333-336.

EFFECT OF ANTIHEPATOCYTOTOXIC SERUM ON DNA SYNTHESIS IN THE RAT

I. N. Alekseeva

UDC 615.373.616.36-002.616-003.93

Incorporation of thymidine-\(^3\)H into parenchymatous and reticulo-endothelial cells of the liver was studied autoradiographically in adult female rats treated with small doses (0.06 \(\mu \text{g} / 100 \text{ g body weight per injection}) of antihepatocytotoxic serum (AHTS), the \(\gamma\)-globulin isolated from it (\(\gamma\)AHTS), and the \(\gamma\)-globulin fraction of normal rabbit serum (\(\gamma\)NRS) to intact animals and to rats with liver damage caused by carbon tetrachloride (CC\(_4\)). Following injection of \(\gamma\)AHTS and, to a lesser degree, of \(\gamma\)NRS into intact animals the index of labeled nuclei of both the parenchymatous and the reticulo-endothelial cells was increased. When given after preliminary CC\(_4\) administration, \(\gamma\)AHTS stimulated reparative regeneration. The action of \(\gamma\)NRS took place in phases: a period of increase in the index of labeled nuclei was followed by a period of decrease, and this again was followed by a fresh period of stimulation of proliferative processes.

KEY WORDS: liver; antihepatocytotoxic serum; carbon tetrachloride; index of labeled nuclei.

A definite role in the activity of organs under normal and pathological conditions is ascribed to antitissue autoantibodies. The possibility of their participation in the growth of organs has been discussed [5]. The problem of their harmful and protective action is in process of solution [7, 10, 13, 15]. The use of heterogeneic antibodies may help to solve this problem.

Small doses of antihepatocytotoxic serum (AHTS) have been shown to have a normalizing action on the functions of the liver and its metabolism, when disturbed by carbon tetrachloride (CC\(_4\)) or by exogenous bile acids [1-3, 8].

The protective action of antibodies is largely ascribed to neutralization of the antigens formed during tissue destruction [6, 7]. However, a stimulating action of antibodies on the organ may also be expected. There are two possible pathways for this to occur: Either antibodies stimulate metabolic processes only in the cytoplasm of the cell and enhance its functional capacity, or, under the influence of antibodies, DNA replication and cell proliferation take place. It has been shown that AHTS increases the mitotic index in the liver of intact rats [4, 14].

The object of this investigation was to study incorporation of thymidine-\(^3\)H into liver cells (parenchymatous and reticulo-endothelial) of rats following injection of small doses of AHTS, of the \(\gamma\)-globulin fraction isolated from it (\(\gamma\)AHTS), and the \(\gamma\)-globulin fraction of normal rabbit serum (\(\gamma\)NRS) into intact animals and to animals with liver damage caused by CC\(_4\).

EXPERIMENTAL METHOD

Experiments were carried out on female Wistar rats weighing 170-200 g. The AHTS for rats was obtained by immunizing rabbits with a saline extract of rat liver. The titer of the serum in the complement fixation test was 1:320. \(\gamma\)-Globulin was isolated from the AHTS and NRS by Kendall's method [12].

In the experiments of series I intact rats were given three injections of γAHTS at intervals of 2 days. In series II intact animals were given whole AHTS by the same scheme. In series III intact rats were given injections of γNRS. The tests in these series were carried out on the 1st and 4th days after the last injection of the sera. In the next series of experiments γAHTS and γNRS were injected into rats with liver damage caused by CCl₄. In series IV the rats received CCl₄ only, by three subcutaneous injections at intervals of 2 days in a dose of 0.5 ml/100 g body weight, the compound being diluted 1:1 with sunflower oil. In series V and VI, γAHTS and γNRS (respectively) were injected into rats on the day after each injection of CCl₄. In all series γAHTS and γNRS were injected intravenously into rats in a dose of 0.06 μg protein/100 g body weight per injection. Whole AHTS was injected in a dose containing the same quantity of protein in its γ-globulin fraction.

At all periods of the investigation, thymidine-³²P (specific activity 12 Ci/mmmole) was injected intraperitoneally into the rats in a dose of 1 μCi/g body weight 1 h before sacrifice. From 3 to 5 animals were used at each time of testing. The control group consisted of 8 intact rats, into which radioactive thymidine was injected 1 h before sacrifice. All tests were carried out at the same time of day.

Histological sections were cut from the liver, stained with hematoxylin, coated with type M emulsion (Photographic Chemical Research Institute project), and exposed for 28 days. After development, the sections were stained with eosin and the index of labeled nuclei determined as the number of labeled cells per 1000 parenchymatous and per 1000 reticuloendothelial cells. The latter group included Kupffer cells, lymphocytes,