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## INFLUENZA A/H1N1 AND PREGNANCY: DIAGNOSIS AND TREATMENT OF PRIMARY INFLUENZAL PNEUMONIA

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*SUMMARY. Analyzed the course of primary influenza pneumonia A /NINI in 47 pregnant women aged 15-38 years. In 31,9 % of pregnant women revealed pathological obstetrical conditions. Both ways pneumonia diagnosed in 63,8 % patients. In 25,5 % confirmed by virus A/NINI using PCR for life. Recovery was achieved in 91,5 %, childbirth in 14.9 %, maintaining pregnancy in 80,9 %. All patients prescribed oseltamivira in a dose of 150 mg per day for 10 days. At VIT starting antibiotics were karbopenemy (Thienam, Meronem). In maternity wards and infectious patients assigned to III generation cephalosporin reserved, reserved penicillin, macrolides. Infusion therapy was carried out for restrictive type, obstetric tactics - according to the obstetric situation.*

**Key words:** pneumonia, influenza virus A/NINI, pregnancy, clinic, treatment.

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## DYNAMICS OF CELLULAR IMMUNITY OF ACUTE RESPIRATORY VIRAL INFECTIONS PATIENTS AGAINST AN AEROSOL INTERFERON TREATMENT BACKGROUND

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*The effect of aerosol interferon treatment on the dynamics of T-lymphocytes and their subpopulations CD3+, CD4+, CD8+ and the CD4+/CD8+ ratio in patients with influenza A, influenza B, adenovirus infection and acute respiratory viral infections (ARVI) of unknown etiology has been studied, laferon in a dose of 1000000 UN once a day for 3 days has been found to possess the best remedial effect. The most effective*

*treatment turned out to be in patients with ARVI of unknown etiology.*

**Key words:** influenza A, influenza B, adenovirus infection, ARVI of unknown etiology, laferon, treatment.

Influenza and other acute respiratory viral infections (ARVI) belong to the most widespread illnesses of human, which during many years prevail

by frequency all other infectious diseases, together. Their part is not less than 50-75 % in the structure of all infectious diseases morbidity [1-4]. However these high indexes do not represent the real distribution of respiratory infections.

The weakening of heterospecific and immunological reactivity of organism stipulated by influenza and other ARVI brings to acuting of base-line chronic illnesses, and also to development of the secondary bacterial complications, which gives to the problem of treatment of the special value and actuality [5, 6].

The treatment of patients with influenza and other ARVI makes considerable difficulties. There is a wide range of remedies which are used for treatment that covers practically all possible methods of influence on infectious process, however often will not give the desired results. Administration of new antiviral drugs, nosotropic, and immune correcting treatment are seldom brought the expected effect [7, 8].

The administration of aerosol interferons (IF) in the treatment of these patients is perspective [4]. However there is no information about experience of such treatment in literature.

Therefore the study of aerosol interferon treatment of patients with influenza and other ARVI has important theoretical and practical value and induces development of the new effective approach to treatment of patients with infectious diseases.

### Materials and methods

964 patients with ARVI were examined and treated. All patients were 18 to 22 years old military men. Influenza A was diagnosed on 194 (20,1 %) soldiers, influenza B – 184 (19,1 %), adenoviral infection (AI) – 196 (20,3 %), respiratory syncytial viral infection (RSV infection) – 178 (18,5 %) and ARVI of unknown etiology – 212 (22,0 %). All patients were admitted to the department of infectious diseases of Chernivtsi military hospital.

All diagnostic and medical procedures were done with the informed written consent of patients. The diagnosis of influenza and other ARVI was done on the basis of characteristic clinical and epidemiological information, results of laboratory studies (serologic studies and immunofluorescent tests). Most patients – 634 (65,8 %) were admitted on the second day of the illness, 242 (25,1 %) – on the first day, 88 (9,1 %) – on the third day of illness.

For description of immunological status of patients with ARVI, changes of the cellular link of immunity, basic subpopulations of lymphocytes were determined by the clusters of determination of CD3+, CD4+, CD8+, by the indirect variant of immunofluorescent method with the use of monoclonal antibodies panel to the superficial leukocytic

antigens, CD4+/CD8+ ratio was calculated. Study was done with the use of the enzyme immunoassay analyzer of "Uniplan" ("Pikon").

With the purpose of study efficiency of the offered treatment, the patients of every etiologic group were divided on 4 subgroups: the patients of I subgroup received traditional treatment (TT), which included disintoxication medications, nonsteroidal anti-inflammatory drugs, mucolytics, antihistaminics, vitamins; the patients of II subgroup received TT, inhalations of laferon in a dose of 200 thousands UN (L-200); III subgroups – TT, inhalations of laferon in a dose of 500 thousands UN (L-500); IV subgroup – TT, inhalations of laferon in a dose of 1 million UN (L-1 of million). The administration of laferon was carried out by nebulizer "Boreal", ("Flaem Nuova", Italy), once a day for 3 days.

The study results are calculated by the method of variation statistics (Statgraf and MS Excel 2000) with the use of Student criterion.

### Study results and their discussion

The important aspect of research was achievement of representativeness of subgroups on the basis of practically identical initial (in the moment of beginning of treatment) level of the studied indexes of cellular immunity.

TT of patients with influenza A caused increase of blood leukocytes (on 20,5 %,  $P < 0,001$ ) without substantial changes of the absolute and relative amount of lymphocytes and CD3+, CD4+, CD8+ ( $P > 0,05$ ).

Patients with influenza B had increase of blood leukocytes (on 15,7 %,  $P < 0,01$ ), the absolute amount of lymphocytes (on 29,5 %,  $P < 0,01$ ), and increase of the relative amount of CD3+ (on 4,0 %), CD8+ (on 7,6 %).

TT of patients with adenoviral infection did not cause substantial changes of blood leukocytes, the relative amount of lymphocytes, CD4+, CD8+, or the absolute and relative amount of CD3+ ( $P > 0,05$ ). At the same time, there was an increase of the absolute amount of CD8+ (on 15,4 %,  $P < 0,001$ ).

TT of patients with ARVI of unknown etiology caused the increase of the absolute amount of CD3+ and CD4+ (on 19,9 % and 27,2 %,  $P < 0,05$  accordingly) and increase of the relative amount of CD3+ and CD8+ subpopulations (on 3,0 % and 3,9 %,  $P > 0,05$  accordingly). The increase of blood lymphocytes, the relative amount of CD4+ and CD4+/CD8+ ratio were observed.

The use of L-200 in complex treatment of patients with influenza A caused increase of the most studied indexes of cellular immunity. The amount of leukocytes was increased on 16,0 % ( $P < 0,01$ ), the absolute amount of lymphocytes – more than twice, their relative

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amount – on 10,6 % ( $P<0,05$ ). The relative amount of CD3+ was increased similarly (on 17,5%,  $P<0,05$ ). The absolute amount of CD4+ was increased on 108,8 % ( $P<0,05$ ), their relative amount – on 18,0 %. The amount of CD8+ was increased as well (absolute amount – on 40,0 %, the relative amount – on 20,4 %). The changes were reliable ( $P<0,001$ ). The changes of absolute amount of CD3+ were irrelevant. The increase of CD4+/CD8+ ratio (on 38,0 %) was observed too ( $P<0,001$ ).

The use of L-200 in complex treatment of patients with influenza B caused more considerable increase of the amount of blood leukocytes (on 15,91 %,  $P<0,01$ ), the absolute and relative amount of lymphocytes (on 55,8%,  $P<0,001$  and 9,2 %,  $P<0,05$  accordingly), the absolute amount of CD3+ (on 41,7 %,  $P<0,001$ ), the relative amount of CD4+ (on 17,7 %,  $P<0,001$ ).

The prescription of L-200 in the complex treatment of patients with adenoviral infection caused reliable increase of all studied indexes. The amount of blood leukocytes was increased on 18,3 % ( $P<0,01$ ), the absolute and relative amount of lymphocytes – on 31,6 % and 23,2 % accordingly ( $P<0,001$ ), CD3+ – on 126,3 % ( $P<0,001$ ) and 8,5 % ( $P<0,05$ ), CD4+ – on 62,1 % and 15,7 % ( $P<0,001$ ), CD8+ – on 90,4 % and 22,4 % ( $P<0,001$ ). These changes assisted the increase of CD4+/CD8+ ratio – on 34,1 % ( $P<0,001$ ).

The use of L-200 in the complex treatment of patients with ARVI of unknown etiology caused increase of the absolute and relative amount of lymphocytes and studied subpopulation of T-

lymphocytes. The amount of lymphocytes was increased more than 30,0 % ( $P<0,001$ ), the relative amount of CD3+ – on 19,1 % ( $P<0,05$ ), and the absolute amount – on 131,3 % ( $P<0,0001$ ). The relative amount of CD4+ and CD8+ was increased on 32,4 % and 43,1 % accordingly ( $R<0,001$ ). Their absolute amount was increased on 97,3 % and 50,4 % accordingly ( $R<0,001$ ). These changes of T-lymphocytes subpopulations caused the increase of CD4+/CD8+ratio on 70,7 % ( $P<0,001$ ).

The aerosol administration of L-500 for patients with influenza A caused greater increase of indexes of cellular immunity (table 1). These patients had increased amount of blood leukocytes on 30,1 % ( $P<0,001$ ). The absolute amount of lymphocytes and CD3+ were increased more than twice, CD4+ – more than 4 times ( $P<0,001$ ). The absolute amount of CD8+ was increased more than one and a half times ( $P<0,001$ ). The relative amount of the studied indexes was increased as well: lymphocytes – on 43,8 %, CD3+ – on 80,8 %, CD4+ – on 66,7 %, CD8+ – on 55,1 %. There was substantial increase of CD4+/CD8+ ratio – more than 2,5 times ( $R<0,001$ ).

The use of L-500 in complex treatment of patients with influenza B caused increase of the amount of blood leukocytes on 24,10 % ( $P<0,001$ ). The absolute amount of CD3+ was increased almost twice, CD4+, CD8+ ( $P<0,001$ ), their relative amount were increased on 34,0 %, 60,7 % and 54,4 % accordingly ( $P<0,001$ ). CD4+/CD8+ ratio was increased considerably – more than twice ( $P<0,001$ ).

Table 1

Dynamics of cellular immunity indexes of patients with influenza A treated by aerosol laferon in a dose of 500 thousands MO once a day (n=30, M±m)

Index	At the time of admission	At the time of discharge	Degree of deviation %	P
Leukocytes, $\times 10^9$ , ЧI-1	5,07±0,15	6,42±0,10	+30,17±4,44	<0,001
Lymphocytes, %	23,93±0,35	34,20±0,62	+43,88±3,54	<0,001
Lymphocytes, $\times 10^9$ , ЧI-1	0,68±0,05	2,05±0,03	+268,7±38,1	<0,001
CD3+, %	41,10±1,22	72,67±0,36	+80,82±4,80	<0,001
CD3+ $\times 10^9$ , ЧI-1	0,49±0,03	1,40±0,02	+222,1±24,8	<0,001
CD4+, %	26,27±0,36	43,57±0,35	+66,73±2,59	<0,001
CD4+ $\times 10^9$ , ЧI-1	0,25±0,02	1,01±0,02	+428,1±52,9	<0,001
CD8+, %	24,43±0,39	37,63±0,24	+55,19±2,68	<0,001
CD8+ $\times 10^9$ , ЧI-1	0,30±0,02	0,75±0,02	+178,7±18,2	<0,001
CD4+/CD8+	0,38±0,02	1,32±0,01	+285,7±24,6	<0,001

Note. P is authenticity of differences between absolute indexes determined at the time of admission and discharge.

The use of L-500 in the complex treatment of patients with adenoviral infection caused increase of the amount of blood leukocytes on 24,8 %, the absolute

and relative amount of lymphocytes – on 57,5 % and 34,5 % accordingly, CD3+ – on 96,5% and 15,2 %, CD4+ – on 114,8 % and 17,7%, CD8+ – on 60,6 %

and 25,4 %, CD4+/CD8+ ratio – on 87,8 %. All found changes were reliable ( $P < 0,001$ ).

The use of L-500 in the complex treatment of patients with ARVI of unknown etiology caused even greater increase of indexes of cellular immunity. The relative and absolute amount of lymphocytes were increased substantially (on 44,0 % and 73,1 % accordingly,  $P < 0,001$ ).

The absolute amount of CD3+, CD4+ and CD8+ were increased on 123,8 %, 107,8 % and 107,5 % accordingly ( $P < 0,001$ ), their relative amount was increased on 19,8 %, 38,3 % and 61,8 % accordingly ( $P < 0,001$ ). All these changes were accompanied by the considerable increase of CD4+/CD8+ ratio – on 95,8 % ( $P < 0,001$ ).

The use of L-1 million in the complex treatment of patients with influenza A caused increase of the amount of blood leukocytes on 25,8 % ( $P < 0,001$ ), the absolute amount of lymphocytes – on 84,2 % ( $P < 0,001$ ). Their relative amount was increased more than 4 times ( $P < 0,001$ ). The absolute amount of CD3+ subpopulation was increased on 35,6 %, CD4+ – on 89,4 %, CD8+ – on 70,5 % ( $P < 0,001$ ). Considerable increase of the relative amount of T-lymphocytes subpopulations – more than 3 times ( $P < 0,001$ ) was found out. All these changes were accompanied by the considerable increase of CD4+/CD8+ ratio – more than 3 times ( $P < 0,001$ ).

The use of L-1 million in the complex treatment of patients with influenza B caused increase the absolute quantitative values of lymphocytes and CD4+ almost twice, CD3+ – on 1,5 times, CD8+ – more than twice ( $P < 0,001$ ). The expressed increase of the relative indexes was observed similarly: lymphocytes – on 55,7 %, CD3+ – on 31,3 %, CD4+ – on 71,1 %, CD8+ – on 50,8 % ( $P < 0,001$ ). More than a double increase of CD4+/CD8+ ratio was found out ( $P < 0,001$ ).

The use of L-1 million in the complex treatment of patients with adenoviral infection caused increase both absolute and relative amount of lymphocytes on 40,8 % and 29,0 %, and CD3+ – on 83,3 % and 28,0 % ( $P < 0,001$ ). The increase of the absolute and relative amount of CD4+ was more expressed – on 144,1 % and 80,4 % and CD8+ – on 96,2 % and 32,9 %, CD4+/CD8+ ratio – on 76,4 % ( $P < 0,001$ ).

The increase of laferon dose to 1 million UN for patients with ARVI of unknown etiology stipulated even greater increase of the absolute quantitative values of lymphocytes on 73,3 % ( $P < 0,001$ ), CD3+ and CD8+ – almost 1,5 times, CD4+ – more than 1,5 times ( $P < 0,001$ ). CD4+/CD8+ ratio was increased on 163,7 % ( $P < 0,001$ ) after administration of L-1 million

in the complex treatment by comparison to an initial period.

Thus, aerosol administration of interferon- $\alpha$  (laferon) in the complex treatment of patients of young age with influenza A, influenza B, adenoviral infection, RS-infection and ARVI of unknown etiology allows to improve immune status of organism considerably, decrease frequency of origin of complications, reduce the terms of patients treatment.

### Conclusions

1. The use of aerosol interferon- $\beta$  (laferon) in the complex treatment of patients with influenza A in a dose 1 million UN once a day for 3 days sets conditions for substantially higher stimulative influence on the indexes of cellular immunity, than traditional treatment with laferon in a dose 200 thousands UN. It increases the relative and absolute amount of lymphocytes, the absolute amount of CD3+ on 35,6 %, CD4+ – on 89,4 %, CD8+ – on 70,5 %, CD4+/CD8+ ratio – more than 3 times by comparison to an initial level.

2. The aerosol interferon treatment of patients with influenza B in a dose 1 million UN caused the expressed treatment effect in addition to the influence on the indexes of cellular immunity: the absolute quantitative values of lymphocytes were increased more than 2,5 times in 1-3 days of treatment, CD3+, CD4+ – more than 1,5 times, the relative indexes of lymphocytes – on 55,7 %, CD3+ – on 31,3 %, CD4+ – on 51,1 %, CD8+ – on 50,8 %, absolute number of CD8+ and CD4+/CD8+ ratio – more than twice by comparison to an initial level. The effect of traditional treatment came later.

3. The aerosol interferon treatment in a dose 1 million UN for patients with adenoviral infection assisted the considerable improvement of general condition of patients in 1-3 days of treatment which was confirmed by increase the absolute amount of blood lymphocytes on 40,8 %, CD4+ – on 144,1 %, CD8+ – on 96,2 %, CD4+/CD8+ ratio – on 76,4 % as compared to an initial level.

4. The use of laferon in a dose 1 million UN for patients with the acute respiratory viral infections of unknown etiology assisted substantial increase of the absolute amount of lymphocytes – on 73,37 %, CD3+, CD8+ – almost 1,5 times, CD4+, CD4+/CD8+ ratio – more than 1,5 times, by comparison to the initial period of treatment.

The minimal treatment effect was observed in subgroups of patients, which received traditional treatment with laferon in a dose 200 thousands of UN.

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### ДИНАМІКА ПОКАЗНИКІВ КЛІТИННОГО ІМУНІТЕТУ У ХВОРИХ НА ГОСТРІ РЕСПІРАТОРНІ ВІРУСНІ ІНФЕКЦІЇ НА ТЛІ АЕРОЗОЛЬНОЇ ІНТЕРФЕРОНОТЕРАПІЇ

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**РЕЗЮМЕ.** Вивчено вплив аерозольної інтерферонотерапії на динаміку Т-лімфоцитів і їх субпопуляцій CD3+, CD4+, CD8+ та співвідношення CD4+/CD8+ у хворих на грип А, грип В, аденовірусну інфекцію і ГРВІ невстановленої етіології. Виявлено, що найкращим лікувальним ефектом володіє лаферон в аерозолі у дозі 1 млн МО 1 раз на день 3 дні поспіль. Найефективнішим було лікування у хворих на ГРВІ невстановленої етіології.  
**Ключові слова:** грип А, грип В, аденовірусна інфекція, ГРВІ невстановленої етіології, лаферон, лікування.

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## ПНЕВМОНІЯ У ВІЛ-ПОЗИТИВНИХ ПАЦІЄНТІВ І ХВОРИХ НА СНІД НА ПРИКЛАДІ ІСТОРІЙ ХВОРОБИ ПОМЕРЛИХ

ДП «Український науково-дослідний інститут медицини транспорту», Одеський обласний центр по профілактиці та боротьбі зі СНІДом

Метою роботи було вивчення захворюваності на пневмонію у ВІЛ-позитивних пацієнтів. На основі використання результатів власних досліджень встановлено, що пневмонія є частим ускладненням перебігу ВІЛ-інфекції/СНІДу, проведено аналіз особливостей перебігу пневмоній у пацієнтів зі зниженим

імунітетом. Висловлене припущення про необхідність застосування більш радикальних схем лікування пневмонії, наприклад, двох антибіотиків та проти-грибкового препарату одночасно.

**Ключові слова:** ВІЛ-інфекція, СНІД, імунітет, CD4, пневмонія.