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⑨ Quarterly report no. 2, 15 Feb - 14 May 1962

SUBJECT OF INVESTIGATION

⑥ STUDIES ON THE MECHANISM OF CELL
DAMAGES IN LIVER AND KIDNEY CELLS
AND IN HEART MUSCLE FIBERS AS
REVEALED BY ELECTRON MICROSCOPY.

RESPONSIBLE INVESTIGATOR

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SECOND QUARTERLY REPORT

On Contract No. DA-92-557-FEC-35699

Inclusive Date: 15 February 1962 to 14 May 1962

SUBJECT OF INVESTIGATION:

STUDIES ON THE MECHANISM OF CELL DAMAGES IN LIVER AND
KIDNEY CELLS AND IN HEART MUSCLE FIBERS AS REVEALED BY
ELECTRON MICROSCOPY

RESPONSIBLE INVESTIGATOR :

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1. Purpose of the investigation: See, first report.

2. The preliminary observation already attained:

a. Intoxication of diphtheria toxin:

Periodical changes of liver cells of rat after intraperitoneal injection of diphtheria toxin (MLD: 0.004 ml for rat) have been observed. Three hours after administration of the toxin, there was an increase of dark cells which were smaller, lean and denser than normal controls and show rather wellpreserved and compactly arranged cell organellae.

Twenty-four hours after the administration the amount of glycogen was definitively decreased. Many dense, shrunken and lean hepatic cells were found in the liver cell strands of the central zone. Irregular shaped cystic or vacuolar structures of uncertain nature occasionally appeared beneath the cell surface facing the sinusoid and near the inter-cellular bile canaliculi. These changes especially the increase of dark and lean cells were remarkable in this experiment.

b. Thioacetamide intoxication:

Thioacetamide (60 mg/kg) was given to rats intraperitoneally. Fifteen minutes after the administration, the liver cells of the central zone showed disarrangement, shortening and falling off of the superficial Palade's granules. Transformation of rough-surfaced endoplasmic

reticulum to smooth type increase of microbody and slight mitochondrial swelling were also noted. These changes were more prominent in the case of three hours. Characteristic appearance of large nucleoli with occasional chromonema formation was observed. Forty-eight hours after the administration, the nucleoli became large, but there was no chromonema formation. Nuclear substance was highly reduced and only small amounts remained beneath the nuclear membrane. Marked disarrangement and decrease of rough-surfaced endoplasmic reticulum with increase of smooth type accompanied by occasional network formation simulating that seen in the cases of CCl₄ intoxication were observed. Changes of mitochondria were also prominent. They showed marked swelling, deformation, vague outer limiting membrane, decrease in stromal density, and occasional cristolysis, but, mitochondrial granules were often well preserved. Irregular and vacuolar structures which are probably made up of infolding of superficial cytomembrane were often found. They contained slightly dense and amorphous or very fine granular substance in the lumen. Microbodies were increased considerably. Lean and dark cells as seen in the cases of diphtheria toxin intoxication and occasional destroying cells were encountered. Bundles of collagen fibers were noted in the Disse's spaces and intercellular spaces of the liver cell strands. Destruction and condensation of the

sinusoidal endothelium and platelet thrombi in sinusoids were also found in the central zones of the lobuli.

Details of the above results together with further observations will be described in the final report.

3. Experiments in progress:

a. Intoxication of yellow phosphor

b. Kidneys following ligation of renal artery and reopening of the circulation in rabbit and rat were already embedded. Soon, they will be examined under the electron microscope.

c. Studies of effects of endoxan on the Yoshida sarcoma and ascites hepatoma:

A single administration of large doses of endoxan and comparison of effectiveness in sensitive (Yoshida sarcoma and AH.130 strain ascites hepatoma) and insensitive (AH. 7974 strain ascites hepatoma) tumor cells are now being studied.