EFFECT OF RADIOACTIVE NEOHYDRIN LABELED WITH Hg^{203} AND Hg^{197} ON THE KIDNEYS AND LIVER

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Neohydrin labeled with Hg^{203} and Hg^{197} was injected into rabbits in various doses. In a dose of 1.5-2 μCi/kg (the dose used in clinical practice) the compound caused no morphological changes in the kidneys or liver. Minimal changes developed in the kidneys when the dose was increased by 6-10 times, and in the liver when it was increased by 15-20 times. Degenerative changes in the kidneys after administration of high doses are reversible in character.

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The compound neohydrin (3-chloromercuri-2-methoxypropylurea) now used for scanning the kidneys is a mercurial diuretic. Its use as a diuretic began in 1949 [6]. Neohydrin-Hg^{203}, with a half-life period of 47.9 days, emitting γ- and β-rays with an energy of 279 keV, and neohydrin-Hg^{197}, with a half-life period of 65 h, emitting γ-rays and x-rays with an energy of 77 keV are used in clinical nephrology.

The localization of mercury in the kidney tissue has been determined experimentally in rats by histoautoradiographic methods [3, 4], showing that the compound administered was localized in the renal cortex and more especially in the medulla. Silvery mercury granules were present in the tubules, but none were found in the medulla and glomeruli. Other workers [1, 2] state that neohydrin-Hg^{203} accumulates selectively in the proximal portion of the convoluted tubules, and that none is found in the medulla. One investigation [5] has shown that during the first 5 h after its administration, 60.5% of the isotope is concentrated in the kidneys and 15.2% in the liver. The remaining organs contain negligible amounts of neohydrin.

From the available local and foreign literature we did not find any information on the possible harmful effects of neohydrin-Hg^{203} or neohydrin-Hg^{197} on the kidney and liver tissues.

In this investigation morphological changes in the kidneys and liver were studied in relation to the dose of the compound administered and the maximal allowable dose was determined.

EXPERIMENTAL METHOD

The kidneys of 40 and the liver of 20 rabbits receiving neohydrin-Hg^{203} and neohydrin-Hg^{197} in an increasing dose from 10 to 100 μCi were investigated. The animals were sacrificed from 3 to 30 days after administration.

The compound is used for diagnostic purposes in a dose of 1.5-2 μCi/kg body weight. In the experiments we increased this dose by 2-30 times (animals weighing from 1800 to 3200 g).

Histological sections were stained with hematoxylin-eosin, picrofuchsin, by Van Gieson's method, and with Sudan III; sections were also impregnated with silver to demonstrate the argyrophilic skeleton.

EXPERIMENTAL RESULTS

After administration of neohydrin-Hg^{203} and neohydrin-Hg^{197} to rabbits in a dose of up to 20 μCi (from 4 to 6 times the clinical dose), no pathological changes were found in the liver.

Minimal changes of the cloudy swelling type in the epithelium (Fig. 1) of the convoluted tubules of the kidneys appeared when the dose was increased by 6-10 times (30 μCi). The glomeruli were unchanged. The degenerative changes were minimal. The epithelium of most convoluted tubules was intact and its

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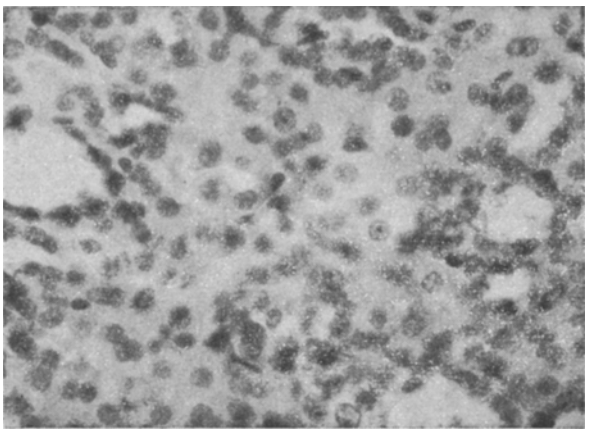

Fig. 1. Cloudy swelling of epithelium of convoluted renal tubules. Hematoxylin-eosin, 400 ×.

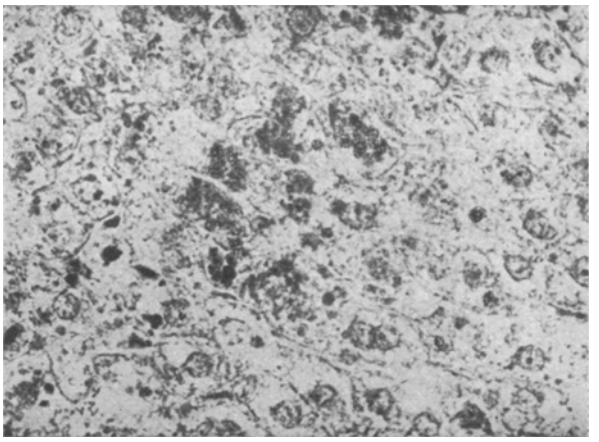

Fig. 2. Fatty degeneration of liver cells. Sudan III, 200×.

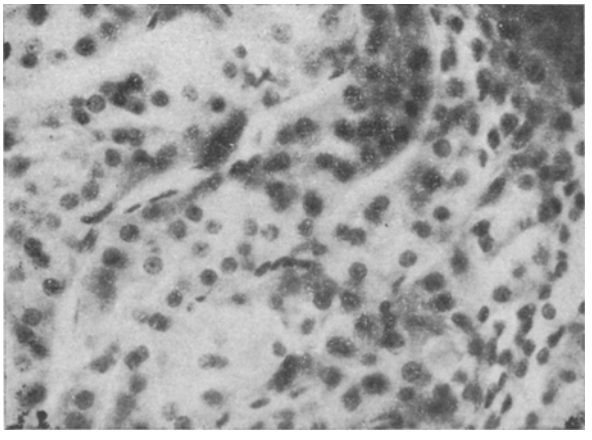

Fig. 3. Regeneration of epithelial cells of the renal tubules. Hematoxylin-eosin, 400×.

cytoplasm transparent. Albuminoid granules were visible only in the epithelium of some tubules, without necrosis of the epithelium. In the liver no pathological changes were found.

After administration of the compound to rabbits in a dose of 40 μCi, besides the picture described above, dilatation and congestion of the blood vessels were found. No pathological changes were observed in the liver.

If the dose was increased by 10-15 times (50 μCi), signs of cloudy swelling of the epithelium of the convoluted tubules were seen more clearly in the kidneys, and the stroma was infiltrated by many lymphocytes and histiocytes. No changes were found in the liver.

Administration of the compound in a dose 15-20 times larger than the clinical dose (60 μCi) produced not only marked changes of the cloudy swelling type in the kidneys, with necrosis of individual epithelial cells, but on staining for lipids (Sudan III) they were present in certain parts of the cytoplasm of the straight tubules. Lipids were absent from the convoluted tubules. Small droplets of fat stained orange with Sudan III were found in the cytoplasm of the liver cells, mainly at the periphery of the lobules (Fig. 2). No gross sclerotic changes were found in the materials stained by Van Gieson's method. The argyrophilic skeleton remained unchanged.

An increase in the dose of the compound by more than 20 times (70-100 μCi) led to sloughing and necrosis of the epithelium of individual convoluted tubules and to infiltration with lymphocytes and histiocytes around the blood vessels, and also to a more clearly defined fatty degeneration of the liver. The liver cells showed hyaline-droplet degeneration and necrosis of individual liver cells with accumulation of lymphocytes and histiocytes around them. These changes were more marked following administration of neohydrin-Hg^{203} than of neohydrin-Hg^{197}.

Cloudy swelling and necrosis, with sloughing of individual cells, were well marked 21 days after administration of neohydrin in a dose of 100 μCi in the proximal portion of the convoluted tubules, but besides these changes evidence of regeneration of the epithelium also was present (Fig. 3).

Hence, it can be concluded from these investigations that the doses of neohydrin-Hg^{203} and neohydrin-Hg^{197} used for diagnostic purposes, namely 1.5-2 μCi/kg body weight, produce no morphological changes in the kidneys or liver. Minimal changes in the kidneys of cloudy swelling type in the epithelium of the convoluted tubules appear after administration of 6-10 times the clinical dose. Minimal changes in the liver,

in the form of cloudy swelling and fatty degeneration appear after administration of 15-20 times the clinical dose. Severe cloudy swelling of the kidneys, with necrosis and sloughing of the epithelium of individual convoluted tubules and fatty degeneration of the liver, with necrosis of individual liver cells, are found after administration of 20 times the clinical dose or more. These changes were more severe when neohydrin-Hg^{203} was given. The degenerative changes in the kidneys are reversible in character, regeneration taking place three weeks after administration of the compound.

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