

DISADAPTIVE EFFECTS IN HUMANS AFTER EXPOSURE TO CHEMICALS CONTAINING DIOXIN

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The actuality of these studies is determined by the disadaptogenic activity of chemical substances like 2,3,7,8-tetrachlorodibenzo-p-dioxin ("Dioxin"). Dioxins' hormone-like disregulatory and disadaptogenic qualities have been shown to be the cascade of correlated pathogenic steps in the mechanism of sub clinical and clinical effects of the long-term consequences' syndrome formation [1,2,3]. The disadaptive effects are studied in the present report on the base of the loading and provocative tests, and by characterizing the reserve potentials of the organism, correspondingly. Two groups of South Vietnam inhabitants were investigated, who had similar specificity of local conditions but principal differences according to exposure with Agent Orange (AO) and dioxin-containing ecotoxicological factor (DEF) [3]. The 1-st group was selected among the inhabitants of control region - without any possible contacts with dioxin; the 2-nd group was selected among those who had been in contact with AO during the war-time and those who had been living on the sprayed territory for 15-20 years. This paper presents the results of all previous findings reevaluations and discussions [1-7].

The human reserve potentials were studied on different levels:

- molecular (N=86), benz-a-pyrene hydroxylase activity of the lymphocyte microsomal system (BAHH) [4];
- vitamin A status homeostasis stability (N=114) [5];
- cytogenetical (N=43, > 9000 metaphase cells). differential analysis of the genetically determined and environmentally induced sister chromatid exchanges (SCE) frequencies, and SCE induced by the additional culture loading with mitomycin C [6,7];
- systemic (N=76), visual analyzer dark adaptation registration [3];
- organism (N=69), respiratory and cardiovascular systems state evaluation while dosed physical loading (PWC-170).

The informativity of the II (Inducibility Index) parameter for the direct inducible effect was revealed by the comparative cohort studies on the diagnostic significance of characteristics for lymphocyte microsomal system state: basal (BAHH), 2,3,7,8-TCDD-induced in cultured cells (IAHH), Inducibility Index ($II = IAHH/BAHH$). II reflects the functional characteristics of lymphocytes, their ability to answer on the loading tests by the substrate-specific activity induction.

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The same peculiarities are registered for the vitamin A status characteristics. The differences in vitamin A status homeostasis couldn't be revealed by application of vitamin A pharmaceutical doses (100 mg/equiv.). Application of vitamin A loading dose (1 mg/kg, p/o) allowed to diagnose the hyposensitive form of hypovitaminosis A (1st group - 3.2%; 2nd group - 35.7%). The increase in vitamin A specific loading apparently provokes the contradictions between its consumption and catabolism. The conditions appear for realization of disadaptogenic alterations formed by dioxin into the concrete medically significant effects. Thus, only an increase of specific loading levels allowed to diagnose the sub clinical alterations in vitamin A status homeostasis supporting systems.

Similar features in reactions to loading were found for the cytogenetic parameters analysed. Their diagnostic significance in relation to dioxin-containing chemicals' exposure increases in the following order: genetically determined sister chromatid exchanges (SCE) < "spontaneous" SCE < environmentally induced SCE < specific mutagen-induced SCE (iSCE, when lymphocyte cultures have been incubated with a direct mutagen - mitomycin C, 0.1 mcg/ml) [6,7]. The enhancement in the informative significance of these parameters we associate with the successive exhaustion of cell reserve potentials (CRP) to self-reproduction as the reaction to a specific loading. The unusual informativity of the iSCE parameter may be explained from the following point of view: additive lesions induced by mitomycin C (above those existing as genetically and environmentally determined) require spending of additional CRP needed for reparative and replicative processes. The common level of CRP spending thus is being exceeded. The conditions for medically significant effects' development are produced on the background of sub clinical disturbances of chromatid structures induced by the environmental dioxin-containing factor. These were manifested by the decrease in the mitomycin-induced SCE levels in the cells of the 2nd group individuals as compared with the controls.

Clinical methods for visual analyzer state evaluation (diseases, keenness decrease in day-time, in the evening, or at night) didn't reveal any significant differences in frequencies of such alterations in two groups. Darkness adaptation study, that is the vision reaction on darkness probe, revealed the three-times' enhancement of time required for adaptation in the 2nd group patients as compared with controls.

The reserve potentials study on the organism level showed the significant increase in the informativity of the cardiovascular and respiratory systems functional activity characteristics when the dosed physical provocations were applied. Special correlation analysis has shown that in the 1st group the physical working capacity is provided by the adequate reaction while provocation test with 100 and 150 W, and by quick restitution during 3-4 minutes of rest. In the 2nd group the high level of physical capacity is provided by the hyperreactive answer of the cardiovascular system on the base of the enhanced tension of the cardiac muscles. So, the specific loading test (PWC-170) allowed to diagnose the sub clinical alterations existing in dioxin-exposed people.

Thus, the comparative cohort studies of the two principally different according to dioxin-containing chemicals' exposure risk groups, the general multilevel medically significant peculiarities were found in the diagnosed manifestations of the long-term medical consequences' effect. This effect is characterized [2,3] by:

- shifts in frequencies of individuals with definite levels of parameters studied;
- appearance of principally new effects, specific for the dioxin-dependent states;

- developing of new - different from the distinct "norm" - stable correlative associations between the functionally related characteristics of homeostasis.

We determine the sub clinical components of the long-term medical consequences' syndrome as specific characteristics. We consider these sub clinical components as the intermediate level of medically significant pathology induction. The important role of the successively aroused disadaptogenic alterations along with the biochemical and hormonal disturbances may be supposed in the process of sub clinical components complex development. This can be attributed particularly to the exhaustion of biological systems reserve potentials. After dioxins' biologically active qualities' realization the new level of functioning develops - when the biological systems can answer adequately only on an insignificant loading. While extraordinary influences the reactive profiles of the systems acquire different, often medically significant character.

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