

*Materials of Conferences***EFFECTS OF HYDROGEN
SULFIDE PRODUCTION
ON MENSTRUAL FUNCTION**

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Environmental factors may have an adverse impact on women's health. Many scientists, such as, A.K. Ailamazyan [1, 2, 3], N.G. Kosheleva et al [5], O.V. Sivochalova et al [7, 8] proved the negative impact of production factors and aggressive factors of the environment in cities with developed chemical industry on the reproductive system of women, proved their role in the growth of gynecological diseases, including menstrual dysfunction.

In 1986 in Astrakhan region there was opened the largest in Europe gas processing complex. Astrakhan gas is characterized by the composition of the aggressiveness and high toxicity. As a result of emergency situations the emissions of harmful substances have occurred in the atmosphere to high and extremely high concentrations.

In Astrakhan gas processing complex employs about two thousands women. They are affected by harmful substances almost during the whole shift (up to 85%) of working hours. So the possibility of chronic exposure of toxic substance is very high.

A.I. Dobrinskaya studied pregnant women from the Astrakhan gas processing complex. She noted the high level of extragenital pathology and placental insufficiency. So, the neuro-endocrine and reproductive systems are developed in the hypoxia conditions. As a result of uterine lesions during adolescence there appear menstrual disorders, including juvenile uterine bleeding. In future these patients suffer both reproductive disorders and infertility [4].

In the Astrakhan State Medical Academy professor A.A. Nikolaev et al conducted research of inhibin A levels as an indicator of ovarian reserve in women working at Astrakhan gas processing complex. It was revealed that after 2,5 years of work the levels of inhibin A are reduced, that indicates a decrease in ovarian reserve. It leads to menstrual irregularities, such as anovulatory uterine bleeding, amenorrhea and infertility as a result [6].

Oxidative stress caused by Astrakhan hydrogen sulfide [9] has a negative effect on woman endocrine system and causes an imbalance of regulation ovulation factor.

It must be admitted that the effects of hydrogen sulfide production in Astrakhan region affects not only the employees, but also the people living in the vicinity.

So, women with high risk of exposure to hydrogen sulfide products must be followed up by gynecologist and have regular rehabilitation courses.

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**INTERRELATIONS BETWEEN
HEART RATE VARIABILITY
AND CYTOKINE SPECTRUM
PARAMETERS IN INFANTS
WITH CONGENITAL
CYTOMEGALOVIRUS INFECTION**

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The work was initiated to study cytokine profile and to analyze heart rate variability in 35 infants with congenital cytomegalovirus infection and in 25 non-infected infants aged $1,81 \pm 0,13$ years. Direct correlations were found between heart rate variability and cytokine profile in cytomegalic in-

fants indicating heterogeneity of ergotropic and tropotropic effect on productions of cytokines. Direct high correlation between functional activity of autonomic regulation sympathetic loop and anti-inflammatory cytokines in peripheral blood of control group infants was established.

Role of autonomic nervous system (ANS) in the regulation of immunity systems is confirmed by the fact that the immune system formation as a whole functional unit in postnatal infants occurs with the direct participation of hypothalamic structures. Ante- and perinatal unfavorable factors leading to imbalance between ANS compartments contribute to the delay of immune system postnatal maturation. Taking into account cytomegalovirus (CMV) tropism to the nervous tissue, it is possible to suggest that intrauterine infection with CMV could affect functional condition of ANS underlying mechanisms. In its turn it will be reflected by condition of immunity. Today heart rate variability (HRV) determination is thought the most informative noninvasive method for quantitative assessment of autonomic regulation of heart rate and a human organism as a whole [1–10]. As applied to the subject of discussion, systemic and multicomponent processes of effect of intrauterine CMV infection on formation of vegetoimmune mechanisms of adaptation of infants are still unexplored. **The work was initiated** to detect statistically significant interrelations between ANS parameters and cytokine spectrum in children with congenital CMV infection.

Materials and methods. Some results of all-up examination of 60 infants (mean age 1.81 ± 0.13) born to mothers with chronic latent TORCH infections. 35 patients with persistent congenital CMV infection were included into group P-1, P-0 group consisting of 25 non-infected infants. The groups were comparable as per age, sex and delivery parity. The newborns were follow-up at the Institute of Gynecology and Obstetrics, Uzbekistan Academy of Sciences from the birth. To determine infection level in the newborns 1–2 days postpartum as well as the virus persistence in those aged 6, 12 and 18 months samples of blood, urine and epipharyngeal scraping for virus genome were investigated by means of PCR method [11, 12]. Immunoenzymatic assay (IEA) was used to measure specific IgM, G by means of a test system («Vector-Best» Closed Joint-Stock Company, Novosibirsk, Russian Federation). To differentiate intrauterine infection and process activity avidity index was used (IEA – anti-G-avidity, «Diagnostic systems»: Scientific-Production Association, Nizny Novgorod, Russian Federation). [13]. At birth neither clinical signs of intrauterine infection nor pathologic course of early adaptation could be registered in the newborn examinees to perform planned vaccination and to discharge them from the maternity house. On

20–25 days of life clinical picture of intrauterine infection was observed in 8 infants (22,6%), manifesting in hepatomegalia, icteric viral hepatitis syndrome and pneumonia in P-1 group and necessitating their hospitalization at the newborns' pathology department. It should be noted that IgGs of low avidity were registered in the infants. Thus, assessment of clinical data of the infected infants showed presence of residual and subclinical infection forms in 25,7 and 74,3 %, respectively, residual one being associated with high degree of stigmatization and anomalies in development of osteocartilaginous tissue and urogenital system [3]. For subsequent 3 years the infants were followed-up at Tashkent Pediatric Consulting-Diagnostic Center. Immunological and cardiorythmographic investigations were conducted in the absence of concomitant infectious or severe somatic pathology in the examinees. Immunoenzymatic assay (IEA) was used to determine content of cytokines (IL-1 β , IL-8, IL-2, IL-10, IFN- α) in pg/ml by means of commercial kits («Vector-Best» Closed Joint-Stock Company, Novosibirsk, Russian Federation). Measurement of optical density at wavelength 450 nm was performed by means of photometer for microplates («Multiscan») at the Institute of Immunology, Uzbekistan Academy of Sciences. Blood samples were taken in the morning 10 minutes after cardiorythmography (CRG). CRG was performed by means of «Rate» (Republic of Uzbekistan) software-hardware complex. RR-intervals were registered for 5 minutes within 0.001s in the morning in resting infants [1]. Absolute values of spectral density were obtained by Fourier method (complete transformation of single series by «Hamming» code variant). CV(%) – coefficient of RR – intervals variability, Amo – amplitude of modal value of RR interval set, SDDN – Standard Deviation of Normal-to-Normal RR intervals, RMSSD – the square Root of the Mean of the Sum of the Squares of Differences between adjacent RR intervals, ABI – autonomic balance index, ARI – autonomic rate index, IRPA – index of regulation process activity, TI – tension index, HF – HRV spectral density in high-frequency range, HF –(1–30) subranges – 0,150–0,300 Hz, LF (21 subranges) – HRV spectral density in low-frequency range, 0,150–0,040 Hz, VLF (5 subranges) – HRV spectral density in very low frequencies, 0,040–0,015 Hz, ULF (3 subranges) – HRV spectral in ultra low frequencies, < 0,051 Hz were the parameters to consider[1]. Processing of the results and their graphic presentation was performed on PC «Pentium 4» with MS Excel-XP and «Statistica» programs [14]. Correlation analysis was performed by Kendall's method (r), relative risk (RR) being calculated by Kelmanson's [15].

Results and discussion. Results of all-up analysis of infants' early post-natal state of health showed significant differences in objective sta-

tus of infants with congenital CMV infection and their non-infected mates. As to structure of general morbidity, in 1-year infants respiratory diseases, such as, pneumonias (RR = 6,1), recurring bronchitis more frequently with obstructive component (RR = 3,4), allergodermias (RR = 2,7), neurological abnormalities (RR = 3,7), such as, hyperactive child syndrome, dyskinesias and vegetovisceral dysfunctions, as well as gastroenterological disturbances (RR = 3,6) were found to prevail. Motor development retardation in 1-year infants manifested as delay in mastering motor skills, the infants could keep the head straight only by 2,5–3 months ($p < 0,05$), turn from back to side and to belly by 5,5–6 months, sit on one's own by 9–9,6 months and started walking later than usual ($p < 0,05$). Physical development retardation (mainly owing to body mass deficiency) was observed less frequently in both groups. Gastro-intestinal disorders, not infrequent at the age, manifesting as constipation in turn with diarrhea ($p < 0,05$), regurgitation ($p < 0,01$), intestinal microbiocenosis abnormalities ($p < 0,05$) were mainly functional and occurred in P-1 group more frequently. Atopic dermatitis (RR = 2,6) and functional gastro-intestinal disorders (RR = 2,0) evidently prevailed in P-1 infants in the 2nd year of life. In infants of the age frequent (more than 6 times a year) episodes of acute respiratory infections (RR = 4,3) and dysmetabolic nephropathies in combination with urinary tracts infection (RR = 3,4) in comparison with the control took place. Incidence of asthenoneurotic and vegetovisceral dysfunctions with speech development retardation remained rather high (RR = 2,9). Only 57 (42,9%) of 133 paired correlations for the control group (P-0) turned out confident. For the P-1 group there were 88 (66,2%) confident correlations. In infants infected with CMV direct correlation between HF and IL-1 β , IFN- α , IL-10, between AMo, ABI, ARI, IRPA, TI and IL-2 was showed indicating heterogeneity of ergotropic and tropotrophic effects on the production of cytokines. Upon production of IL-2, IL-8 and IL-10 in P-1 group maximum tendency to reduction in effect of autonomic regulation (AR) sympathetic loop was observed, for IL-1 effect of only autonomic loop. Infants of the control group showed diametrical dynamics, that is predominance of vasomotor center (LF) and suprasedimentary level of regulation.

Upon production of IL-1 in P-1 infants presence of intermediate direct correlation with HF, effect of AR parasympathetic loop can be observed, while in P-0 infants this power is distributed on LF, spectrum of low frequency waves only. This distribution of powers is confirmed by IL-1 concentration in the peripheral blood, confident increase of its production being registered in P-1 group as compared with the control ($p < 0,001$). IL-1 is an immunotransmitter, producing direct ef-

fect on the central nervous system (CNS) structures, on hypothalamo-hypophyseal-adrenal axis, in particular. In high concentrations IL-1 favors necrosis and nerve cell apoptosis. Clear logical correlation between perinatal injury of CNS in the CMV infected infants ($p < 0.001$) and IL-1 content was established. This can be considered as a sign of the brain ischemic injury upon persisting CMV infection and inadequate response of AR central loop. Differentiating effect of sympathoadrenal mechanism can be seen upon production of IFN- α . In P-1 group close direct relations with high-frequency waves (HF) (5,3%) add, their complete absence in the control group evident. IFN- α production naturally increases in the group by 4,2% as compared with the control to confirm unsoundness of antiviral activity.

Predominant effect of high-frequency spectrum (HF) on IL-8 with positive vector in P-1 group was established. Similar synchronicity could be seen in IL-8 concentration as compared with the control ($p < 0,01$). Increased IL-8 level is associated with chronic inflammatory process upon CMV infection and correlates with functional gastro-intestinal disorders ($p < 0,01$). Close multidirectional correlations in respect to IL-2 and IL-10 were observed in the examined groups too. Peculiarities of interrelations between AR parasympathetic loop and IL-2, IL-10 are of special interest. For IL-2 positive vectorial effect in P-0 group gives place to the contrary one in P-1 group. For IL-10 antagonistic effect of AR humoral loop with predominance of central link can be seen in the control group, humoral link in the infected infants activating production of interleukin. IL-10 is the key link in pathogenesis of allergodermias (AD). By its immune suppressive activity IL-10 favors formation of chronic allergic inflammation. Confident dependence between IL-10 content and AD recurrences in infants ($p < 0,05$) was found. Thus, cytokine spectrum of infants infected with CMV persisting form is regulated by the parasympathetic effect.

Conclusion. In infants with persistent congenital CMV infection diagnostically significant confident differences in correlation density between HRV and cytokine profile have been established. The natural dependences are found to characterize degree of imbalance in the system of regulation of cytokine reactions with predominance of autonomic loop regulation. Synchronic alterations in concentrations of peripheral blood cytokines confirmed prognostic value of HRV parameters. As the result, new approaches to development of methods of anticytokine therapy and prevention of persistent CMV infection in infants are possible.

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