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## SECTION OF BIOLOGICAL AND MEDICAL SCIENCES

### THE ROLE OF ENVIRONMENTAL FACTORS IN THE PROGRESSION OF RHEUMATOID ARTHRITIS

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#### Abstract

The results of dispersion analysis indicate that clinical, radiological and sonographic signs of articular syndrome and extra-articular manifestations in RA depend on the degree of contamination of atmospheric air and soil with xenobiotics. It means that changes in the trace element composition of the soil and atmospheric air (NO<sub>2</sub>, FH, Cd, Al, Pb and HF), depending on the RA patients' living areas, contribute to the rate of disease progression.

**Keywords:** rheumatoid arthritis, ecologic factors, climate geographic zone.

Geographical factors, according to a study conducted under the auspices of the WHO are estimated as external risk factors that could adversely affect to function of all systems of the human body, as well as the course and outcome of various diseases, including rheumatic diseases [1, c. 28-30]. In recent years, it began to discuss the possible connection of the current and future features of rheumatoid arthritis with unfavorable environmental factors [2, c. 68]. RA is a multifactorial disease in which the interaction of genetic component and environmental factors determines not only the disease but also its pronounced clinical polymorphism [3, c. 2206]. Weighting of disease occurs under the simultaneous influence of environmental factors [46, c. 1747; 5, c. 7-8; 6, c. 86].

To date, Uzbekistan is the object of many investigations of medical and geographic directions, as Republic is distinctive by its geographical location, climate and nature of the development of industry and agriculture. Moreover, special attention should be paid to the environmental problem in certain areas of the Republic. As it is known, deterioration of the nature does not occur immediately or instantly, this process is observed for a long time, in other words, the environmental situation gradually accumulates. The big environmental problem in Uzbekistan is the high degree of soil salinity. The real threat was extensive contamination of soil by various types of industrial and household wastes. One of the major problems is the quality of water resources, the problem of the disappearance of the Aral Sea and the threat of ecological safety in the country and contamination of air space. Our Republic of Uzbekistan is located in the arid zone and characterized by the presence of major natural sources of atmospheric dust as the Karakum and Kyzylkum deserts with frequent dust storms [9, c. 78]. Therefore, we believe that actual study in this field, particularly in matters of environmental rheumatology, in particular on the issues of RA in various climatic and geographical regions of

Uzbekistan. We are interested in properties of development and duration of RA associated with environmental factors.

The aim of this study was evaluate the influence of environmental factors to articular syndrome in patients from various regions of Uzbekistan.

#### Material and Methods

The study included 460 patients with a documented diagnosis of RA at the age of 50,6 ± 9,1 years, disease duration 9,9 ± 4,7 years: I zone, the northern region - Tashkent - 144 patients; II zone, the western region - Khorezm region - 112 patients; III zone, the eastern region - Namangan region - 104 patients; IV zone, the southern region - Surkhondaryo region - 100 patients

These hygienic assessment of environmental pollution, in particular xenobiotics in its three objects - air, soil and water (surface water and underground water sources) were obtained as a result of laboratory tests of sanitary stations, government offices of regional committees in the field of hydrometeorology, control of natural condition and environmental safety, as well as governmental Committee of Uzbekistan by protection of nature. Total emissions of air pollutants from stationary and mobile sources characterize the general anthropogenic load to the air. According to these data, the level in the atmospheric emissions to the area of the experimental zones includes following for 5 years:

- in I zone it was 302,76 ± 96,12 t / km<sup>2</sup> per patient with RA - 17,2 ± 29,16 kg; in II zone - 81,2 ± 16,2 t / km<sup>2</sup> per 1 patient with RA - 31,2 ± 1,8 kg; in III zone 68,51 ± 11,4 t / km<sup>2</sup> per 1 patient with RA - 9,1 ± 1,1 kg; in IV zone 90,5 ± 8,9 t / km<sup>2</sup> per 1 patient with RA - 35,1 ± 3,4 kg.

Integral indicators of environmental burden to the atmosphere (v), water (σ) and soil (ω) were used to compare them with clinical signs of RA (F) on the number of patients and with integral criterion in the study areas of Uzbekistan (G).



We evaluated average values ( $M$ ), their errors ( $m$ ), the standard deviations ( $s$ ), the correlation coefficients ( $r$ ), the criteria of dispersion ( $D$ ), the Student ( $t$ ), Wilcoxon - Rao ( $WR$ ),  $\chi^2$  McNemar - Fisher and reliability of statistical parameters ( $p$ ).

#### Results and discussion

Allocation of risk factors among the chemicals, which have adverse environmental burden on the environment ( $\psi$ ), water ( $\sigma$ ) and soil ( $\omega$ ) plays a practical value, because this will determine their role in the progression and development of mechanisms of RA, as well as particular anatomical defects in the joints and the process of destruction in them. As the results of our analysis, hydrogen fluoride ( $FH$ ) is an environmental factor of risk affecting the course of RA, as against its anthropogenic load in ambient air (IV zone) significantly progressing disease activity (DAS28 and SDAI;  $p=0.024$ ) and reduced the duration of clinical remission ( $p=0.048$ ). Moreover, increasing the concentration of  $FH$  leads to more frequent incidence of systemic manifestations of RA, polymorbidity and reproductive disorders in patients, which suggests it as a risk factor in relationship to this disease. In turn, recess autoimmunity in RA occurs on the background of increasing its concentration in the air because significantly reducing the overall pool of T lymphocytes ( $p = 0.0302$ ), T-helper cells ( $p=0.041$ ) and T suppressor ( $p = 0.045$ ). However, also it progresses apoptosis of T lymphocytes

in patients since greatly reduces quantities of CD 95+ cells and also activates factor of phagocytosis nonspecific protection ( $p=0.0481$ ). Therefore, this shows the significant role of  $FH$  in violation of the immune imbalance in RA.

Another factor that has been identified in a study it was sulfur dioxide ( $SO_2$ ) which is also unfavorable in relation to the Republic of Armenia.

In turn, RA progresses with an increase in the concentration of carbon monoxide ( $CO$ ) (II zone;  $p=0.041$ ). It should be noted, with increased rates of dust in the air significantly increases polymorbidity (II zone);  $p=0.024$ .

Study showed that the main clinical manifestation of RA, the severity of the articular syndrome depends on the degree of contamination of water and soil. With increasing concentration of Al and Ni it becomes aggressive. So with the increase of Ni accumulation (IV zone) RA becomes more frequent cases with ankylosis (radiographic stage IV RA) joints (Figure 1), and in particular leads to progress of Larsen index ( $p=0.0023^{\$}$ ;  $p=0,033^{\$}$ ). This means that the cause of the aggressiveness of the articular syndrome in these cases is linked to the development of mechanism of early joint destruction. Inflammatory process is amplified in the joints on the background of the accumulation of Al.

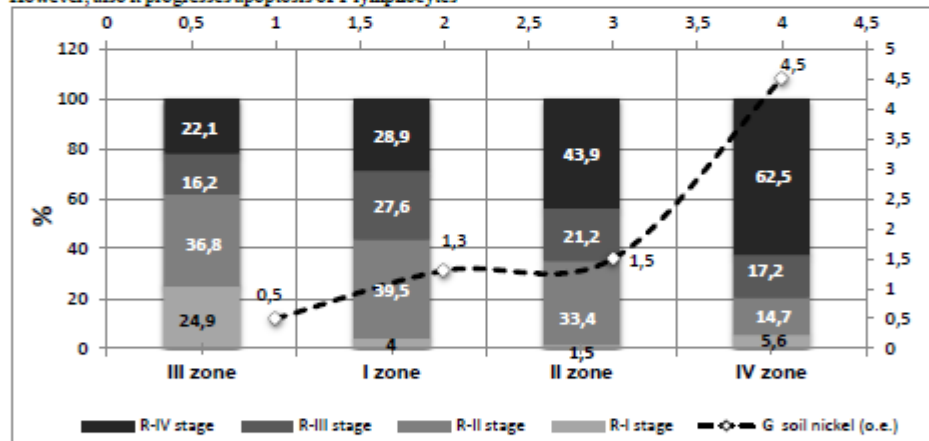


Figure 1. Dependence of the X-ray changes by G soil nickel.

According to information received, one of the external factors that affect the articular syndrome is also Zn, (II and IV zones) functional possibilities of joint become worse as with a reduction in its concentration in the soil (HAQ index:  $p = 0.0034$  \$;  $p = 0,0431$ ) and indicators of T-cell immunity reduce ( $p < 0.05$ ).

The results showed that with increasing salinity of the soil in the areas caused anatomical defect in the joints of RA patients accommodation (II zone), as increasing cases of tenosynovitis ( $p=0.033$ ), Baker's cyst ( $p=0.054$ ).

The results show that the frequency of occurrence of extra-articular manifestations of RA depends not only on the  $FH$  concentration in atmospheric air, but

also by  $NO_2$ , Cd, Al, Pb, F, and Ni, as well as the degree of salinization. Therefore, this means that zones II and IV zone were unfavorable in respect of extra-articular manifestations of RA.

In turn, the comparative analysis showed the influence of the environment to RA patients living areas, in particular environmental factors on the reproductive system. According to the data, against adverse factors reproductive system it is not only the  $FH$ , and a high degree of salinity,  $SO_2$  and  $CO$ . This means that the violation of the reproductive system depend on the above xenobiotics. According to ANOVA Pb accumulation in soil contributes to the disruption of the dynamics of female sex hormones in

RA women of reproductive age. Progesterone deficiency becomes pronounced with increasing concentrations of Pb. Therefore, zone IV zone was unfavorable risk zone against Armenian women of reproductive age.

**Conclusions:** Thus, we have proved and substantiated role of xenobiotics (Al and Ni) in the development of a mechanism of early joint destruction, aggression contributes to the progression of articular syndrome in rheumatoid arthritis. Progression of apoptosis of T cells occurs against the load of hydrogen fluoride (FH) and proved its role in the imbalance of the immune system in RA. In turn, environmental risk factors, such as NO<sub>2</sub>, FH, Cd, Al Pb contribute to the formation of systemic manifestations of the disease.

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### РОЛЬ МАРКЕРІВ ЕНДОТЕЛІАЛЬНОЇ ДИСФУНКЦІЇ ТА АПОПТОЗУ В РАННІЙ ДІАГНОСТИЦІ ПОРУШЕНЬ В СИСТЕМІ МАТИ-ПЛАЦЕНТА-ПЛІД

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### ENDOTHELIAL DYSFUNCTION AND APOPTOSIS MARKERS IMPORTANCE FOR THE EARLY DIAGNOSIS OF MOTHER-PLACENTA-FETUS SYSTEM DISTURBANCES

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#### Анотація

**Мета роботи** – показати роль маркерів ендотеліальної дисфункції в ранній діагностиці порушень в системі мати-плацента-плід.

**Матеріали і методи.** Нами були вивчені в 100 вагітних жінок з порушеннями в системі мати-плацента-плід в терміни 18-24 і 28-38 тиж. гестації в сировотці крові маркери ендотеліальної дисфункції, апоптозу, клітинної проліферації і енергозабезпечення клітини. Жінок було розподілено на дві групи з врахуванням наявності преєклампсії та екстрагенітальної патології.

**Результати.** Отримані результати дозволяють патогенетично обґрунтувати вилучення розроблених критеріїв плацентарної дисфункції і ступеня її тяжкості, разом з ультразвуковою складовою, в програму діагностики даного ускладнення вагітності з метою підвищення її точності. Результати ранньої діагностики плацентарної дисфункції та оцінки ступеня її тяжкості під час вагітності, засновані на лабораторному та ультразвуковому тестуванні, в зіставленні з гістологічно верифікованим діагнозом показали, що діагноз правильно поставлений в 91% спостережень, неспівпадіння складало 9%. Аналіз збігу клінічних і гістологічних діагнозів при важких формах плацентарної дисфункції показав підвищення точності діагностики при використанні модифікованої шкали на 39,5% в порівнянні із вживанням шкали, заснованої лише на ультразвукових критеріях.

**Заключення.** Розроблений на основі діагностичної шкали (ультразвукове і лабораторне тестування) клінічний алгоритм ведення вагітних жінок групи ризику підвищує точність діагностики плацентарної дисфункції на 26,1%, її важких форм на 39,5%, сприяє вибору адекватної акушерської тактики, поліпшенню перинатальних результатів при важких формах плацентарної дисфункції на 60%. Отримані результати дозволяють рекомендувати методику ранньої діагностики важких форм плацентарної дисфункції в практичну охорону здоров'я.