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The work was submitted to International Scientific Conference «Fundamental and applied research in medicine», France (Paris), 14-21, October, 2012, came to the editorial office on 18.10.2012.

#### THE KIDNEYS' CYTOMORPHOLOGICAL STATE UNDER THE INDUSTRIAL POLYMETALLIC DUST INFLUENCE

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The structural condition research of the experimental animals' kidney tissue (e.g. rats) under the inhalation influence of the polymetallic ore dust of Temirtau has been conducted. The non-purebred white rats-males and pregnant females, in quantity of 108, weight is 180–220 grams, have been used in the experimental work, the animals have been on a standard diet. The level control of the rats' kidneys defeat has been carried out under the cytomorphological condition. The chronic illness of kidneys model (which has been caused) reproduced, according to the standard techniques, has been used in the work. These animals have been contained under the vivarium conditions of the National center of hygiene and occupational diseases factory in Karaganda. The level control of the rats' kidneys defeat has been carried out under the cytomorphological condition. The experiment has been lasted for 3 days, 70 days and 4 months, the experiment duration has been defined by time of the tissues' cellular updating.

The Central Kazakhstan – is the large and the major industrial Region, where a lot of companies and the enterprises have already been concentrated on the metals' mining and its processing [1].

So, the anatomical and physiological peculiarities and their characteristics of the kidneys: the high blood flow, the complex and the renal tubular transport processes, the renal route of the elimination of a large number of the metabolites – they are made the human organ extremely vulnerable at the prolonged exposure to dust on the human organism.

In this connection, it is necessary to be determined the etiological significance of the dust factor in the occurrence of the renal disease and their pathology under the experimental conditions, and up to date there is no any information on the early stages of the cytomorphological changes of the

kidney tissue cells, when they are exposed to the adverse and the quite unfavorable factors of the industrial dust.

**The purpose of the work** is the structural condition of the kidneys tissue study of the experimental animal (e.g. rats) under the inhalation influence of the of the polymetallic ore dust of Temirtau.

**The Materials and Methods of the Study.** The study of the possible adverse influence and the unfavorable effects of the metal complex in the dust composition on the children organism of the Temirtau town has been held during the special toxicological experiment. So, the special feature and its peculiarity of this dust is that it is highly fibrogenic (e.g.  $\text{SiO}_2 > 70\%$ ), it, moreover, is contained more than 30 metal compounds and the natural radionuclides of the uranium and the thorium families, in excess of ПДЧ in 3 times [2].

So, the level control monitoring of the kidneys damage in the rats has been carried out on the cytomorphology state. Then, the animals of the I-st experiment have already been divided into 2 main groups:

The 1-st group – is the control one, it has been included 16 animals (e.g. the intact ones), the 2-nd group – 20 animals, which have been administered the Temirtau dusk by the intratracheal way, at 50 mg/ml a dose. The term – is 3 days (e.g. 72 hours) (it is the acute experiment). So, the control group has also been consisted of the 16 intact animals in each subsequent experiment

The II experiment – the 20 animals, which have been poisoned by the subacute industrial dust of the Temirtau town, at 50 mg/ml a dose by the intratracheal way. The term – is 3 days (e.g. 72 hours).

The III experiment had been lasted 4 months (e.g. 120 days), when the rats received the dust in the inhalation chamber at the concentration of  $0,25 \text{ mg/m}^3$ , that it is exceeded the daily average dust concentration in 5 times (MPC –  $0,05 \text{ mg/m}^3$ ), and it is corresponded to the real dust load for the residential areas of the town. The study group has been consisted of 20 animals.

The powder substances dispensers, having permitted to be taken into account the aerodynamic laws of the dust flow distribution and simultaneously to be subjected exposure to the large group of the animals, have been used for the dust low concentration to be created in the chamber poison.

So, the kidney tissues of the experimental animals have already been by the cytomorphological study material.

Thus, the experimental part of the work has been conducted at the National Center for the Occupational Health or the Labor Hygiene and the Occupational Diseases in the Karaganda town in the framework of the R & D SC HT (GT) and CT on the theme: GR № 0106PK00241 «The Medico – Biological Monitoring Biomarkers Development for Hygienic Safety of the Population Provision in the Terms of the Ecological Trouble».

**The Results and Discussion.** Before one can be judged on the possible changes nature in the kidneys, the kidney tissue morphology of the animals from the control group has already been studied.

So, the white rats have already been selected by us in our experiment, because they are the most resistant to the toxic metals, and they are much easier to be reproduced the long – termed chronic intoxication in the small doses of the chosen xenobiotics.

At the dose of 50 mg/ml, in the period of 3 days (e.g. 72 hours), just after the Temirtau polymetallic dust poisoning in the rats' renal tissue, the pathological processes have already been revealed, in the form of the further reduction in the number of the small tubular cells (STC) in 2 times, the further increase in the number of the neutrophilic leukocytes (NL) in 6 times, and the further increase in the number of the fibroblasts in 2 times.

It had also been revealed the further increase in the number of the degenerated small tubular cells (DSTC) in 3,1 times at the pregnant females in the kidney cells, in the period of 3 days (e.g. 72 hours), at the dust dose of 50 mg/ml, which was more frequently met the albuminous degeneration or the proteinosis, but more pronounced changes have already been observed in the cellular composition of the renal tissue at the males, and they were acutely sensitive to the toxic effects and the adverse influence of the Temirtau polymetallic dust. It has also been revealed the further increase in the number of the DSTC in 4,2 times, the degenerated neutrophilic leukocytes (DNL) in 1,8 times, the fibroblasts in 2 times, at the males in the kidney cells, in the period of 3 days (e.g. 72 hours), at the dust dose of 50 mg/ml, that it is suggested on the pathogenic effect of the polymetallic dust, under the influence of which the enhanced dissolution of the large tubular cells (LTC) and STC at the males and the females of the studied group is also taken its place.

It had also been revealed the further increase in the number of DSTC in 1,5 time at the pregnant females in the kidney cells, in the period of 70 days (e.g. 1,680 hours), at the dust dose of 50 mg/ml, but more pronounced changes were found and observed in the kidney cells of the males. It had also been revealed the pathological processes, in the form of the further reduction in the number of STC in 1,9 time, the further increase in the number of DSTC in 2,3 times, the number of the fibroblasts were increased in 10 times at the dose of 50 mg/ml, in the period of 70 days (e.g. 1,680 hours), after the poisoning by the Temirtau polymetallic dust in the kidney tissue of the male rats.

It is being observed the further increase in the number of DSTC in 77% after the intratracheal poisoning by the Temirtau polymetallic dust in the kidneys of the animals, when the dose of 50 mg/ml receiving, in the period of 70 days (e.g. 1,680 hours), which is indicated, that along with the albuminous degeneration or the proteinosis, and the presence of the dystrophic – generatively changes.

It has also been revealed the further increase in the number of DSTC in 2,3 times and the further increase in the number of the fibroblasts in 13 times at the pregnant females in the kidney cells, in the period of 4 months (e.g. 120 days), at the dose of the Temirtau polymetallic dust of 0,25 mg/m<sup>3</sup>, in comparison with the control group of the animals, which are quite characterized for the dystrophic – generatively changes. It has also been found more pronounced changes in the composition of the degenerative cells at the pregnant females with the chronic poisoning in the period of 4 months (e.g. 120 days), at the dose of the Temirtau polymetallic dust of 0,25 mg/m<sup>3</sup>, in comparison with the males, and it is indicated on the depletion of the compensatory mechanisms of the pregnant females' organism and, moreover, on more rapid development of the sclerotic processes in the kidney tissue of the animals.

The number of fibroblasts (e.g. the connective tissue further proliferation of the intermediate cells) has been increased in 13 times just after the inhalation of the Temirtau polymetallic dust in the kidneys of the animals, at the dose of 0,25 mg/m<sup>3</sup>, in the period of 4 months (e.g. 120 days), which is indicated, that the sclerotic processes in the kidney tissue of the animals.

It has been marked the very delicate zone of the nephrogenic tissue and the nephrons' low content of the first generations in the juxtglomerular zone at the histological examination of the rats' kidneys after the inhalation poisoning by the Temirtau dust, in the period of 4 months (e.g. 120 days). From the side of the kidney cells, the structural changes are being observed, in the form of the single glomerular cysts presence with the vascular cell collabirovation or the mesangial cells proliferation with the glomerules vascular loops fragmentation. So, the greatest changes have been noted in the tubular system of the nephron, in the form of the severe – pronounced vacuolar dystrophy of the tubular epithelium and with the foci of its necrosis.

Thus, the cytomorphological studies of the kidney tissues of the rats, having carried out by us, have been shown, that the Temirtau polymetallic dust is possessed more pronounced cytotoxic effect. In the acute experiment, it is characterized more pronounced cytotoxic, but in subacute experience, the chronic inflammatory process in the urinary excretion system is caused the renal cells morphology. In the early stages, the poisoning by the Temirtau polymetallic dust has the moderately toxic effect and the adverse influence. The sharp decline in the cells' resistance is suggested on the pathogenic effects and the adverse influence of the dust factors action. So, the enhanced and the amplified nephrons' decay has been taken its place under the influence of the phagocytized dust particles.

All the dust samples have been decreased the nephrons' total content at the experimental rats that is attributable to the further growing number of the destructive cells.

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The work was submitted to the International Scientific Conference «Fundamental research», Israel (Tel Aviv), 16-23, October, 2012, came to the editorial office 13.09.2012.

**THE IMMUNE STATUS AND VASCULAR BED STIFFNESS INDICES AT THE RHEUMATOID ARTHRITIS PATIENTS DURING THE INFlixIMAB THERAPY**

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The indices study results of the cytokine status in the blood serum, and the functional state parameters of the vascular wall and its dynamics during the infliximab medical treatment at the 38 patients with the advanced stages ACCP – negative variant of the rheumatoid arthritis have been presented in the given paper. So, the significant increase in the serum concentration of the proinflammatory cytokines (e.g. TNF- $\alpha$ , IL-1 $\beta$ , IL-6, IL-8, and IL-17) at the patients with the RA advanced stage, compared with the control group, has been found. The significant decrease at all the examined RA-pulse wave propagation time, the stiffness and the augmentation indices increase, having reflected the vascular wall elasticity decrease patients, have been revealed. The pulse wave velocity (PWV) determination has been shown its further increasing up to  $14,2 \pm 1,2\%$  (e.g.  $p < 0,05$ ), that it is indicated in the arterial bed stiffness increase at the examined RA patients. The multivariate correlation analysis carrying out has been shown, that there is the significant inverse correlation between the pulse wave propagation time, the IL-1 $\beta$ , IL-6, IL-8, IL-17, TNF- $\alpha$  serum concentration, and the direct one – between the proinflammatory cytokines, the pulse wave velocity (PWV), and the augmentation index at the deployed RA patients. So, the infliximab medical therapy is associated with the content significant reduction of the IL-1 $\beta$ , IL-6, TNF- $\alpha$ , IL-8, IL-17 blood serum, the stiffness decrease and the vascular wall elasticity increase (e.g. by the lower pulse wave velocity, by the augmentation and the stiffness indices) at the RA patients.

The rheumatoid arthritis (RA) is one of the most common and wide – spread chronic inflammatory diseases in the humans; it is characterized by

the symmetrical chronic erosive arthritis (e.g. the synovitis) of the peripheral joints and the systemic immuno-inflammatory visceral injuries [4]. As the important and the significant challenge, in this pathology condition, the premature mortality rate is considered (e.g. up to 50% of the cases) from the cardio-vascular system diseases, having caused by the atherosclerotic vascular disease (e.g. the myocardial infarction, the congestive heart failure, the sudden death, the acute ischemic stroke), having developed for 10 years earlier, than in the population [8]. So, the cardio – vascular events (CVE) risk at the RA is quite significantly higher, than in the general population, and at the patients, having suffered from the diseases with the proven high – level cardio – vascular risk (e.g. the diabetes mellitus and the arterial hypertension) [8,9,11]. The CVE development risk increase at the RA is associated with the immuno – inflammatory mechanisms, having underlied in the basis of the RA pathogenesis and the atherosclerosis [2]. So, it is believed, that the inflammation, having contributed to the lipids deposition in the vascular wall, is the significant pathogenetic factor «destabilization» of the atherosclerotic plaque and the atherothrombotic complications [11]. It has been shown, in the recent years that the high frequency of the «subclinical» atherosclerotic vascular disease is characterized for the RA. The endothelium dysfunction, the small and the large vessels of the elasticity decrease, the systemic vascular resistance increase are reflected the earliest stage of the atherosclerotic vascular disease, and they have already been detected the RA onset, though these changes degree manifestation is practically increased with the disease duration further increasing.

The atherosclerosis development and the increased risk of the premature death at the RA are associated with the extra – articular manifestations, the disease progressive course, the inflammatory process activity, and the sulphur-positivity for the RF. However, in the overwhelming majority of the cases, the cardio – vascular complications are further developed at the RA patients, with the low or the moderate risk, according to the traditional factors risk, that is why the pressing challenge of the new predictors finding out of their occurrence is the most actual one [2, 11].

The effective anti – inflammatory therapy carrying out is played the important role in these complications prevention, having taken into consideration the chronic inflammation and the autoimmune disorders place, in the atherosclerosis development and the CVE related with it at the RA [6].

Recently, the genetically engineered biological agents (GEBA) are successfully used, that are permitted to be controlled the immuno-pathological processes further development for the patients' medical treatment with the RA high level activity [7]. However, up to the present time, there is no clear understanding and its presentations on the genetically