections (NCI) are confounding the course of the disease among patient, make the treatment more difficult and expensive, prolong the period of hospitalization and can be life-threatening [1]. Recent studies in Europe have shown that NCI affect from 4,6% to 9,3% of hospitalized patients [2-8]. About 5 million cases of nosocomial infections are registered in Europe per annum; annual mortality is 50000 - 135000 and the damages reach from 13 to 24 billion Euro [9, 10].

Opportunistic pathogenic microflora is the etiological agent of the NCI. Biological spectrum of the agents is varied and there is no single opinion on the issue of etiological role of different microorganism groups [11, 12].

This defines the topicality of the research on the structure of nosocomial infections agents, their persistence and namely the factors for their resistance to biocides.

The aim of the research was to study the structure and patterns of nosocomial infections agents' resistance to antibacterial medications that were identified in the Military clinical hospital of the Ministry of defense of the Republic of Kazakhstan in the period of 2004-2010.

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EPIDEMIOLOGIC SURVEILANCE OVER ANTHRAX IN KAZAKHSTAN IN MODERN CONDITIONS

Resume. *The article presents results of epidemiologic monitoring of anthrax in Kazakhstan over the period of 2002-2013. It was identified that range of anthrax infection has changed. Farm animals morbidity (FAM) and people are registered on the territory of only 2-3 regions on an annual basis, usually in South-Kazakhstan (SKR), East-Kazakhstan (EKR), West-Kazakhstan (WKR) and Almaty regions. Over 10 years (2002-2012) the number of anthrax cases among people has decreased 3,6 times compared to previous decade (1991-2001). Based on the results of epizootic and epidemic processes analysis, which characterize modern situation with anthrax in Kazakh-*

stan, priority directions have been identified for preventive anti-anthrax activities depending on the degree of epizootic and epidemiologic adversity of the territories.

The term "epidemiologic surveillance" was first developed in 1969 by the participants of the seminar, organized by WHO European regional bureau in Hague. According to B.L. Cherkasskiy "Epidemiological surveillance is a system of dynamic and multifacet monitoring of epidemic process of a specific infectious disease or epidemiologic situation in general in a given period of time for the purpose of rationalization and increasing efficientcy of preventive activities" [1].

State sanitary-epidemiologic surveillance over anthrax among people and farm animals in Kazakhstan includes:

1) monitoring of anthrax morbidity among people and farm animals;

2) monitoring of Bacillusanthracis agent circulation;

3) identification, recording and certification of the areas with adverse situation on anthrax;

4) preventive vaccination to the individuals, whose activities are related to anthrax infection threat;

5) assessment of activities efficiency;

6) forecasting the development of epidemic situation.

Threat of lethal outcomes after anthrax infection for people, large funds to liquidate the outbreaks require study of epizootic and epidemic situation on the territory of Kazakhstan, identification of old disease sites and registration of new ones.

Anthrax is a sapronosis-zoonotic infection. Currently in Kazakhstan it is manifested in small outbreaks, sporadic disease cases among people and animals. Sapronosis nature of B. anthracis agent's existence defines its natural disease sites. The peculiarity of the agent lies in the fact that development of epizootic infection hotbeds is generally related to activity of human beings. Creation of new infection sites as a result of natural factors influence, such as carrying soil particles and spores with wing or water (rain or flood) is possible as well. Climatic and geographic peculiarities influence the development of persistent anthrax infection sites on the territory of Kazakhstan.

Aim of the research: monitoring of anthrax morbidity among people and farm animals; study of the nature of infection prevalence in modern conditions.

UDC 616.98:578.825.12

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LABORATORY CHARACTERISTIC OF CYTOMEGALOVIRUS INFECTION AMONG PATIENTS IN KYRGYZ REPUBLIC

Resume. *The work is devoted to studying the state of new-born, children and patients CMV infection.*

Among the children in all age groups tested specific titers IgG are identified most often, in fact the share of children with high levels of antibodies 1:400 and 1:800 was 39,5%±1,3 and 3,1%±0,4 respectively, and with average antibodies level – 26,5%±1,2, and in adults high levels of IgG 1:800 were identified in 14,7%± patients, antibody levels of 1:400 were identified in

47,5%± patients, with average antibody titers– 14,8%± patients. Intrauterine infection of newborns, as well as subsequent infection of children in first year of life was identified. The titers of antibodies to CMV infection were higher in women of 30 to 40 years (68,9%). Among women under 20 the risk of intrauterine transmission of CMV to the fetus was almost 3 times higher than among children of older age.

CMV virus has special significance in children due to high level of infection, possibility of severe clinical forms development and prognostic unfavorable consequences in future, even in subclinical course options. The main transmission way in children is intrauterine infection from infected mothers. According to the data of modern studies in the Russian Federation intrauterine infection is seen among 0,2-10% of newborns [2]. In the USA for 4 million births per year and approximately 1% of intrauterine infected newborns about 8700 children suffer from early and late complications of CMV infection [1].

In Germany for 810 000 births per annum the share of intrauterine infected newborns is 0,2-0,3%, 500 children have early and late CMV damages.

In cases of intrauterine infection CMV easily penetrates placenta and can be a cause for incomplete pregnancy, congenital diseases of fetal infection development [3]. Intrauterine CMV-infection takes significant place in fetus and newborns pathology and is one of the most frequently diagnosed at this age.

UDC 61.577.212.3(005)

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STRUCTURAL AND FUNCTIONAL ORGANIZATION OF VIRIONS AND COMPONENTS OF INFLUENZA A VIRUS

Review paper

Abstract. *The article describes the structural and functional organization of influenza A virus virions. Each segment and functional roles of proteins - genome expression products – are discussed in detail. The article presents data that indicate possible ways of antigenic variation of influenza A virus, main methods for the identification of influenza viruses and determine their relationship to other strains.*

The family *Orthomyxoviridae* includes three genera of influenza viruses: genus *Influenzavirus A*, genus *Influenzavirus B* and *Influenzavirus C*. In recent years, this family also includes Thogo-like viruses [**Ошибка! Источник ссылки не найден.**].

Influenza A viruses differ from each other by antigenic properties of surface proteins - hemagglutinin and neuraminidase. At present, regardless of the host type from which the viruses are isolated, there are 16 serosubtypes of hemagglutinin and 9 serotypes of neuraminidase, of which only serosubtypes H1N1, H2N2, H3N2 are human influenza viruses [**Ошибка! Источник ссылки не найден.**,**Ошибка! Источник ссылки не найден.**]. Influenza viruses of B and C are not divided into serosubtypes.

The chemical composition of influenza virus virions is determined approximately

because viral populations are heterogeneous and largely depend on the composition of the host cell. A viral particle includes: 1-2% RNA, 50-70% protein, 18-37% of lipids, and 5-9% of carbohydrates. Virions are spherical (80-120 nm in diameter) or a pleomorphic form of the same diameter. The length of filamentous virus particles 20 nm in diameter can significantly exceed the diameter of the spherical particles [**Ошибка! Источник ссылки не найден.**]. Filamentous forms are characteristic mainly for particles that are freshly isolated from human or animal strains, after passages in cell culture or in embryonated chicken eggs. In the process of adaptation to the cell they become round. [**Ошибка! Источник ссылки не найден.**].

A characteristic morphological feature of Orthomyxovirus particles is the lipid membrane 4-5 nm thick at a distance of 42.5 nm from the center of the particles. About 500 surface spikes, which project by 10-14 nm high from the membrane surface and are 4-8 nm thick, are integrated in the lipid layer. Distribution of spikes on the virion surface is uneven. Approximately 5 adjacent spikes are around each spike. All they seem to relate to each other like a bee honeycomb [**Ошибка! Источник ссылки не найден.**]. These spikes are formed by proteins of two types: rod-shaped spikes HA and mushroom-shaped spikes NA. The correlation of subunits HA and NA from different strains of the A genus virions varies in the range of 5:1-10:1 [**Ошибка! Источник ссылки не найден.**]. An electron-dense layer that consists of a membrane protein MI is under the lipid bilayer [**Ошибка! Источник ссылки не найден.**].

The internal part of the virion consists of RNP-containing structures of different sizes: 50 to 130 nm long, from 9 to 15 nm in diameter, which contain 8 RNA different segments with helical asymmetry [**Ошибка! Источник ссылки не найден.**]. It is suggested that the RNP-containing structure is formed by a thread, rolled back on itself and then twisted into a double helix [**Ошибка! Источник ссылки не найден.**]. Ribonucleoproteins contain 4 proteins. NP is a dominant protein subunit of nucleocapsid; it is calculated that one molecule reacts with about 20 nucleotides. Three proteins associated with RNP are in smaller amounts and designated as PB1, PB2 and PA [**Ошибка! Источник ссылки не найден.**].

Genetic information of the influenza virus is encoded in 8 segments of linear minus filiform single-stranded RNA with molecular weight 5106 and the total length of 12,000-15,000 nucleotides. The number of nucleotides of the biggest segment encoding PB2 protein is 2,300-2,500, the second segment (PB1 protein) – 2,300-2,500, the third segment (PA protein) – 2,200-2,300, fourth segment (AT) – 1,700-1,800, fifth segment (NP) – 1,500-1,600, the sixth segment (NA) – 1,400-1,500, the seventh segment (M1, M2, M3 proteins) – 1,000-1,100, the eighth segment (NS1, NS2 proteins) - nucleotides 800-900 [**Ошибка! Источник ссылки не найден.**].

PB1, PB2, PA Proteins

PB1 and PB2 polypeptides are relatively basic proteins, and PA polypeptide is relatively acidic protein [**Ошибка! Источник ссылки не найден.**]. Although it was found that 1 and 2 segments of RNA contain the same number of nucleotides and encode similar proteins PB1 and PB2, there is no homology in their sequences. PB2 protein recognizes and binds to the 5-cap site of cellular RNA. This fragment is split by the endonuclease and, after conformation changes, participates in priming of transcription of virion RNA [**Ошибка! Источник ссылки не найден.**]. PB1 protein catalyzes the processes of polymerization (elongation) of RNA transcript, cRNA and vRNA [**Ошибка! Источник ссылки не найден.**]. PA protein participates in the synthesis of vRNA, but the mechanism of this process is still unclear. There are data that RNA protein induces proteolysis in the nucleus co-expressed proteins [**Ошибка! Источник ссылки не найден.**, **Ошибка! Источник ссылки не найден.**].

Nucleoprotein

This polypeptide is a basic protein enriched in arginine residues and has a positive charge of + 14 at pH 6.5. It is calculated that about 20 nucleotides interact with one subunit NP. It is assumed that RNA are outside RNP because they can be replaced with polyvinyl and are sensitive to cleavage by ribonuclease without destroying the structure of RNP [**Ошибка! Источник ссылки не найден.**]. After translation, the phosphorylation of a part of NP molecules at Ser residue, which explains the presence of two NP protein fractions with different electrophoretic mobility [**Ошибка! Источник ссылки не найден.**]. Another explanation for the presence of forms NP56 and NP53 is posttranslational proteolytic degradation of newly synthesized protein NP and NP of parental influenza virus [**Ошибка! Источник ссылки не найден.**]. Nucleoprotein is a multifunctional protein as it interacts with itself within the RNP and with vRNA. It forms a transcriptase complex with proteins PB2, PB1 and PA NP [**Ошибка! Источник ссылки не найден.**]. NP promotes polymerase protein activity at the stage of synthesis tRNA, vRNA and cRNA. It is shown that the role of NP in infected cells in the synthesis of complete complementary RNA copies is in anti-termination in the termination end points of viral mRNAs [**Ошибка! Источник ссылки не найден.**]. NP closely interacts with M-protein in the plasmamembrane [**Ошибка! Источник ссылки не найден.**]. NP in influenza virus is a protein that is genus-specific, which is used to detect A, B and C viruses. However, significant inter-genus differences are observed in antigenic properties of the NP [**Ошибка! Источник ссылки не найден.,Ошибка! Источник ссылки не найден.,Ошибка! Источник ссылки не найден.**]. There are differences in the positions of 30 amino-acid residues between the NP of A/RR/8/34 strains (N0N1) and A / NT 60/68 (H3N2) [**Ошибка! Источник ссылки не найден.,Ошибка! Источник ссылки не найден.**]. When comparing the peptides labeled as 35S, 61 strain, it was possible to isolate 6 groups of NP of human influenza A viruses, and 2 groups of NP proteins of animal viruses, which is consistent with the division [**Ошибка! Источник ссылки не найден.**] on the NP group with the use of homogenous antibodies.

Experiences with homogenous antibodies showed that NP molecule has from 3 to 5 antigenic sites, one of which is conservative in all studied strains of monoclonal antibodies [**Ошибка! Источник ссылки не найден.,Ошибка! Источник ссылки не найден.**]. Monoclonal antibodies to a conservative site inhibit in vitro the transcription of viral RNA or due to steric hindrance. This may occur due to interference with the function of NP, which differs from its structural role in the complex RNP. It is possible that NP plays a key role in determining the species specificity. Thus, the genetic analysis of a large number of influenza virus strains using the method of competitive RNA-RNA hybridization has found that segments of 5 RNA-avian viruses fall into two groups of equine viruses - form two other groups, and one group consists of human influenza and swine viruses [**Ошибка! Источник ссылки не найден.**].

The importance of NP in determining the host specificity is in a series of experiments with strains of subtype H3N2 isolated from different hosts. Mechanisms that control the host range of influenza virus through the NP, remain obscure. Perhaps the restriction recognition of NP cytotoxic lymphocytes (gene products of major histocompatibility complex) is one of the mechanisms of viral tropism to a particular host [**Ошибка! Источник ссылки не найден.**].

NP is a major target antigen for cross-reactive anti-influenza cytotoxic T lymphocytes (CTL) [**Ошибка! Источник ссылки не найден.**]. In polypeptide chains of NP exposed on cell membranes, CTLs recognize epitopes 50-63, 147-161/365-379 [**Ошибка! Источник ссылки не найден.**] in their close relationship with strictly defined gene products of major his-

tocompatibility complex expressed on the cell surface [**Ошибка! Источник ссылки не найден.**]. In the mice experiment, purified NP protein induces a high level of cross-reacting cytolytic T-lymphocytes, which protects animals from death after infection with a heterological virus in 75% of cases [**Ошибка! Источник ссылки не найден.**,**Ошибка! Источник ссылки не найден.**]. Due to this, there is an actual possibility of using NP protein or antigenic determinants in anti-viral vaccines and drugs.

Neuraminidase

The tetramer is the oligomeric complex of NA; its size is 100 x 100h60A on the leg, which is 140a^{o} high [**Ошибка! Источник ссылки не найден.**]. The distal end of peplomer NA is separated from the membrane surface by 160Ao, while HA peplomer - by 135a. NA peplomer consists of four identical subunits joined by covalent and non-covalent bonds [**Ошибка! Источник ссылки не найден.**]. In contrast to HA, NA polypeptide is immersed in its lipid membrane, and the N-terminus is not cleaved after the translation: its signal peptide initiating methionine and C-terminal sequence remain in the molecule [**Ошибка! Источник ссылки не найден.**].

As a result of sequencing of the gene, NA amino acid sequences of all four subtypes have four structural and functional domains: N-terminal conserved hexapeptide (residues 1-6), which is a cytoplasmic "tail," a hydrophobic transmembrane segment (residues 7-35), a thin "leg," stabilized by carbohydrates and intermolecular disulfide bonds (residues 36-61), "head" (residues 62-654) [**Ошибка! Источник ссылки не найден.**,**Ошибка! Источник ссылки не найден.**].

NH2 – a terminal domain is multifunctional, as it serves not only for “anchoring” in the lipid bilayer, but also provides the signal function for translocation and is required for intracellular movement between organelles [**Ошибка! Источник ссылки не найден.**]. Polypeptides of neuraminidase N1 and N2 contain methionine residues 7-8, 19-22 half-cysteine residue, one of which is in transmembrane domain, residues 1-2 in the area of the “leg,” and the rest – in the “head.” There are 5-8 potential glycosylation site in the molecules of neuraminidase N1 and N2 at asparagine residues in the “foot” and “head” [**Ошибка! Источник ссылки не найден.**,**Ошибка! Источник ссылки не найден.**].

The study of three-dimensional structure “head” of NA showed that each monomer consists of 6 topologically identical β-sheets arranged like a propeller. The peplomer of the enzyme consists of four identical and symmetrically arranged polypeptides and is partially stabilized by metal ions associated with the axes of symmetry. The oligosaccharides are attached to asparagine residues 86, 146, 200, and 234 [**Ошибка! Источник ссылки не найден.**]. Residues 86 and 234 are arranged on the lower surface of the monomer at a distance of 11Ao from each other. Residue 146 is on the upper surface of the head in β23 structure. The oligosaccharide attached to the residue is of complex type and serologically reacts with the host antigen of chicken embryo [**Ошибка! Источник ссылки не найден.**]. This glycosylation site is conservative in all the examined strains except for neurovirulent A/WSN/33 virus [**Ошибка! Источник ссылки не найден.**]. It is also unique due to the high content of N-acetylglucosamine [**Ошибка! Источник ссылки не найден.**]. Direct or indirect participation of oligosaccharide at residue 146 in the catalytic activity of NA is of considerable interest. Glycosylation site at residue 200 is located on the inter-subunit surface of the monomer and interacts with surface residues on the adjacent monomer. Approximately half of the carbohydrates is localized at the N-terminal transmembrane domain of the “leg,” they are partially included in the interchain bonds.

The catalytic sites are located in cavities on the surface of the upper corners of the oligomer “head” [**Ошибка! Источник ссылки не найден.**]. Like other enzymes that catalyze the removal of terminal groups,

the morphology of the active site is more similar to the "pocket" than to the "cleft." The walls of the "pocket" are formed with amino acid residues, most of which are conservative to A and B viruses, charged to the site that binds sialic acid, and identical in A and B viruses. One peplomer of the neuraminidase contains four catalytic centers that are located at a distance of 40Ao from each other. When the sialic acid is bound with the active site, there is no noticeable change of the quaternary structure of the enzyme [**Ошибка! Источник ссылки не найден.**].

The active center of the enzyme and receptor site of hemagglutinin have certain similarities, such as presence of tyr98, his193, glu190, trp 153, leu 194. There is evidence that a change at position 226 in HA1 by leu changes the specificity of the binding with sialic acid from nen aca2 → 3 gal to neu ac l2→6gal [**Ошибка! Источник ссылки не найден.**].

The examination of NA A/Ri/5/57 (H2N2) with moAbs showed that the enzyme molecule contains four independent antigenic areas [**Ошибка! Источник ссылки не найден.**]. Sites 1 and 4 are remote from each other and no competition between moAbs to these sites is revealed. Site 2 is divided into four overlapping zones 2a, 2b, 2c and 2d. Only moAbs to site 2 have virus-neutralizing activity and ensure selection of antigenic variants. The topographic map of neuraminidase was created on the basis of antigenic mapping and biological properties of influenza viruses. It is suggested that sites 1 and 4 are arranged in the lower part of the molecule, and site 3 – in the upper part, at a distance from the catalytic center. Site 2 is probably located in the upper part, while 2d zone is closely related to the enzymatic center and adjacent zones 2a and 2b. [**Ошибка! Источник ссылки не найден.**].

NA cleaves α-ketose connection between the terminal sialic acid and adjacent sugar residue. NA, similar to HA, is the glycosylated protein but owing to the enzymatic activity both glycoproteins do not contain the normal level of terminal sialic acid [**Ошибка! Источник ссылки не найден.**].

M1, M2, M3 Proteins

The seventh RNA segment encodes membrane proteins M1 and M2, and probably peptide M3. As a result of the transcription, three separate mRNA are synthesized, one of which is a collinear transcript segment M1, and the other two are spliced mRNA that contain discontinuous portions of genes M2 and M3 [**Ошибка! Источник ссылки не найден.**].

Proteins M1 and M2 overlap by 14 amino acids, as splicing is combined with a shift of the reading frame. Reading of mRNA for M3 protein occurs in the same frame as the mRNA in M1, but closer to the C-terminus. M1 and M2 proteins consist of 252 and 97 amino acid residues, respectively. Four domains of hydrophobic neutral amino acids in M1 protein were identified, the first three of which are built into the virion lipid membranes [**Ошибка! Источник ссылки не найден.**]. M2 protein is expressed as tetramers on the surface of infected cells, and also found in the virion envelope (from 16 to 68 molecules per virion). It is suggested that M2 functions as an ion channel during uncoating of the virus and controls the progress of HA during maturation [**Ошибка! Источник ссылки не найден.**,**Ошибка! Источник ссылки не найден.**].

Identification of differences between conservative areas in M1 and M2 proteins that are specific to avian and human viruses confirms the hypothesis of the existence of antigenic determinants of hosts and resistance to rimantadine [**Ошибка! Источник ссылки не найден.**]. However, M1 protein is a type-specific antigen. This is the most conservative protein in the virus; the homology of that gene in different strains of avian and human influenza viruses reaches 92% [**Ошибка! Источник ссылки не найден.**]. Four antigenic sites were identified using moAbs, one of which is conservative, type-specific, and others are subject to change. Antigenic differences can be identi-

fied both within the subtype and between virus subtypes [**Ошибка! Источник ссылки не найден.**].

The molecular weight of the protein M1 is 25,000 D; it accounts for 15% of all viral proteins, the number of molecules M1per virion does not exceed 800. M1 protein inhibits the RNA synthesis in the early stages [**Ошибка! Источник ссылки не найден.**]. In conditions of acidic pH, M1 is involved in the process of uncoating, is involved in nuclear transport and assembly of virion RNP. In addition to providing structural stability of the virion envelope, M1 recognizes virion glycoproteins and forms domains on the inner surface of the plasma membrane, which then provide the binding sites for RNP segments during assembly of virions [**Ошибка! Источник ссылки не найден.**].

Reduction of the relative concentration of M1 leads to increased brittleness of viral particles. Under experimental conditions, unstable particles with low M1 are described in ts-mutant influenza virus in virus progeny produced during abortive infection of Ehrlich ascites tumor cells [**Ошибка! Источник ссылки не найден.**], as well as during long persistent infection [**Ошибка! Источник ссылки не найден.**]. A limited amount of matrix protein in BHK cells with abortive infections can be caused by the defect of 7 gene transcription and reduced amount of mRNA for Ehrlich M1 [**Ошибка! Источник ссылки не найден.**]. Modifications of M1 protein are probably necessary to control the interaction with lipids on the one hand and for binding a viral RNP on the other hand. The latter regulates the function of RNP as a matrix for transcription of the genome and/or as a member of the assembly of viral particles [**Ошибка! Источник ссылки не найден.**]. The ability of the matrix protein to inhibit the transcription on the RNP matrix is demonstrated in experiments in vitro [**Ошибка! Источник ссылки не найден.**].

Non-structural proteins NS1 and NEP

The eighth segment of influenza virus RNA encodes two proteins that are found in infected cells: NS1 (MW ~ 26,000) and NEP (MW ~ 14,000). Mapping and sequencing of the gene revealed that NS1 and NEP proteins coincide in 70 amino acids, which are translated from different reading frames [**Ошибка! Источник ссылки не найден.**]. NS1 and NEP are type-specific proteins [**Ошибка! Источник ссылки не найден.**]. NS1 is synthesized in large quantities in the early stages of infection and accumulates in the nucleus. NEP protein is produced in the last stage of infection and is found in the cytoplasm. It is assumed that the NS1 protein is involved in elimination of the protein synthesis of the host cell and induces the synthesis of the virion RNA [**Ошибка! Источник ссылки не найден.**].

NS1 protein is encoded by the 8th fragment of the viral genome and plays an important role in the replication cycle of influenza A viruses [**Ошибка! Источник ссылки не найден.**]. The effect on the synthesis of cellular mRNA, splicing, action on protein kinase, induction of apoptosis is connected with the multiple functions protein. A feature of this protein is that it specifically binds to poly-A sequences of mRNA, small nuclear RNA such as U6 and double-stranded RNA of various origins. According to X-ray analysis, this protein forms dimers. Probably, binding to ds-RNA dimers tend to NS1. NS1 protein is only active as a dimer. Even a deleted version of the protein that retains the ability to dimerize remains active for suppressing the activation of interferon type 1.

Understanding the structural organization of the NS1 protein plays a key role in the identification of mutations that are responsible for high pathogenicity of influenza virus (including avian origin). Besides, it is obvious that the NS1 protein is the most promising target for the development of drugs that ensure suppression of immunosuppressive effect of influenza viruses on the system IFN type 1.

The most detailed study of the function of the protein NS1 in the blockade of production of IFN-α / β during influenza infection was published by Wang et al. (2000) from the laboratory R.Palese [**Ошибка! Источник ссылки не найден.**].

The group's work was based on the use of the deletion mutant of A/RR/8/34-del NS1 virus with deletion of the NS1 gene sequence in 8 segment of the virus genomic RNA. To obtain direct evidence of the role of the NS1 protein in the blockade of IFN-response during infection, the authors [**Ошибка! Источник ссылки не найден.**] investigated the induction of IFN-α and-β with a wild strain of A/RR/8/34 virus and its deletion mutant A/RR/8/34- del NS1. As a result, it was found that the induction of I-IFN type is observed in the MEF cells only in the case where a deletion mutant virus A/RR/8/34-del NS1 is used. When cells are infected with a wild type of the virus, the induction of gene expression of IFN-α / β was virtually absent.

Hemagglutinin

The protein of the HA influenza virus has been well examined both structurally and functionally. It is the principal viral antigen which is targeted by protective antibodies, and its variability is the main driving force of the evolution of the virus that occurs during epidemics. HA is the first membrane protein, the structure of which was established by X-ray tests [**Ошибка! Источник ссылки не найден.**]. Three-dimensional structure of NA head was detected using the same methods [**Ошибка! Источник ссылки не найден.**].

Hemagglutinin of influenza virus is synthesized as a single polypeptide chain that consists of 550 amino acids. As a result of subsequent cleavage with removal of residue Arg-329 form two chains, HA1 and HA2, that are covalently linked with a disulfide bond between positions 14 in HA1 and 137 in HA2. These double-stranded monomers are combined with non-covalent bonds in trimers and arranged on the membrane surface. The spatial structure of the trimer is installed X-ray test [**Ошибка! Источник ссылки не найден.**]. The monomer of hemagglutinin is an extended structure that protrudes from the membrane to 135A. It contains a stem at the top and a globular structure. This structure is formed by a part of the HA1 chain, and the “trunk” contains a part of the HA1 chain and the entire chain of HA2. The polypeptide has an extremely stretched configuration.

To initiate the infection, the influenza virus glycoprotein must contact the surface receptor of the target cell. The virus binds with the receptor that contains the sialic acid via the section located at the distal end of the HA. Initially, this section was located based on the results of determining amino acid sequences: Tyr-98, His-183, Tgr-153, Leu-194, Glu-190, etc. [**Ошибка! Источник ссылки не найден.**].

After infection of the cell with the virus that retains its envelope, the immune system of the cell forms antibodies against viral membrane glycoproteins. These antigens are also the targets for serum antibodies, which are formed as a result of vaccination [**Ошибка! Источник ссылки не найден.**]. Interpretation of the structure of influenza virus glycoprotein [**Ошибка! Источник ссылки не найден.**] allowed not only to identify a portion of this glycoprotein which is recognizable by antibodies, but also to understand how antigenic variations change. All antibodies that neutralize the influenza virus are antibodies to HA.

Based on the homology of amino acid sequences of HA1 (35%) and HA2 (53%), and conservative disulfide bonds, one can suggest that the structures of HA in viruses of subtypes H3 (1968-1983) and H1 (1933-1956) are generally similar [**Ошибка! Источник ссылки не найден.**]. Antigenic sites - loops, spirals, etc. are surrounded in H3 subtype strains by conserved residues, which are also in H1strains. An interesting difference is noted: section 165-167, which is an extension to the section B in HA virus in 1934, is masked by the oligosaccharide chain in HA of 1968, that is why the strain was not recognizable by antibodies. Similar

findings are observed in strains of influenza B virus.

As follows from the above, influenza viruses are a unique family of viruses that pose a real threat to the population of our planet. The main feature of this virus family is the ability to antigenic variation. The influenza virus is characterized by two main types of variability - antigenic drift and antigenic shift. The first type of antigenic variation, so called antigenic drift, is a gradual mutational change (point mutations) accompanied by changes in the antigenic structure of surface antigens: hemagglutinin (HA) and neuraminidase (NA). The second type - antigenic shift includes significant changes in antigen specificity, which occurs as a result of gene reassortment between viruses that are phylogenetically very distant from each other. These "new" viruses have the subunits of HA and NA that are completely different from those that have been circulating among people before the new virus appeared.

One of the earliest methods for detecting the interaction between the antigen and the antibody was based on detecting and analyzing the complex using the precipitation in gels [**Ошибка! Источник ссылки не найден.**], where monoclonal antibodies (moAbs) were used as antibodies to specific determinant of HA subunits [**Ошибка! Источник ссылки не найден.**].

The results of determination of HA amino acid sequences (in natural or laboratory selected antigenic variants of influenza H3 viruses) suggested that the three-dimensional structure, which is subject to structural changes during the antigenic drift, is responsible for the interaction with antibodies [**Ошибка! Источник ссылки не найден.**]. It is found that HA molecule has four major antigenic sites [**Ошибка! Источник ссылки не найден.**]. Section A is located at the projecting loop formed by amino acids 140-146. The portion B includes the projecting loop over residue 155 and exterior residues 187-198 around a-helix at the distal end of the molecule. Section C (residues 53, 54, 275, 278) is a bulge in the tertiary structure below globular domain. Section D (residues 207, 174) covers the residues on the surface of HA, and possibly some amino acids on the surface that separates monomers. In the study [**Ошибка! Источник ссылки не найден.**], a conclusion was made that viruses isolated during a certain period of the epidemic contained at least one mutation in each of above-described four antigenic sections that allowed them to avoid neutralization with antibodies.

These results were confirmed in studies of the HA virus A/Bangkok/1/79 (H3N2) that caused the flu epidemic in 1979. These experiments revealed additional changes in each of potential antigenic regions [**Ошибка! Источник ссылки не найден.**]. The analysis of a large number of 1968HA options that are selected using monoclonal antibodies directly confirmed the presence of A and B sections, and E section, which are recognized by antibodies [**Ошибка! Источник ссылки не найден.**]. Monoclonal antibodies, which helped to select substitution from Asn to Asp at position 63, are of particular importance because the oligosaccharide is introduced in this position. This explicitly indicates that carbohydrates can affect the immunological recognition of a steric structure of a glycoprotein by masking the surface of protein molecules. Carbohydrates can also simulate recognition of hemagglutinin and mask a part of antigenic zones in some strains [**Ошибка! Источник ссылки не найден.**].

Currently, molecular genetic tests, in particular the phylogenetic analysis, are used to determine both the antigenic drift and antigenic shift variants of influenza virus. The phylogenetic analysis of molecular data is one of the approaches to the theoretical study of the structure and function of genetic macromolecules (RNA, DNA, protein) and their evolutionary changes. The main purpose of the phylogenetic analysis is to study the evolutionary divergence of the sequences of genes and proteins, or their portions, and to recover the lists of evolutionary

events (substitution of nucleotides, deletions and insertions) in the ancestral lines of these macromolecules.

The main instrument of the phylogenetic analysis is comparison of genes or proteins, which have a similar structure or functions, and especially comparison of their primary sequences. The most important property of functionally important structures of macromolecules is their evolutionary conservatism. The conservatism of genes allows identifying a distant relationship between their representatives, which diverged a long time ago in the course of the evolution and sometimes perform different functions. However, the phylogenetic analysis requires a certain level of variability of genes. Mutations, deletions and insertions are marks, which help to restore the ways of evolution of modern forms of macromolecules. The polymerase chain reaction (PCR) followed by the nucleotide sequence analysis has been widely used recently for exact identification of influenza viruses and determine their affinity for the other strains. Restriction analysis of PCR products is also performed for comparative characteristics of genomes of different virus strains. Data of nucleic acid sequences are generally used for construction of the phylogenetic tree. The phylogenetic tree shows very clearly the relationship between viruses, if a large number of isolates are analyzed. For these purposes, there are a lot of software applications. The most popular software packages are PHYLIP (PHYLogeny Inference Package), PAUP (Phylogentic Analysis Using Parsimong), CLUSTAL and MEGA.

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RETROSPECTIVE ANALYSIS AND ASSESSMENT OF INFLUENCE POF HARMFUL PHOSPHOR PRODUCTION FACTORS ON THE HEALTH OF THE WORKERS

Resume. *The issues of multiple organ and systems damage on the initial stage of professional intoxication development have not been studied sufficiently. Assessment of interrelation of professional morbidity of phosphor production workers and some most significant factors of production environment and labor process has not been done.*

The aim of our work was retrospective study of the peculiarities of toxic organ and systems damage among the workers of phosphor production with correlation analysis to identify interrelations between professional morbidity of the workers and factors of production environment and labor process.

In-depth retrospective analysis of clinical materials of 200 patients with chronic phosphor compounds intoxication as professional disease. The age of studied patients differed from 26 to 49 years (28,0±0,7 years), work experience in phosphor production was from 6 to 19 years (15,8±0,5). The study allowed establishing peculiarities of toxic damage of organs and systems

among the workers of phosphor production depending on the stage of professional intoxication. Syndrome clinical characteristic of chronic intoxication with phosphor compounds with different degree of manifestation was analyzed with account of the nature and degree of toxic organ and systems damage while developing a professional pathology.

Clinical criteria for stages of damage have been identified for practical use by the professional pathologies physicians in order to identify early signs of professional intoxication within the framework of periodic preventive medical check-ups. Assessment of the degree of harmful factors influence in phosphor production on health of the workers has been done. Some clear positive correlation has been established between some adverse factors of production environment, labor process and professional and general morbidity of the workers. The most significance have the relations between professional morbidity due to chronic intoxication with phosphor compounds with loss of working capacity and such harmful factors as furnace charge dust, ferrophosphorus (r-0,94); phospholic anhydride (r-0,92); yellow phosphor fumes (r-0,95), hydrofluoric acid (r-0,93); phosphine (r-0,93). Relations between the general morbidity and such factors as labor heaviness (r-0,9), labor intensity (r-0,91) and uncomfortable working position (r-0,92) are also significant. There was also high positive correlation between microclimate conditions in the working premises and general morbidity (r-0,91).

UDC: 613.6.027

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REHABILITATION ALGORITHM OF THE PATIENTS AND DISABLED INDIVIDUALS WITH EFFECTS OF THE CHRONIC PHOSPHOR COMPOUNDS INTOXICATION

Resume. *The issues of disability prevention and improvement of approaches to decreasing disability indicators is one of the relevant problems of medical-social expertise and rehabilitation of patients with chronic phosphor compounds intoxication (CPCI). The problem of rehabilitation process evaluation and rehabilitation prognosis with account of CPCI course peculiarities has not been studied.*

The aim of this work was to develop algorithm and technology of rehabilitation process, which includes prevention, identification and rehabilitation of disability. The study allowed to develop and test rehabilitation technology for the patients and disabled individuals, who suffer from CPCI. Stages of rehabilitation technologies in cases of professional CPCI are presented. Rehabilitation technology for the patients with CPCI includes the following stages:1) expert rehabilitation diagnostics; 2) identification of rehabilitation potential;3) identification of clinical-rehabilitation groups (CRG); 4) medical-social expertise;5) development of individual rehabilitation program;6) individual rehabilitation program implementation; 7) assessment of rehabilitation efficiency.

Identification of rehabilitation potential (RP) has been done in order to forecast recovery of damaged functions and possibility of the patient's return to labor activities.

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EXPERT ASSESSMENT OF NEUROPROTECTING MEDICATIONS, USED IN PHARMACEUTICAL THERAPY FOR THE PATIENTS WITH ISCHEMIC STROKE

Resume. *The article provides the results of expert assessment of the neuroprotecting agents range, used in pathogenic based treatment of patients with ischemic stroke. It was identified that among the factors, influencing the prescription of medications, the most significant are efficiency of medications, data of clinical studies, as well as pharmacotherapeutic characteristics and rationality of forms of production. According to the studies for each of the 20 medications average weighted estimates were identified based on the parameters of efficiency, frequency of prescription, perspectives, availability in pharmacies and side-effects. In order to take into account all analyzed parameters for each medication multidimensional averages were calculated. It was identified that out of 20 studied neuroprotecting agents the experts gave their preference to the following medications: citicolin, magnesium sulfate, cerebrolysin, actovegin, cortexin and betagistin.*

Vascular-cerebral diseases of population are relevant medical and social-economic problem both for domestic healthcare and society in general. According to the data of World health organization, about 10-12% patients after ischemic stroke die, 20% of patients need constant care and only 20-25% people can get back to work [1].

Currently the problem of cerebrovascular pathology treatment efficiency is still relevant, as well as the schemes of pharmacotherapy, which are rather expensive. Despite wide range of medications on a pharmaceutical market of the Ukraine, the population does not have adequate access to vitally needed medications. Furthermore, significant number of the medications are of foreign origin, which makes it more difficult to use them in the FT process. [2, 3]. In the given conditions research on the issues of optimizing pharmaceutical provision of medications to people with ischemic stroke gains special significance.

In order to solve the abovementioned problems it is necessary to form the registry of neuroprotecting medications (NPM), which will satisfy the requirements of specialists, providing medical care to patients with ischemic stroke. In order to do this we suggest use of expert evaluation method, the aim of which is to define the most efficient and perspective medications.

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ROLE OF DIFFERENT RESPIRATORY VIRUSES IN DEVELOPMENT OF SARI INADULTS (BASED ON THE MATERIALS OF ASTANA INFECTIOUS DISEASES HOSPITAL)

Key words: *Sentinel surveillance, severe respiratory infections, standard case definition, influenza virus, Astana, Kazakhstan*

Abstract. *Every year influenza epidemics cause approximately 3-5 million cases of severe illness and about 250,000-500,000 deaths. The goal of this study was to evaluate the role of respiratory viruses in the development of severe acute respiratory infections (SARI) based on materials of city infectious diseases hospital in Astana.*

Patients were selected based on the standard case definition of SARI. Clinical, epidemiological, and etiological aspects of 272 SARI cases, including 30 pregnant women at different stages of pregnancy for 2010 -2013 were analyzed.

In 2010-2011 season, the DNA of influenza virus was isolated in 57 (50.4%) examined patients. In 2011-2012 epidemic season, influenza viruses were isolated in 32 (43.8%) examined patients; other ARI viruses were isolated in seven SARI patients: rhinovirus (hRv) in 3 (42.9%), respiratory syncytial virus (hRSv) in 2 (28.5%), parainfluenza 1 (hPiv) in one patient (14.3%) and coronavirus (hCov) – in one patient (14.3%). In 2012-2013 season, samples of 77 SARI patients were collected. Positive results of the PCR test were received from 20 (26.0%) SARI patients. Other respiratory viruses were isolated from 19 (24.6%) patients: rhinovirus – from 12 (63.2%) patients, respiratory syncytial virus – from two (10.5%) patients, adenovirus – from 3 (15.8%) patients, parainfluenza 1 – from two (10.5%) patients. Influenza viruses A/H1N1-pnd 09, A/H1N1V, influenza B were isolated from 30 pregnant women with SARI.

Sentinel surveillance enabled to select SARI and identify the cases by etiology. Not only influenza viruses but also other respiratory viruses are important in development of SARI. Out of 263 SARI patients, influenza viruses were isolated from 109 patients: influenza A virus - from 82 patients, influenza B virus – from 27 patients. Early detection of SARI during sentinel surveillance and hospitalization of patients with timely start of treatment helped to avoid severe complications and death outcomes among SARI patients.

Introduction

Epidemic increase in influenza and ARI incidence is observed in many countries of northern hemisphere in October-January with different intensity. Influenza causes a significant number of influenza cases [1]. According to data of the World Health Organization (WHO), severe influenza affects 3-5 million people in the world every year, and 250,000-500,000 people die from complications. In developed countries, majority of death cases associated with influenza are reported among people of 65 years and older [2]. Due to this, enhanced epidemiological surveillance of influenza and ARI is determined as one of the priorities in the whole number of international initiatives [3], including in the Republic of Kazakhstan, where epidemiological surveillance is aimed at reducing incidence and mortality associated with influenza.

Since November 2009, Astana infectious diseases hospital became one of the sentinel sites for recording SARI patients. From 2009 to 2011, registration of patients who meet the standard case definition (SCD) under sentinel surveillance and laboratory testing for respiratory viruses was performed according to the criteria that met SARI SCD: fever 38.0ºC and above, cough or sore throat, shortness of breath or difficulty breathing with the duration of the disease for no more than 72 hours.

Since 2011, we started using the new WHO Regional Office for Europe guidance for sentinel influenza surveillance in humans [4]. According to the guidance, SARI is diagnosed in case of the disease with onset during the previous 7 days (7 days – to count cases and 3 days - to collect a sample) requiring overnight hospitalization and is characterized with the following signs: 1) history of fever 38.0C^{o} and above or high fever temperature; 2) cough (sore throat was removed from the new standard case definition of SARI due to lack of specificity of this symptom); and 3) shortness of breath or difficulty breathing.

The goal of this study was to evaluate the role of different respiratory viruses in devel-

opment of SARI based on the materials of the Astana city infectious diseases hospital.

Materials and methods

All patients who visited the City Infectious Diseases Hospital and met the SARI SCD were admitted to the hospital and underwent comprehensive examination. Laboratory throat and nasal samples were collected upon the admission in a special viral transport medium, were stored at– 190°C in liquid nitrogen until they were transported to a zonal virology laboratory of the Astana Center for Sanitary and Epidemiological Expert Examination. In addition, a questionnaire was filled in for each patient. The questionnaire indicated the patient's sex, age, social status, comorbidities, status of influenza vaccination, and use of antiretroviral drugs. Laboratory samples were collected by a trained nurse of the admissions department.

In 2011 - 2012 epidemic season, patients were selected in accordance with the criteria of the new SARI SDC. According to the rules of sentinel surveillance, material was collected and survey was performed as follows: every day at least one patient but no more than three patients who visited for medical consultation during the week were selected from each age group (15-29, 30-64, 65 and older). A standard questionnaire was completed and its hard copy was submitted once a week to the surveillance section in the department for Astana State Sanitary and Epidemiological Surveillance.

To evaluate the role of influenza viruses and other respiratory infections in the development of SARI in pregnant women, we observed 30 women with different periods of gestation with clinical signs that met SARI SDC.

Results

According to the information of Epi Info database, data of influenza electronic tracking in sentinel surveillance, SARI patient record logbook, and medical charts of the hospital patient (form 003-u), we analyzed clinical and epidemiological and etiological aspects of 263 SARI cases (130 men, 133 women). The following underlying diseases were identified in SARI patients: purpura rheumatica - 1, otitis - 1, chronic maxillary sinusitis - 2, chronic obstructive lung disease - 4, including tuberculosis pleurisy - 1, pulmonary tuberculosis - 1, hypertension - 1.

Results of virology tests of data of SARI patients are presented in table 1.

Epidemic seasons	Total ARI and influenza patients	Number of virologically tested patients selected by sentinel surveillance criteria	Results			
			RNA of influenza virus "+" n (%)	Among them		RNA of influenza virus "-" n (%)
				Influenza A virus n (%)	Influenza B virus n (%)	
2010/2011	1254	113	57 (50.4)	39 (68.4)	18 (31.6)	56 (49.6)
2011/2012	1534	73	32 (43.8)*	27 (84.3)	5 (15.6)	41 (56.2)
2012/2013	1440	77	20 (26.0)**	16 (80.0)	4 (20.0)	57 (74.0)
Total	4228	263	109 (41.4)	82 (31.1)	27 (10.3)	154 (58.6)

*other ARI viruses were isolated from 73 patients, except for influenza viruses in seven patients

** other ARI viruses were isolated from 77 patients, except for influenza viruses from 19 patients

Table 1 – *Role of influenza viruses in SARI development during 2010–2013 epidemic seasons (based on materials of Astana City Infectious Diseases Hospital)*

In 2010 - 2011 epidemic season, 113 SARI patients were examined, out of which RNA of influenza virus was isolated in 57 (50.4%) patients. In this epidemic period, influenza A virus dominated 2.2 times more frequently in SARI patients.

In 2011 -2012 epidemic season, all 73 patients were examined; influenza viruses and other ARI were isolated from 39 (53.4%) patients.

In 2012-2013 epidemic season, samples and data of 77 SARI patients were collected. PCR positive results with influenza virus isolation were detected in 20 (26.0%) SARI patients. Influenza A virus that was detected in 16 (80.0%) patients played a key role. Influenza B virus – 4 (20.0%) was detected in SARI patients four times less frequently. Besides, other respiratory viruses were isolated in 19 (24.6%) SARI patients. The frequency of detection of influenza viruses from SARI patients is presented in figure 1.

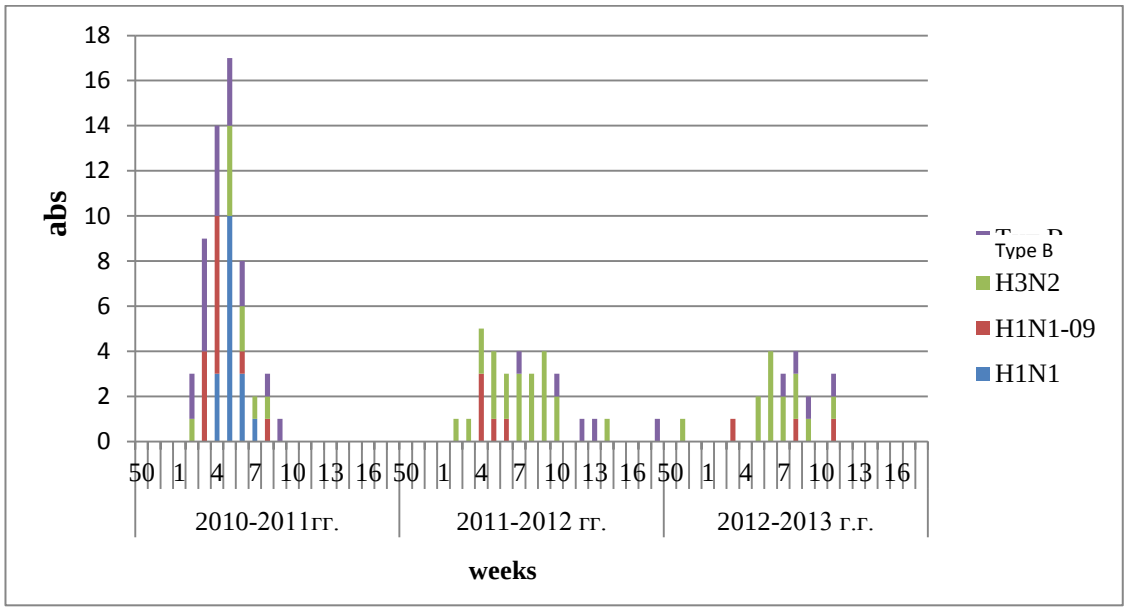

***Figure 1** – Etiology of SARI in the period of epidemic seasons by weeks in 2010-2013 (based on the materials of Astana City Infectious Diseases Hospital)*

In 2010 - 2011 epidemic season, influenza viruses were mainly isolated from patients from week 2 to week 9 of 2011, with isolation of subtypes A/H1N1 и A/H1N1 – pnd 09 of influenza A and influenza B. However, influenza viruses of A/H1N1 and A/H1N1–pnd 09 caused further development of SARI equally frequently - 17 (43.6 %) and 13 (33.3%), respectively, while A/H3N2 virus caused development of SARI twice as less - 9 (23.1%).

In 2011-2012 epidemic season, A/H1N1 did not play a role in development of SARI.

Influenza virus B started to appear among tested patients at the end of the epidemic seasons. This virus was isolated from 5 (15.6%) SARI patients, which is 3.6 times lower than in the previous season.

In 2012-2013 epidemic season, A/H1N1 was not isolated from SARI patients as in the previous season. During the whole epidemic season, A/H3N2 played a main role in development in SARI patients. This subtype was isolated from 13 patients (81.3%); subtype of influenza virus A/H1N1–pnd 09 was detected from 3 patients (18.7%). Influenza B virus was still isolated from SARI patients at the end of the epidemic season.

It should be noted that other respiratory viruses also caused SARI. Data are presented in figure 2. In 2011-2012 epidemic season, the following viruses were isolated

from seven (9.6%) SARI patients: rhinovirus (hRv) from 3 (42.9%) patients, respiratory syncytial virus (hRSv) from two (28.5%) patients, parainfluenza 1 (hPiv) from one patient (14.3%) and coronavirus (hCov) – from one patient (14.3%).

In 2012-2013 epidemic season, the following viruses were isolated in 19 SARI patients: rhinovirus – in 12 patients, respiratory syncytial virus – in two patients, adenovirus – in three patients, parainfluenza 1 – in two patients. In two patients, SARI was caused by a co-infection: combination of rhinovirus and coronavirus; combination of parainfluenza 1 and parainfluenza 3.

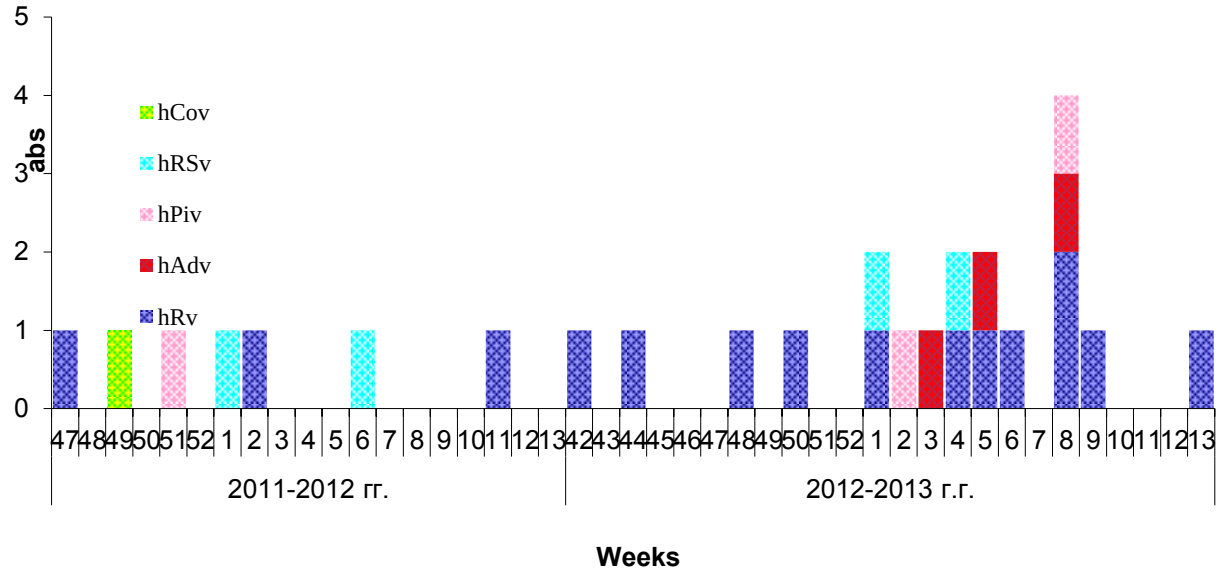

***Figure 2** – Role of different ARI viruses in development of SARI n=(26) in 2011-2013 epidemic seasons (according to the materials of the Astana City Infectious Diseases Hospital)*

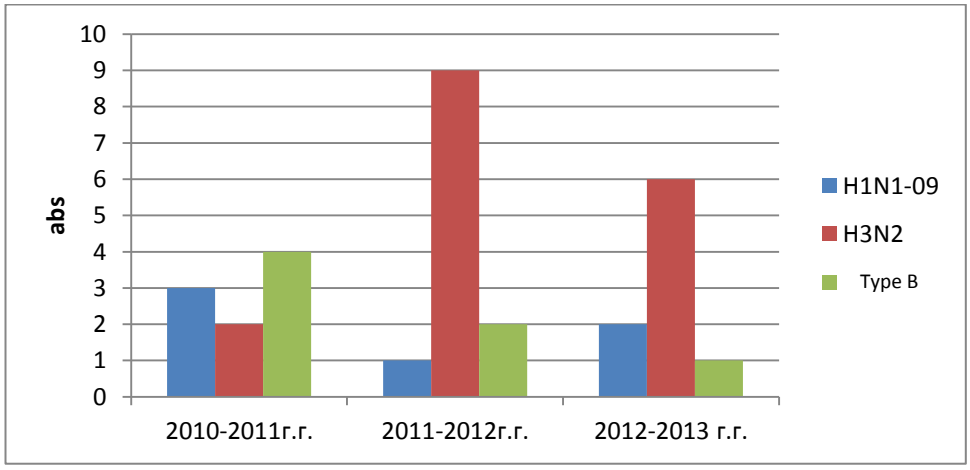

***Figure 3** – Role of viruses in development of SARI in pregnant women (n=30) in 2010-2013 (based on the materials of the Astana City Infectious Diseases Hospital)*

The role of influenza viruses in development of SARI in pregnant women during 2010-2013 is presented in figure 3. In 2010-2011 epidemic season, nine positive PCR results were received from pregnant women with SARI. Overall, six pregnant women

with SARI were registered (66.7%) in the first trimester of pregnancy, and three (33.3%) women in the second trimester of pregnancy, in each of whom one A/ H3N2 virus, one influenza B virus, and one A/ H2N-pnd 09 influenza virus were isolated.

In 2011-2012 epidemic season, influenza virus was isolated in 12 pregnant women with SARI. There were two pregnant women with SARI in the first trimester of pregnancy (16.6%); eight (66.7%) in the second trimester; there were two pregnant women in the third trimester.

In 2012-2013 epidemic semester, influenza viruses were in nine pregnant women with SARI. Overall, there were two pregnant women with SARI (22.2%) in the first trimester of pregnancy

In addition to main symptoms of the SDC, such symptoms as nausea, vomiting, accompanied by increasing headache lead to suspected development of meningitis in SARI patients in the hospital. Besides, SARI patients had catarrhal symptoms such as runny nose, sneezing. Such complication as pneumonia was reported in 10.6% of SARI patients. Aggravation of chronic bronchitis was associated with SARI in 6.2% cases, meningitis in 2.6%, and aggravation of chronic pyelonephritis in 5.2% cases. The clinical course did not allow identifying SARI. Only because of sentinel surveillance in Astana, it was possible to differentiate SARI as the disease of multiple etiologies.

The condition improved in the majority of cases from the second day of admission. There were no deaths among SARI patients monitored by us.

However, three pregnant women who stayed in obstetrics facilities died in 2009. They were admitted on the 4-5th day of illness. A/H1N1–pnd 09 virus was isolated from the material of the patients. One pregnant woman had unfavorable pre-morbid condition – chronic obstructive bronchitis. Late hospitalization and pre-morbid condition caused early development of severe virus pneumonia with death outcome.

Discussion

The study results suggest that the etiological factor in development of SARI in patients included not only influenza viruses but also other respiratory viruses. In 2009–2010, mainly patients who met SCD were admitted to pulmonology departments with early development of such complications as pneumonia including virus pneumonia. These departments did not perform sentinel surveillance, and that is why virology tests of agents of respiratory infections that were observed in this department were not performed. In 2011-2012 and 2012-2013 epidemic periods, no influenza virus A/H1N1 was isolated from tested influenza viruses. In 2012-2013 epidemic period, influenza and other ARI viruses were isolated with the same frequency. According to the SARI SCD, hospitalization was required for all 263 patients; we considered only 10 SARI patients out of them as severe according to the clinical condition. In addition to the symptoms indicted in the SCD, patients had other symptoms that were not included in the definition: headache, myalgia, joint pain, seizures, intoxication that worsened the condition and required hospitalization of patients.

Taking into account the 2009–2010 epidemic season, we started paying attention to pregnant women who become more susceptible to bacterial complications of SARI. They included pneumococcal, hemophilic, staphylococcal infections, especially in the third trimester of pregnancy. We considered the condition of all pregnant women as moderately severe irrespective of the influenza type. Severe conditions were observed in one pregnant woman with SARI from who influenza B virus was isolated. In 2010-2013 seasons, influenza A (H1N1) was not detected in pregnant women with SARI. There were no peculiarities depending on the etiological factor in the course of SARI in pregnant women. No death outcomes of pregnant women were observed. Thus, detection of patients based SARI criteria allowed conducting timely hospitalization of patients to prevent development of complications and deaths.

Conclusions

Sentinel surveillance helps diagnose SARI during the patients' first visit and identify the case according to the etiology, and determine the time for the beginning of the influenza season. SARI can be caused not only by influenza viruses but also by other respiratory viruses. Early detection of SARI in sentinel surveillance and timely hospitalization of SARI patients, and prescription of targeted treatment helps to avoid severe complications in SARI patients and deaths.

Thus, use of sentinel surveillance provides a standard mechanism for monitoring conditions associated with severe influenza.

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SERODIAGNOSTIC TESTING OF INFLUENZA VIRUS IN PIGS IN NORTHERN KAZAKHSTAN

Key words: *swine influenza virus, serological test, Northern Kazakhstan*

Abstract. *After the 2009 swine flu pandemic, the attention to the influenza in pigs increased worldwide. However, in Kazakhstan, swine influenza is studied insufficiently. Due to this, we studied the infection of pigs with influenza virus in the Kostanai region of Northern Kazakhstan.*

Blood serum samples were selected from 70 pigs in farms of the Kostanai region in Northern Kazakhstan. In November 2012, ten blood samples were collected from ten pigs of two-month age, 15 – from animals born in August and 15 from four-month pigs. In spring 2013, 30 blood samples were collected from animals born in November-December 2012. Blood serum samples of animals were studied for antibodies to influenza virus using enzyme immunoassay (EIA) and the hemagglutination-inhibition test (HAI).

The analysis of swine blood serum samples by EIA showed antibodies to influenza virus in 24.2% of samples from the total number of samples, 23.5% out of which were the subtype H1N1 and 29.4% were H3N2. According to HAI results, specific antibodies to influenza virus of Hsw1N1 subtype were detected in 31.5% of samples, to influenza virus H1N1 – in 15.7% and H3N2 – in 21%. It was found that classical swine influenza virus is dominant among pigs in the Kostanai region.

Because pigs can be considered as the reservoir for influenza A virus, regular surveillance of circulating types of swine influenza with further molecular study is important.

Introduction

The pig population plays an important role in the evolution of influenza A virus; moreover, the body of these animals is a suitable reservoir for mixing viruses from different hosts [1].

It is known that the increased frequency of mutations in the genome is a unique capability of the influenza virus. This occurs most often as a result of the 'gene drift', where the antigenic specificity of surface proteins (hemagglutinin and neuraminidase) changes as a result of mutations, which can lead to annual epidemics [2].

Such phenomenon as 'gene shifting' occurs more rarely but with certain regularity. Virus proteins are fully replaced by analogous but completely new antigenic specificity and new virus variants – reassortants – appear as a result of such mutations [2]. Simultaneous replication of human and avian influenza virus in pigs are most likely to lead to a new reassortant. Such phenomenon occurred in 2009 in Mexico. The influenza epizootic among pigs led to the announcement by the WHO of the sixth stage of influenza pandemic caused by the swine virus [3].

The goal of our study was to test swine sera for the presence of swine influenza virus from pigs in hog farms of the Kostanai region in Northern Kazakhstan. To our knowledge, no such studies have been done in Kazakhstan before.

Materials and methods

In the period from November 2012 to April 2013, 70 blood serum samples were collected from animals in farms of Northern Kazakhstan. Selection was mainly performed from pigs aged 2-6 months given that animals are susceptible to the diseases of different origin [4].

Blood serum samples were collected from healthy animals (n=45), animals with the signs of a respiratory disease (n=17), and from animals with suspicion of having bacterial infections (n=8 heads). Sera were collected in private farms in the Kostanai region of Northern Kazakhstan. The conditions in the farms at the time of collection conformed to zoo-hygienic standards. In November 2012, blood samples were collected in ten pigs aged two months, 15 – in animals, born in August, and 15 – in four-month pigs. In spring 2013, 30 blood samples were collected from animals, born in November-December 2012.

Blood from animals was taken from the auricular veins. To obtain the serum, blood tubes were put in the thermostat with the temperature +37°C after separating the blood clot from tube walls with the heat-treated wire. In 1-1.5 hours, stagnant serum was transferred into special transportation tubes and delivered in cold conditions to the laboratory with further storage at -20°C.

EIA and HAI

To determine antibodies to influenza H1N1 and H3N2 viruses, a test system of PPDP LLC (Saint Petersburg) was used in EIA.

It is known that EIA is the most sensitive method for detection of specific antibodies; however due to the lack of test systems to influenza virus of subtype Hsw1N1, testing of serum to this antigen in this test was not performed. Therefore, we used HAI to detect antibodies to influenza virus of subtype Hsw1N1.

HAI was performed by a standard method using influenza diagnosticum of H3N2, H1N1 and Hsw1N1 of PPDP LLC (Saint Petersburg).

To release non-specific inhibitors, serum samples were processed with RDE (receptor - destroying enzyme) (300 µl of RDE per 100 µl of serum), then preheated for 30 minutes at +56°C.

Results

During the first stage of our study, EIA was performed to detect antibodies to influ-

enza A of subtypes H1N1 and H3N2. Out of the total number of samples, antibodies to the influenza virus were detected in 24.2% samples, out of which 23.5% were referred to subtype H1N1 and 29.4% to H3N2.

According to HAI results with reference strains, antibodies to the influenza virus H1N1 were detected in 15.7% samples; to H3N2 – in 21% samples. But the highest number of tested sera in HAI was referred to the subtype Hsw1N1 – 31.5% from the total number of samples (Fig.1).

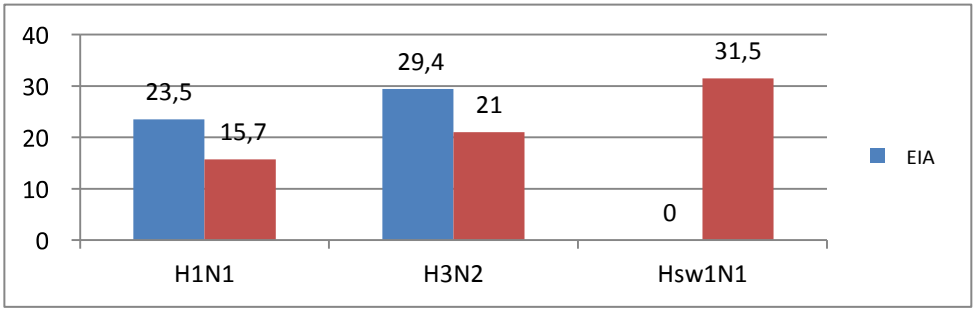

***Figure 1** – Detection of Antibodies to Influenza Virus in Swine Blood Sera by EIA and HAI (n=70)*

As the figure shows, the swine seropositivity to influenza subtype Hsw1N1 defined in HAI was much higher than the seropositivity to H1N1 and H3N2.

HAI results also demonstrate detection of antibodies to influenza virus, subtype H1N1 in 23.5% samples, and H3N2 in 29.4%, which conforms to HAI data. Out of two subtypes of influenza virus H1N1 and H3N2, the highest number of specific antibodies was detected to subtype H3N2. One cannot exclude that when using test systems for EIA to the influenza virus, subtype Hsw1N1, we could detect antibodies to this subtype.

Discussion

The results of EIA demonstrated antibodies to influenza viruses of H1N1 and H3N2 in the blood of examined animals. Perhaps, it is determined by the entry of an infection into a pig farm by the staff as shown by previous studies [5]. Out of two subtypes of influenza virus H1N1 and H3N2, the highest number of specific antibodies was detected to subtype H3N2.

A review of reference literature shows that three subtypes of influenza H1N1, H3N2 and H1N2 prevail in the pig population [6]. Data obtained when typing swine sera in HAI deny the information in relation to the circulation of these variants in Kazakhstan.

The results of the serum test by HAI showed that 31.5% of samples tested are referred to the subtype Hsw1N1. International studies of isolates A (H1N1) obtained from pigs in different regions of the world showed that two antigenic variants of these viruses are circulating among pigs: “avian-like” and “classical swine influenza virus” [1]. During the serological test by HAI, it was found that the influenza virus, subtype “classical swine influenza virus” prevails among the pig population in Kazakhstan.

Data regarding antibodies to influenza virus H1N1 and H3N2 in tested serum samples, which constituted 15.7% and 21% respectively, confirm the theory that pigs can be considered as a reservoir for influenza A viruses. According to certain studies, human viruses can be “conserved” in pigs for a long period [1]. Subtypes of H1N1 and H3N2 are the result of interspecies transit of influenza virus from humans to pigs.

Influenza viruses with unusual antigenic subtypes: H4N6 – in Canada [6], H3N6 – in Kazakhstan [7], H1N7 – in UK [7] were isolated sporadically from pigs. Influenza viruses of serotype C similar to human influenza C were also isolated from pigs [8]. Therefore, newer variants of influenza virus

continue to be registered which increases the probability of formation of reassortants. The risk of high virulent swine like virus similar to A/California/04/2009 in the human population necessitates systematic monitoring of pigs for the earliest detection of potential pandemic strain of influenza virus.

Animals are becoming more often the source of infections for humans as zoonoses continue to pose a serious risk for health of humans and animals. [9] Approximately three fourth of all new infectious diseases are zoonoses. As for influenza, pigs pose a high risk. According to the experts' opinion, swine influenza can be transmitted from animals to humans. The most important thing is to prevent a human-to-human transmission of swine influenza, although such cases cannot be excluded. Xian Qi et al. inform about 50 cases of affecting people by swine influenza virus; that is why this infection is referred to dangerous zoonoses [10], which also necessitates specific prevention of influenza in pigs. Most commercial swine influenza vaccines used in North America and Europe create a protective immunity to influenza A virus of subtypes H1N1 and H3N2 for about two months [11]. A swine influenza vaccine has not yet been developed in Russia or Kazakhstan.

One can ask whether there is a sense in influenza vaccination of pigs that live maximum two years. Another question is whether a vaccine strain, if it is a live vaccine with persisting virus in pigs, can provoke a mutant virus and pose a new risk for humans.

Changes in the practice of pig farming that suggest separation from people and in particular from swimming birds are required to prevent future pandemics regardless of whether the vaccination of pigs was performed or not [7]. Regular surveillance of circulating types of swine influenza virus with further molecular tests is of great importance.

Conclusion

Thus, circulation of influenza A, serotypes Hsw1N1, H3N2 and H1N1, was found in pigs of farms in Northern Kazakhstan. Data obtained about the spread of influenza virus among pigs are very limited and do not reflect the situation with swine influenza in Kazakhstan, which dictates the need to perform further monitoring of this disease among pigs.

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ACUTE RESPIRATORY VIRAL INFECTIONS WITH AND WITHOUT DIARRHEA BASED ON MATERIALS OF THE BISHKEK INFECTIOUS DISEASES HOSPITAL, KYRGYZ REPUBLIC, 2009-2010

Key words: *acute respiratory viral infection, association of the acute respiratory viral infection with diarrhea, Kyrgyz Republic*

Abstract*. In 2009, the number of registered ARVI patients in the Kyrgyz Republic exceeded 242,000 (4,840 per 100,000 population). Cases with diarrhea occurred among patients with ARVI and influenza. We analyzeв ARVI cases with and without diarrhea and determineв whether they met WHO case definitions of the severe acute respiratory infection (SARI).*

We analyzed the logbooks of daily registration of patients in the Republican Clinical Infectious Diseases Hospital (RCIDH) in the influenza epidemic season from week 40 of 2009 to week 13 of 2010. We also performed a retrospective study of medical charts of patients with ARVI (n=3,101) and ARVI with diarrhea (n=2,073) admitted to the RCIDH for the given period and evaluated whether the condition of patients meets the WHO standard case definition of SARI (2009). Among ARVI patients with diarrhea, cases where patients had loose stool more than twice per day prior to admission, with duration of more than two days together with SARI symptoms, were united into a separate group – SARI with diarrhea. Stool culture was collected from 2,073 ARVI patients with diarrhea to test for enteric pathogens. SARI patients included in sentinel surveillance (220 cases) were examined using the PCR method for influenza viruses. Data obtained were entered in Excel and analyzed.

During the epidemic season connected with influenza pandemics 2009-2010, RCIDH bed capacity was occupied by 80-97% with ARVI patients. 40% (n=2,073) ARVI patients had diarrhea. The proportion of SARI in cases of ARVI without diarrhea coincided with the proportion of SARI patients with diarrhea. The highest exposure to SARI was observed among children of the first year of life.

In the epidemic season of 2009-2010 influenza season in Bishkek, ARVI patients with and without diarrhea (40% and 60%, respectively) were registered. A high proportion (99%) of diarrhea of unknown origin was noted in ARVI patients and requires further tests to identify the role of viruses in development of the diarrhea syndrome in case of ARVI.

Introduction

ARVI and acute enteric infections (AEI) in the structure of infection incidence consistently occupy 1st and 2nd places and represent an important issue of children's infectology [1-3]. Over the recent years of epidemic tracking, 2009 was the most tense by incidence with ARVI and influenza, when the number of registered patients in the Kyrgyz Republic exceeded 242,000 cases (4,840 per 100,000 population) [4].

WHO's initiative *Global Agenda on Influenza Surveillance and Control* implemented in 2002 set several priorities, one of which is to enhance clinical and virological influenza surveillance. Due to WHO's alert of A (H1N1)-2009 influenza pandemic, and in order to promptly respond to pandemic and perform integrated clinical, epidemiological and laboratory surveillance, SDC of SARI were recommended separately for children under 5 years of age and persons 5 years of age and older who require hospitalization and SCD of influenza-like illnesses (ILI) for persons who do not require hospitalization. The case definition of SARI is deemed to provide the international standard method for registration and analysis of morbidity with severe influenza [4].

In addition to ARVI and AEI, cases with diarrhea among cases of ARVI symptoms, when AEI-associated ARVI is diagnosed, are registered in the country. Therefore, the goal of this study was to examine characteristics of ARVI with and without diarrhea, and determine the SARI proportion among ARVI patients.

Materials and methods

RCIDH of Bishkek provides medical care the population of the capital and has 250 beds; patients with all infection pathologies are admitted to the hospital. ARVI patients who require hospital and emergency care also visit this hospital.

We studied the logbook of daily registration of patients who are admitted for treatment to this hospital. All patients admitted from week 40 of 2009 to week 13 of 2010 were grouped at admission and distributed according to the week of the given season. Then the proportion of ARVI in the structure of weekly hospitalization was determined.

We performed a retrospective study of hospital medical charts of 3101 ARVI patients (n=3,008) 97% of whom were children under 14 years of age and 2,073 AEI-associated ARVI patients 96% of whom (n= 1990) were children under 14 years of age hospitalized in the RCIDH over the given period. We evaluated whether ARVI patents with and without diarrhea met the SDC of SARI. SDC recommended by WHO for children under 5 years was used as the main tool for evaluation of SARI: *cough or difficulty breathing, breathing ≥ 40 per minute, any sign that can be dangerous for the child's life: unable to drink or breastfeed, vomits everything, convulsions, lethargic or unconscious, or chest indrawing or stridor in a calm child.* Children above 5 years – *sudden increase in temperature >38°C, cough or sore throat (pharyngitis) and difficulty breathing or shortness of breath.* [4].

Among ARVI patients with diarrhea, cases of SARI with diarrhea were united into a separate group: *cases with loose stool more than twice per day by admission, with duration of SARI symptoms for more than two days.* Stool culture was taken from all 2,073 ARVI patients with diarrhea for enteric pathogens. SARI patients included in sentinel surveillance (n=220) were examined in the virology laboratory using the PCR method for influenza viruses. Data obtained were entered in Excel for further analysis.

Results

Over 2009-2010 epidemic season, 8,661 patients with different infection pathologies were admitted to the RCIDH. ARVI was detected in 60% (n=5174), of 60% whom had an independent course of ARVI, and 40% (n=2,073) had ARVI associated with diarrhea. Out of hospitalized patients 23% of patients were diagnosed with AEI. 17% patients received hospital care due to air-borne, zoonotic and other infections (Fig. 1).

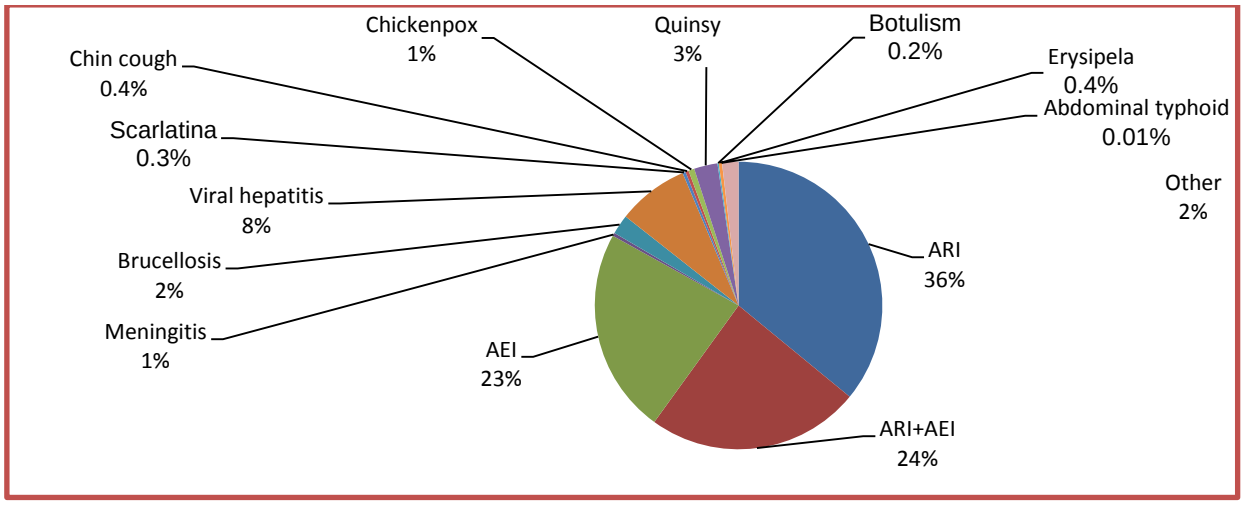

***Figure 1** – Nosological structure of admissions in RCIDH, Bishkek, Kyrgyz Republic, week 40 of 2009 – week 13 of 2010, N=8,661*

Weekly distribution of all admissions to the RCIDH, as well as the proportion of ARVI in the structure of admissions during the analyzed season is presented in figure 2. As it can be seen from the chart that 60% of all admissions were ARVI patients; moreover, 80-97% of admissions to the RCIDH from week 47 of 2009 to week 1 of 2010, during the influenza pandemic in the country were ARVI cases.

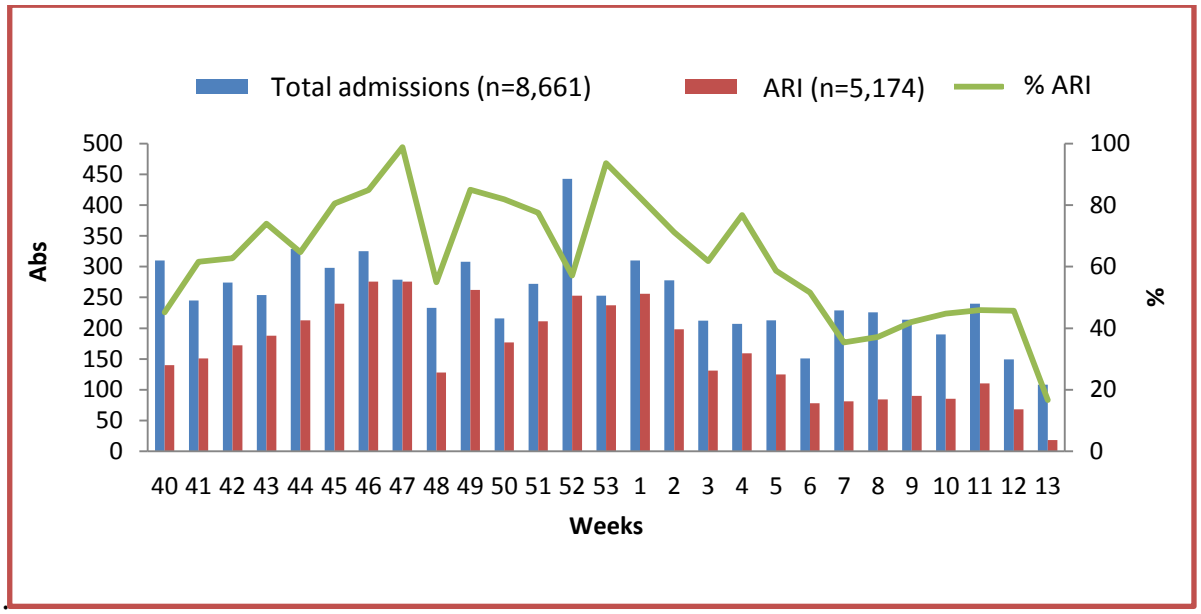

***Figure 2** – Admissions with infectious diseases, including with ARVI, by weeks, RCHID, Bishkek, Kyrgyz Republic, week 40 of 2009 – week 13 of 2010*

SARI detected in ARVI cases with and without diarrhea were distributed by weeks of the season (Fig. 3). SARI was observed equally frequently in compared groups and had a similar dynamic during the epidemic season.

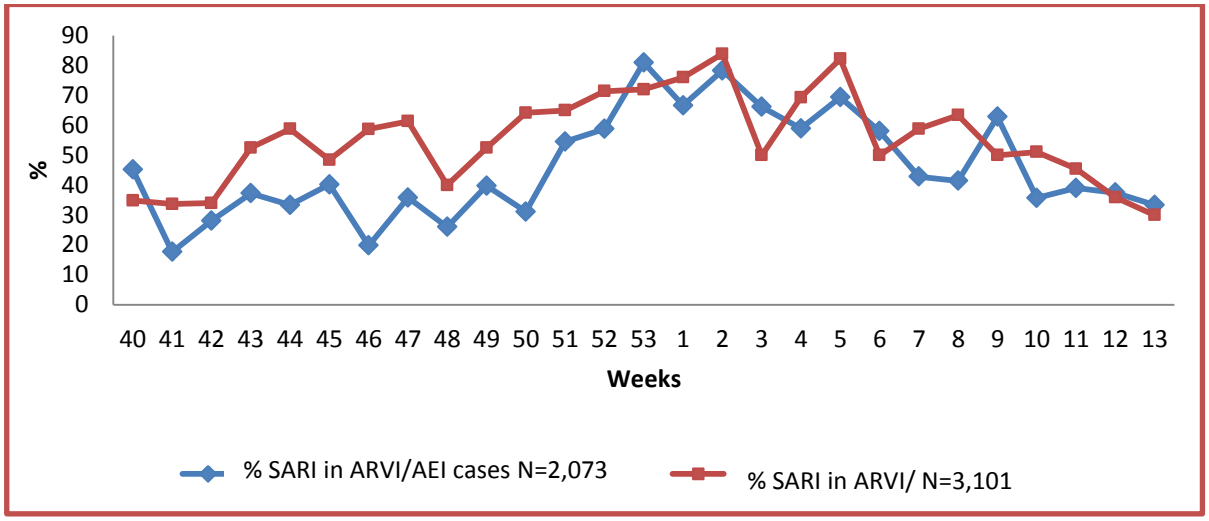

***Figure 3** – Proportion of SARI in ARVI cases with and without diarrhea, week 40 of 2009 – week 13 of 2010, n= 5174*

ARVI with a different degree of severity was diagnosed in 2,570 (83%) patients, 155 (5%) of whom had acute constrictive laryngotracheitis. Adenovirus infection was clinically diagnosed in 9 (0.3%) cases. There were 239 patients (7.7%) with the affected respiratory system in the form of obstructive bronchitis, pneumonia; toxic injury of the central nervous system in the form of convulsions was detected in 30 patients (1%).

Influenza viruses were identified in 105 (3.4 %) patients, pandemic influenza A (H1N1) -2009 was detected in 86 (81.9%) cases, seasonal influenza A H1N3 was detected in other 19 cases (18.1%) (Fig. 4a).

The analysis of medical charts of ARVI patients with diarrhea showed that ARVI complicated with bronchitis and pneumonia with underlying diarrhea were observed in 122 (5.9%) patients. The proportion of patients with bacteriologically confirmed forms of dysentery associated with ARVI was 1% (20 cases). Adenovirus infection and respiratory syncytial infection (RS) was clinically diagnosed in the setting of diarrhea – each infection in six patients (0.3%), parainfluenza – in 10 cases (0.5%). Remaining 1,907 (92%) patients whose bacteriological tests were negative had a final diagnosis “AEI-associated ARVI” (Fig. 4b).

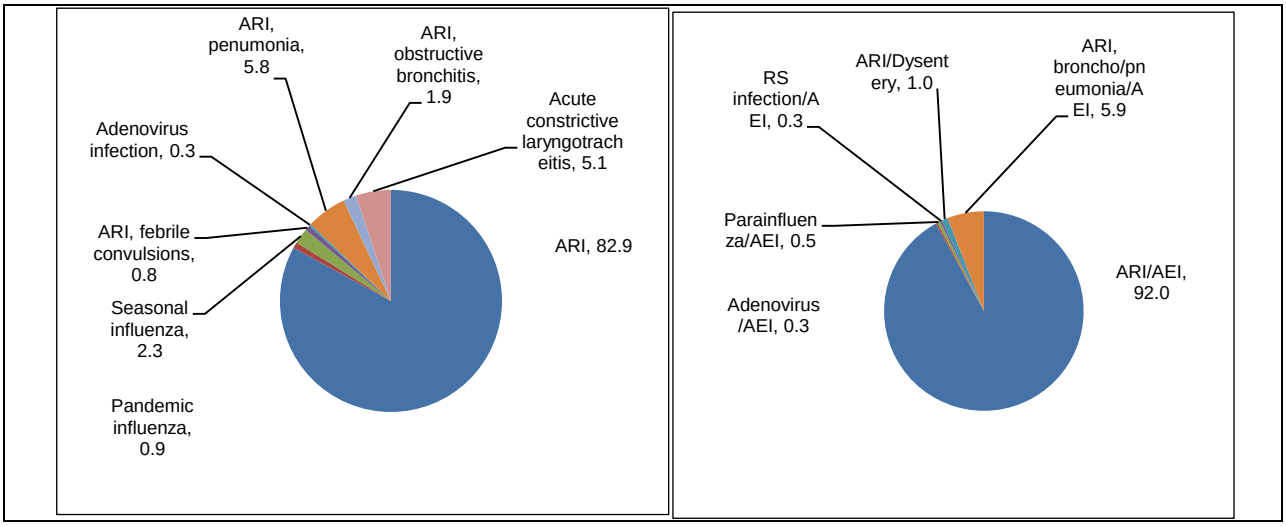

Fig. 4a. Nosological structure of ARI patients, n=3,101, RCIDH, Bishkek, Kyrgyz Republic, week 40 of 2009 –week 13 of 2010

Fig. 4b. Nosological structure of ARI patients with diarrhea, n=2,073, RCHIDH, Bishkek, Kyrgyz Republic, week 40 of 2009 – week 13 of 2010

The proportion of each age group in the epidemiological process was determined. To determine the age incidence, calculations were made based 100,000 population of respective age. Comparative data are presented in figure 5a,b.

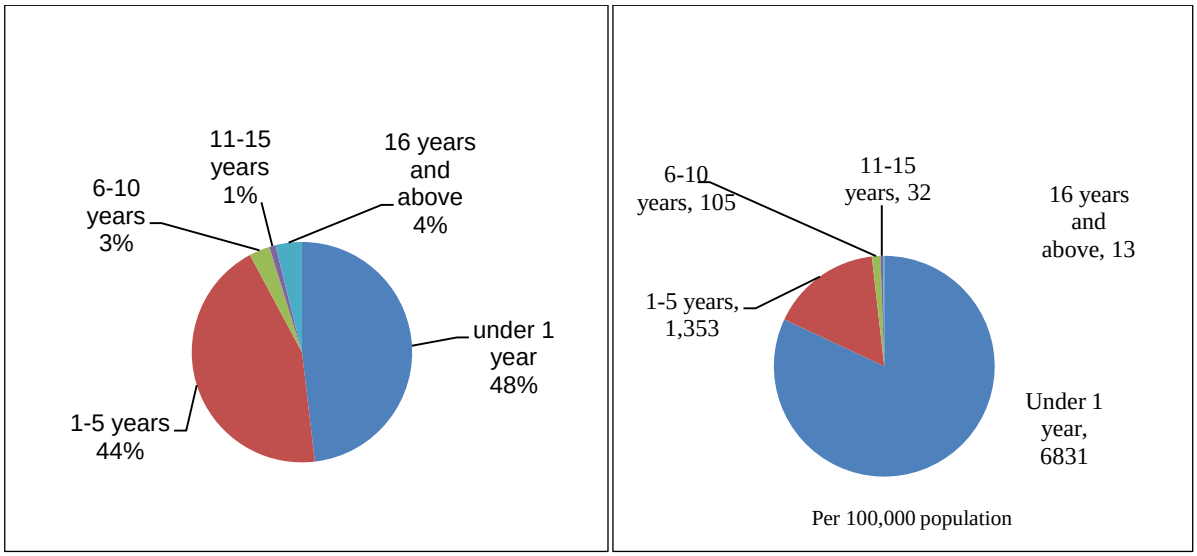

Fig. 5 a. Age distribution of SARI admissions to RCIDH, Bishkek, week of 40, 2009 –week 13 of 2010, N= 2,849

Fig. 5b. Age incidence of SARI admissions to RCIDH per 100,000 population of respective age, Bishkek, week 40 of 2009 –week 13 of 2010, N= 2,849

Children under 1 year and children of 1-5 years had almost equal proportions (48% and 44%, respectively) and accounted for a large number of SARI patients. A similar proportion was observed in children 6-10 years of age and persons 16 years of age and older (4% and 3%, respectively) but they accounted for 1/50 of all patients. The calculation of incidence rates per 100,000 population showed that SARI incidence among children under 1 year was 6381, and 1353 in the age group of 1-5 years, and the decrease in the intensity of the disease with the increase in patients' age.

Discussion

ARVI accounted for 60% among patients admitted to the RCIDH from week 40 to

week 13 of 2010. During week 47 of the epidemic season, patients with the pathology accounted for almost 100% of admissions, short-term decrease in consultation rates of ARVI patients associated with the increase of the bed capacity in other hospitals of the capital was noted. However, the spread of influenza pandemic A (H1N1)-2009 in the country determined a high consultation rate (80-90%) from week 50 of 2009 to week 10 of 2010.

Acute constrictive laryngotracheitis (5.1%) that has a high correlation with parainfluenza infection and adenovirus infection (0.3%), which have characteristic signs of illness in ARVI patients without diarrhea, was diagnosed using the clinical method because the facility was unable to perform etiological interpretation of ARVI. Disorders of the pulmonary system such as obstructive bronchitis, pneumonia (7.7%) together with the severe process indicated the possibility of late consultation by patients. Isolation of pandemic virus A (H1N1)-2009 from patients of this group proved the spread of influenza pandemic in the country.

The dynamic of consultations by AEI-associated ARVI had a similar trend of consultation rate of ARVI patients, which suggested that the disease in these patients was caused by respiratory viruses rather than enteric pathogens. Bacteriological tests were positive for Shigella only in 1% (20) of patients. It is known that diarrhea diseases are caused by roto-, entero- and other viruses in the fall-winter period [5]; however, examined patients were not tested for viruses. Due to this, the etiological factor of diarrhea in ARVI patients remained unrecognized. But we can assume that diarrhea in ARVI patients was caused by viral agents. The proportion of patients with bronchitis and pneumonia (5.9%) clinically identified by the adenovirus infection in the setting of diarrhea was not statistically important in comparison with ARVI patients without diarrhea.

Symptoms of SARI occurred almost with equal frequency in ARVI and AEI-associated ARVI. This trend maintained during the whole period of ARVI; moreover, the peaks of severe forms in compared groups coincided.

The comparative analysis of data of the structure and incidence by age groups of SARI patients shows that the results can give ambivalent conclusions. If the proportion of each group indicates that children under 1 year and children 1-5 years of age prevailed, incidence rates conclusively indicate that children under 1 year of age (6,831 per 100,000 population) suffer from severe acute respiratory infection five times more than children of 1-5 years (1,353 per 100,000 population). Children 5-10 years of age are 8 times more susceptible to SARI (105 per 100,000 population), and children 11-15 years of age are susceptible 2.5 times (32 per 100,000 population) more than adults (13 per 100,000 population). This situation is perhaps connected with incomplete development of the immunity in breastfed children when the body responds to the primary exposure to the virus agent. Decrease in the susceptibility to ARVI with the increase in age is also explained by increased herd immunity.

Difficulties in introducing laboratory interpretation of ARVI in the country posed difficulties in determination of etiological participation of viruses in the development of ARVI with the diarrhea syndrome. Testing for influenza viruses within sentinel surveillance covered persons 1 year of age and older due to the difficulty of collecting nasopharyngeal swabs of children under one year of age and lack of special tools for this. This circumstance did not allow identifying the etiological structure of ARVI with and without diarrhea in the most vulnerable group of population – children of breastfeeding age.

Conclusion

ARVI patients with and without diarrhea (40% and 60%, respectively) were registered during 2009-2010 epidemic season in Bishkek. The proportion of SARI cases in these groups was similar (80-90%). Chil-

dren under 1 year of age were most susceptible to SARI. High proportion of diarrhea (90%) of unknown etiology was noted in ARVI patients, which requires further studies on determination of the role of viruses in development of the diarrhea syndrome in ARVI case.

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PREVALENCE OF BREAST CANCER AMONG WOMEN EXPOSED TO RADIATION IN EAST-KAZAKHSTAN REGION IN DISTANT PERIOD AFTER THE RADIATION DOSES EXPOSURE

Resume. *A study was done in radiation risk groups, who were subject to ionized radiation as a result of Semipalatinsk testing ground activities. The main population group is represented by people with radiation dose of 250 mSv, comparison group was formed from the people with radiation dose 75 mSv, control group – people, who were not subject to radiation exposure. Breast cancer prevalence was studied among women in distant time after radiation exposure.*

Analysis of average age of women with diagnosed breast cancer in the research groups allowed to confirm its reliable decrease among the main group by 3,7±0,12 years and in comparison group by 2,6 ±0,1.

The ratio of breast cancer in the main group has reached 2,7, in the comparison group - 1,74.

Breast cancer with regards to its prevalence among population is the third nosological form among malignant tumors after lung and gastric cancer. In the structure of women population breast cancer takes the leading place.

On an annual basis in the world there are about million cases of cancer of this localization, and the forecasted growth of patients to 2010 was 1.5 million [1].

More than half of the breast cancer cases are diagnosed in the industrial developed countries: 361,00 in Europe; 230,00 in North America [2].

Breast cancer prevalence in Kazakhstan on average is on a stable high level – 20,3 - 20,8‰ [3].

Over the last 20 years the prevalence of breast cancer in the radiation risk groups among the population of Kazakhstan, which suffered after the nuclear weapons testing in Semipalatinsk

testing ground, has significantly grown, which affected the structure of oncologic morbidity and mortality in general [4].

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ANALYSIS OF INVESTMENT ACTIVITIES IN IMPLEMENTATION OF THE ONCOLOGICAL CARE DEVELOPMENT PROGRAM IN THE REPUBLIC OF KAZAKHSTAN FOR 2012-2016

Abstract. *One of the priority directions for the health care system development is oncologic service. The funds, allocated for Oncology service development program in Kazakhstan for 2012-2016, should be used in a targeted way and assist in the achievement of aims and objectives: improvement of oncologic diseases prevention by means of early diagnostics (screening) program development, increasing accessibility to high-tech diagnostics and treatment methods with evidence-based efficiency, creation of rehabilitation and palliative care system for oncological patients.*

There is systematic work done in Kazakhstan for implementation of new medical technologies, enhancing the medical care quality management, including the oncological service.

In order to increase life expectancy and quality among the citizens by means of decreasing the mortality level of oncological patients the Oncological care development program in the Republic of Kazakhstan for 2012-2016 by the Ministry of healthcare of the Republic of Kazakhstan. Funds from republican and local budgets will be allocated for implementation of the Oncological care development program. Within the framework of this program funds are used for infrastructural modernization of the oncological service of the RK with implementation of innovative projects in order to increase quality of specialized and highly specialized care for oncological patients.

Within the framework of the objectives implementation it is necessary to conduct procurement of modern equipment for medical organizations in all regions of the Republic of Kazakhstan. Monitoring of equipment procurement will allow evaluation of preliminary results of Program implementation: in the analyzed period budgetary funds, allocated for implementation of the Oncological care development program are fully used according to the Road map and action plan under the «Oncological care development program in the Republic of Kazakhstan for 2012 – 2016 ».