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ABSTRACTS

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INHIBITING EFFECT OF OXIDATED CHOLESTEROL DERIVATIVES ON PHAGOCYTIC ACTIVITY OF PERITONEAL MACROPHAGES OF MICE

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Oxidated cholesterol derivatives are present in many foodstuffs and can appear as a result of endogenous metabolism of cholesterol (with monooxygenase participation) in an organism. Their increased content is characteristic of hypercholesteremia accompanied by a depression of some functions of the immune system. Hydroxylated cholesterol was shown to have a pronounced immunomodulating activity, in particular, suppressive effect on humoral immune response and ability for lymphocyte proliferation inhibition. In this connection, it can be supposed a possible influence of oxidated cholesterol metabolites on effector and immunoregulatory functions of macrophages.

In this work , it was studied the effect of cholesterol oxi-

dation products: 25-hydroxycholesterol and 7-ketocholesterol on the phagocytosis rate of corpuscular antigen-SRBC- by mice peritoneal macrophages. Macrophages, isolated from peritoneal cavity of (CBA x C57BL)F1,mice were used in experiments in vitro. Macrophages have been incubated with different concentrations of 25-hydroxycholesterol, 7-ketocholesterol, cholesterol and serous lipoprotein of low density for 2,6 and 22 hours. Then opsonized SRBC were added. Fc-dependent binding and SRBC phagocytosis were estimated by photometric method using 8-channel photometer "Multiscan" with 405 nm.

25-hydroxycholesterol and 7-ketocholesterol at 0,5, 1 and 5 mkg/ml concentrations were found to have a dose-dependent suppression of Fc-mediated SRBC phagocytosis after 22 hours of macrophage incubation with cholesterol metabolites studied. At 5 mkg/ml concentration, the degree of inhibition was 55% and 50% for 25-hydroxycholesterol and 7-ketocholesterol correspondingly. Shorter incubation (2 and 6 hours) did not exert considerable influence on SRBC phagocytosis. Cholesterol added to macrophages alone or supplemented with lipoproteins (unmodified and acetylated) did not affect the phagocytosis intensity in mentioned incubation periods.

In order to define more exactly the mechanism of 25-hydroxycholesterol and 7-ketocholesterol action on phagocytosis, we have studied the influence of these cholesterol derivatives on the intensity of SRBC Fc-dependent binding with macrophages. 22 hour macrophage incubation with 5 mkg/ml of 25-hydroxycholesterol or 7-ketocholesterol resulted in 30% and 35% decrease of Fc-dependent SRBC binding with macrophage mambrane. A phagocytosis decrease under the influence of oxidated cholesterol derivatives appeared to be partially mediated by Fc-dependent SRBC binding diminuation. This effect might be explained by a decrease in Fc-receptor number on macrophage membrane.

Mice macrophages have been previously shown to be able to metabolize cholesterol with appearance of its oxidated derivatives. Perhaps, this process is performed by cytochrome

P-450-dependent monooxygenase, which activity in macrophages is rather high. Taking it into consideration, it can be supposed that oxidative cholesterol metabolism in macrophages is physiologically sufficient process and changes of its intensity can cause the modulation of cell functional activity alterations of the immune reaction intensity.