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Histological and Histochemical Investigations of the Influence of Metizol on the Function of the Kidneys When Given During Pregnancy

Badania histologiczne i histochemiczne wpływu Metizolu, podawanego podczas ciąży, na funkcję nerek

Therapy for thyroid hyperactivity during pregnancy is complicated. Usually it consists in administration of antithyroid drugs which depress the activity of this gland almost to its physiological level, but do not block it completely. With this aim in view the doses of drugs are reduced to one half, for instance Metizol is given over the entire pregnancy period in the amount of 30 mg daily (2). This drug appears in the urine as early as 30 min after administration, the main pathway of its excretion being the kidneys. This drug is also known to enhance iodide clearance from the kidneys. It seemed, therefore, useful to evaluate the activity on certain cell enzymes and the physiological state of nephrons under the specific conditions of pregnancy and after Metizol application.

MATERIAL AND METHODS

The experiments were performed with female Wistar rats of mean body weight 200—250 g. They were divided into three groups, five in each. The control group consisted of pregnant females receiving no medication, group I — nonpregnant females receiving the drug for 21 days and group II — pregnant rats treated with the drug for 21 days of pregnancy.

Metizol ("Polfa") in 5 mg tablets was given in the form of aqueous suspension with a gastric tube in a volume of 2 ml. The dose for each female was 0.15 g/kg/day. The control group was given intragastrically 2 ml of distilled water. After 21 days of this treatment with Metizol the rats were decapitated and the kidneys were prepared out for examination. The tissue was divided into two parts:

1. The segments were fixed in a mixture of Bacer's solution at 4° for 24 hrs and cut on a freezing microtome (8 mg). They were subjected to the reaction for acid phosphatase (AcP) and alkaline phosphatase (AlP) after Gomori (9).

2. The kidney segments were fixed in Carnoy's fluid and embedded in paraffin. The PAS reaction was run on the 8 mμ sections which were stained with hematoxylin and eosin (H+E) (8).

RESULTS

Experimental group I

The kidneys showed morphological changes as compared with the controls (Fig. 2). These consisted in shrinking of the blood vessels of the renal bodies and thus, extension of the space between the laminae of Bowman's capsule (Fig. 2). The tubules here were dilated, the epithelium in some places markedly lower with the brush border. Within the lumen of the convoluted tubules of the second order inclusions in the form of glomerules were visible. The stroma was endematous because of accumulation of inflammatory infiltration, mainly of lymphocytes. The AlP activity in the brush border of the convoluted tubules of the first order was distinctly weaker and nonuniform as compared with that in the control group. A difference in AcP activity in the particular nephrons was observed in the kidneys of this group of animals. Convoluted tubules of the first order were noted with a large accumulation of granular material filling almost uniformly the cytoplasm of epithelial cells as well as tubules with a granular reaction weaver than in the control (Figs. 4, 5). The PAS reaction in the brush border of convoluted tubules of the first order was weaker as compared with that in the control.

Experimental group II

The microscopic picture of kidneys in this group of animals was similar to that in group I. The tissue stroma exhibited swelling at the site of accumulation of infiltration (Fig. 3). In the main tubules the epithelial cells were lower with brush border destroyed in some places. In the lumen of the convoluted tubules of the second order inclusions were visible. The lumen of the main tubules was obscured nonuniformly by the reaction product indicating the presence of AlP. The intensity of appearance of this enzyme was weaker than in the control group and resembled that in nonpregnant animals in group I. The phosphatase activity reaction was positive, its intensity, however, was markedly lower than in the control group (Fig. 6). A positive PAS reaction was noted in Bowman's capsule and mesangium of the renal bodies. In the brush border the reaction was but little pronounced like in group I.

DISCUSSION AND CONCLUSIONS

Comparison of the results in the present paper indicates similar results in groups I and II. This suggests that the changes in the kidneys were due to Metizol, notwithstanding pregnancy. Among the symptoms caused by the drug were changes in the tubules and stroma such as destruction of the epithelium together

with the brush border in the contorted tubules of the first order, leucocytic infiltration, edema of the stroma and tubuler inclusions (1, 4, 8).

It is possible that the observed injury to the tubular epithelium after Metizol produced a state of tubulopathy. The most frequent of the latter is poor reabsorption of sodium, leading to an avalanche reaction of excitation of the periglomerular apparatus, a centraction of the arterioles and ischemia (5). The distention of the peritubular capillaries and the increase of their permeability were probably a further consequence of the local hypoxia (3, 6). It is possible that these facts were the cause of leucocytic infiltrations and edema in the renal stroma in the animals receiving Metizol. The fact of increase of the AlP level and its participation in transport through the cell membranes in the pregnancy period is known (7). The reduced AlP activity after Metizol application in pregnant females is probably a subsequent symptom of drug-evoked nephropathy. The correctness of this interpretation of the results is supported by the fact that, after administration of the drug, the PAS reaction also diminished in the brush border of the first order contorted tubules. The noted similarity of both reactions (AlP and PAS) is understandable. AlP causes dephosphorylation of hexose phosphate, thus taking part in active glucose absorption. The decrease in AcP activity after Metizol points to a reduction of the lysosomal apparatus and decline of the digestive reactions of the cell.

It may be concluded on the basis of the obtained results that application of Metizol in a definite dose was the cause of appearance of nephropathy. This state was reflected in morphological changes within the numerous renal glomeruli, destruction of the epithelium of the tubules belonging to them and disturbances in the function of the intracellular enzymes. It would seem that both pregnant and nonpregnant females reacted here similarly to the nephrotoxic factor.

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EXPLANATION TO FIGURES

Fig. 1. Kidney of control rat. Hematoxylin and eosin staining (H + E). Magn. ca 50 ×.
Fig. 2. Rat kidney experimental group I. H + E. Magn. ca 50 ×.
Fig. 3. Rat kidney experimental group II. H + E. Magn. ca 50 ×.
Fig. 4. Kidney of control rat. Reaction for acid phosphatase (AcP). Magn. ca 50 ×.
Fig. 5. Rat kidney experimental group I. Reaction for AcP. Magn. ca 50 ×.
Fig. 6. Rat kidney experimental group II. Reaction for AcP. Magn. ca 100 ×.

STRESZCZENIE

W wyniku podawania Metizolu w dawce 0,15 g/kg c.c./dzień w okresie 21 dni stwierdzono zmiany w strukturze anatomicznej nerek oraz zaburzenia: przepuszczalności przez błony komórkowe (Fz), przemian węglowodanowych (PAS) i trawienia wewnątrzkomórkowego (Fk). Wydaje się, że stosowana dawka Metizolu powodowała podobne efekty u samic zarówno ciężarnych, jak i nie będących w ciąży.

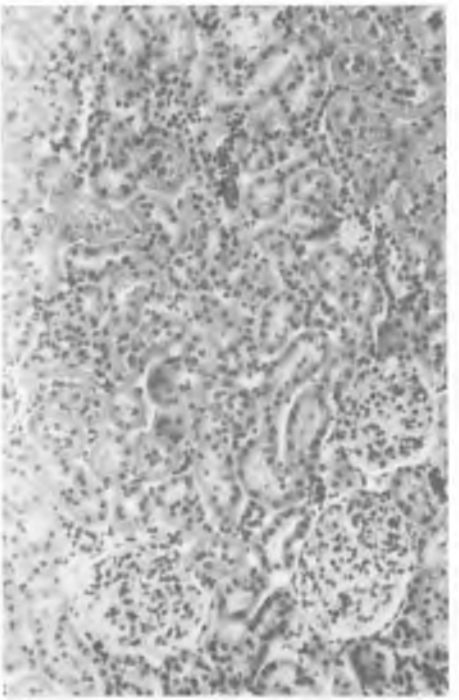

Fig. 1

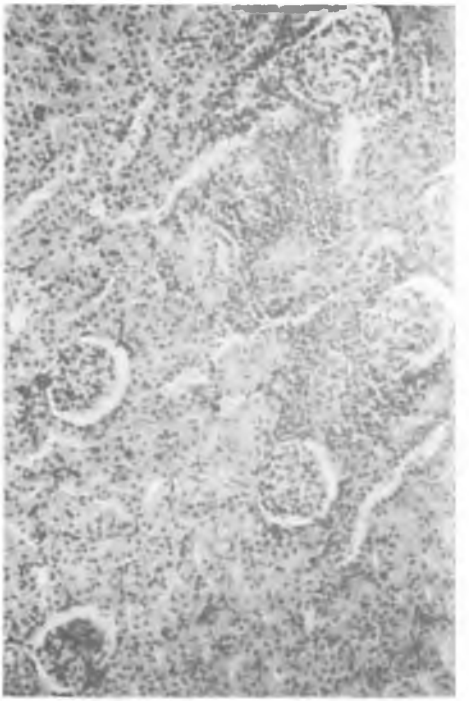

Fig. 2

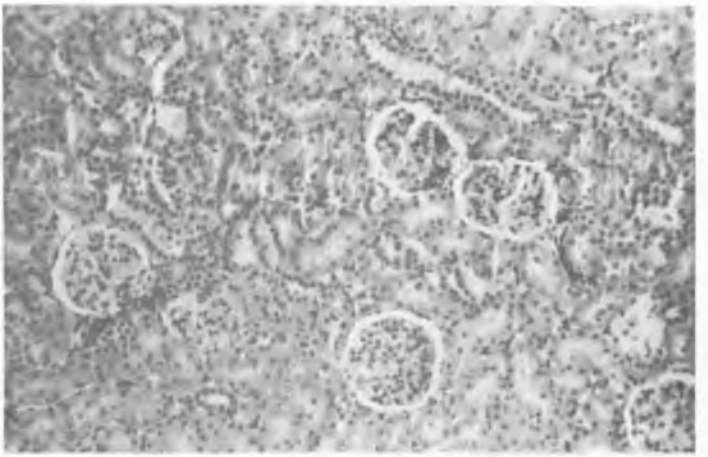

Fig. 3

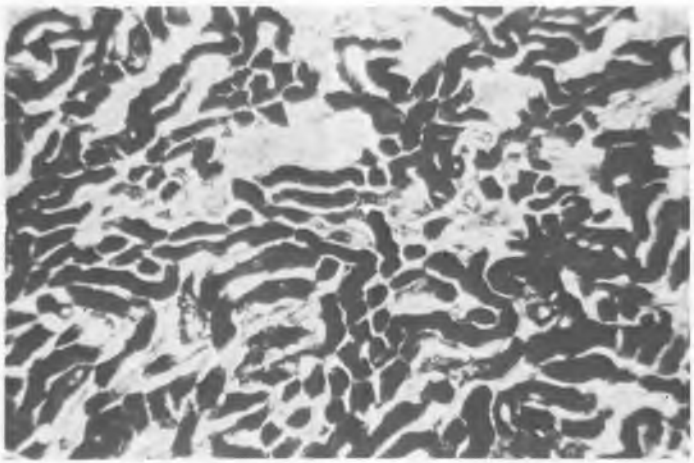

Fig. 4

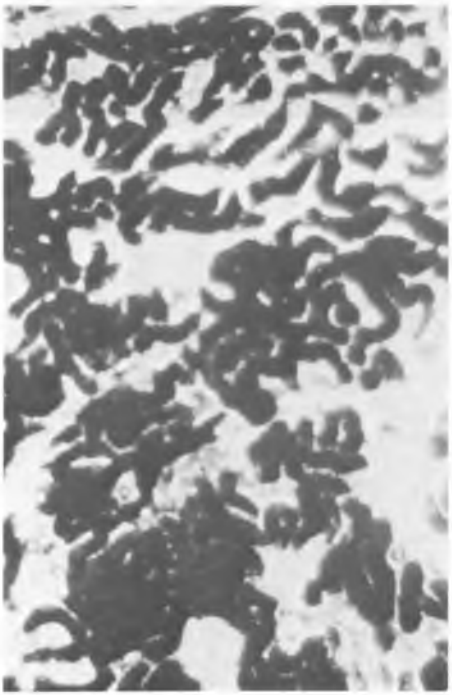

Fig. 5

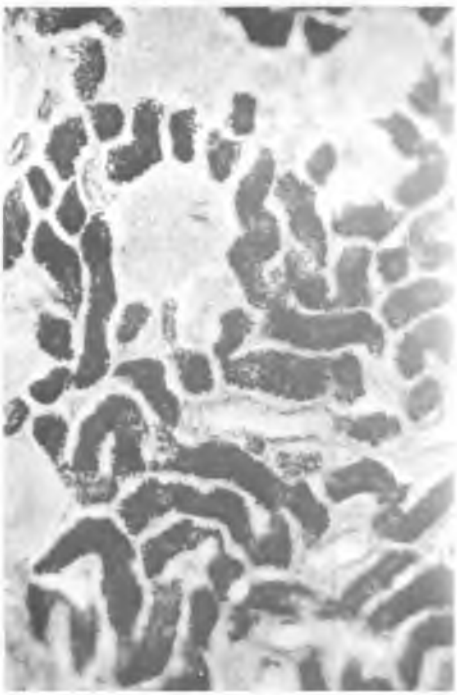

Fig. 6