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The Effect of Torecane on the Female Rat Spleen During Pregnancy

Wpływ torekana na śledzionę samic szczurów w okresie ciąży

Влияние торекана на селезенку самок крыс в течении беременности

Torecane (*Thiethylperazine maleate*) is a derivative of fenotiazine of quick antivomitary and sedative action. Because of its beneficial therapeutic action this drug is often taken by pregnant women. Considering its contraindications (4) the effect of torecane on the female rat spleen during pregnancy has been investigated.

MATERIAL AND METHODS

Female rats weighing 120—150 g were divided into 6 groups:

Control group I — 5 non-pregnant animals, not receiving the drug.

Experimental group I — 5 non-pregnant animals, receiving torecane (Torecane, Sandos S. A. Bazylea) in the dose of 0.5 mg/kg of body mass.

Experimental group II — 5 non-pregnant animals, receiving the drug in the dose of 5 mg/kg of body mass.

Control group II — 5 pregnant animals, not receiving torecane.

Experimental group III — 5 pregnant animals, receiving the drug in the dose of 0.5 mg/kg of body mass.

Experimental group IV — 5 pregnant animals, receiving torecane in the dose of 5 mg/kg of body mass.

The animals were given the drug by intraperitoneal injection in 0.5% methylcellulose solution for 3 successive days before fertilization and for the whole period of pregnancy. The animals of experimental groups I and III received about 1.8 mg each and animals of experimental groups II and IV — about 18 mg of torecane. The female rats were decapitated 1—2 days before the end of pregnancy. Some sections of spleen were fixed in 4% neutral formalin for review staining by hema-

toxylin and eosin, and other sections — in Carnoy's solution for detection of nucleic acids. In order to detect acid phosphatase and alkaline phosphatase activities the spleen was fixed in Baker's solution and cut by freezing microtome.

The photographs were taken by microscope and Carl Zeiss — Jena photographic apparatus.

RESULTS

NON-PREGNANT FEMALE RATS

Staining with hematoxylin and eosin

No histomorphological differences were found in the spleen of non-pregnant animals when the control group and animals receiving torecane in the dose 0.5 mg/kg of body mass were compared.

After administration of a larger dose (5 mg/kg) of body mass the quantity of lymphatic papules increased in the organ.

RNA staining by Brachet's method

The cells with pyroninabsorptive cytoplasm were present in the whole parenchyma of the spleen of control animals. There were: a) a number of big cells located in the reproductive media of lymphatic papules; b) cells similar to the above-mentioned but present in a big number (very often in concentrations) in the red pulp; c) cells of medium size with a spoken nucleus and predominantly irregular shape present in the red pulp; d) very big multinuclear cells scattered in the red pulp. Microscopic pictures of the spleen of animals treated with torecane in the dose 0.5 mg/kg of body mass showed a greater number of different types of pyroninabsorptive cells in comparison to that found in control animals. A larger dose of the drug (5 mg/kg of body mass) caused further increase in the number of cells with the cytoplasm rich in RNA in the red pulp. Numerous cell divisions occurring in the white and red pulp were observed in the spleen of both groups of animals.

Alkaline phosphatase

A positive reaction to alkaline phosphatase was found in the cell membranes of numerous red pulp cells and in the internal membranes of blood vessels in the spleen sections of control animals. In the lymphatic comparison with control slides was observed. Moreover, the reaction was visible in the walls of sinuate vessels.

Acid phosphatase

Strong acid phosphatase activity was observed in numerous cells of the spleen red pulp. The enzymes were found in the cells in the condensed zone and in the reproductive medium of lymphatic papules. A slight increase in acid phosphatase activity has taken place in both experimental groups of nonpregnant animals when compared with the control.

PREGNANT FEMALE RATS

Staining with hematoxylin and eosin

Typical well-developed lymphatic papules were present in the spleen of control pregnant animals (Fig. 1). The microscope slides of pregnant female spleen from experimental groups III and IV (Fig. 2) showed identical changes in relation to control that is a reduction of lymphatic papules quantity and the appearance of lymphocyte concentrations which did not form papules.

RNA staining by Brachet's method

The quantity of cells containing cytoplasm rich in RNA decreased in the spleen of animals which were administered torecane in dose 0.5 mg/kg of body mass in comparison with control. However, after administration of 10 times larger dose the number of cells rich in RNA increased chiefly in red pulp (Figs. 3 and 4). Large, multinuclear cells were also present in this part of spleen pulp.

Alkaline phosphatase

The distribution of enzyme activity in the spleen of pregnant control animals was very similar to that of the comparative group of non-pregnant animals (Fig. 7). However, alkaline phosphatase activity was greater in the sinus walls of pregnant animals.

The dose of torecane in amount 0.5 mg/kg of body mass did not cause any change in alkaline phosphatase activity but a 10 times greater dose brought about a slight decrease in the enzyme activity (Fig. 8).

Acid phosphatase

Some increase of acid phosphatase activity in comparison with control was observed in pregnant animals only after the dose in amount 5 mg/kg of body mass (Figs. 5 and 6).

DISCUSSION

This experiment showed that torecane given to non-pregnant female rats in dose 0.5 mg/kg of body mass did not cause visible histomorphological changes in the spleen except for a slight increase of macrophages and plasmatic cells and a insignificant increase in acid and alkaline phosphatase activities.

The treatment of the spleen of pregnant animals with this same drug dose suggest a modified sensibility of the organ in this period.

In relation to control slides no difference in acid phosphatase activity was observed and the number of cells rich in RNA in the red pulp was slightly decreased.

Alkaline phosphatase showed a slight increase in its activity similarly to the comparative group of non-pregnant animals. The changeable sensibility of some organs to Biseptol during pregnancy has been reported by Haliniarz and Sikorski (1). These observations can suggest that the spleen is an organ resistant to torecane dose in amount 0.5 mg/kg of body mass also in the period of pregnancy.

The application of 10 times greater dose of torecane to non-pregnant animals did not cause any visible histological and morphological changes in the spleen, either. However such changes were observed in pregnant females. They consisted in the decrease in the number of typical lymphatic papules and the formation of many lymphocyte concentrations in the red pulp. Most probably the administration of the drug in this dose enlarged the request for lymphocytes in the organism and caused their rapid removal from lymphatic papules to red pulp. Simultaneously an increase in macrophage and plasmatic cells number in red pulp was observed. The increase in plasmatic cells quantity under intoxication with pesticide "Zolon" was observed by Zlatera and Softova (6). A similar influence of the pesticides has been reported by Olefir (3) and Kasakova (2).

The described changes can be considered as functional phenomena connected with administration of torecane in the period of pregnancy and suggest that a greater dose of the drug can be worse tolerated by

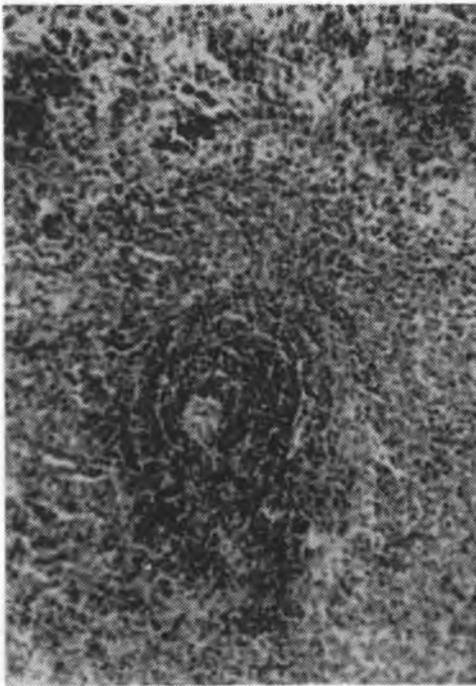


Fig. 1

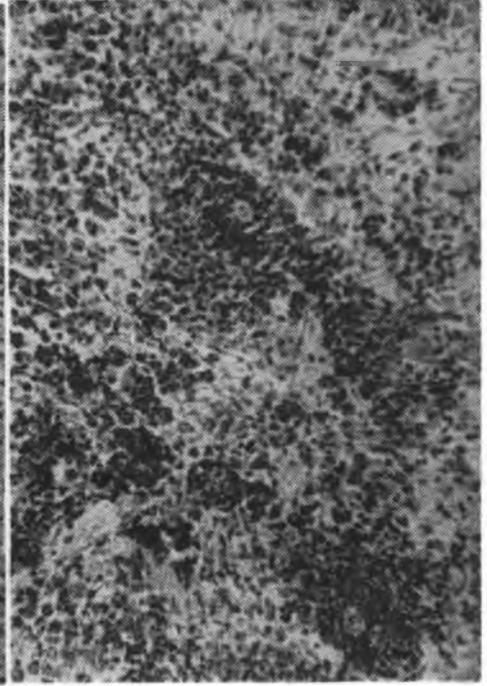


Fig. 2

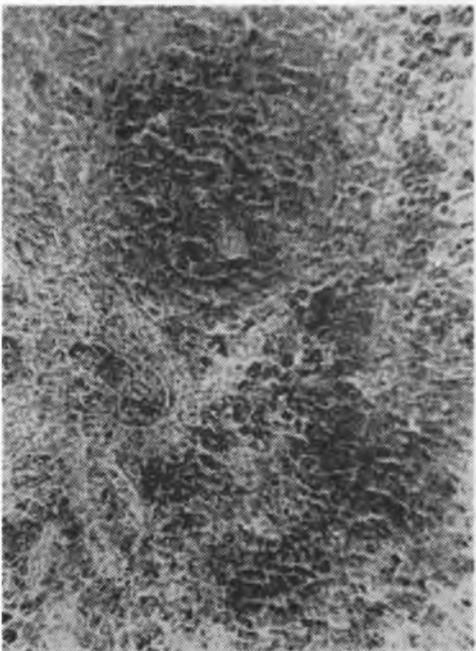


Fig. 3



Fig. 4

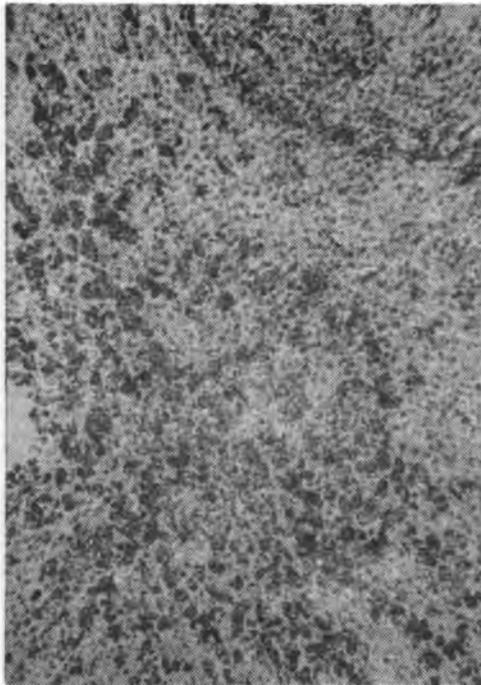


Fig. 5

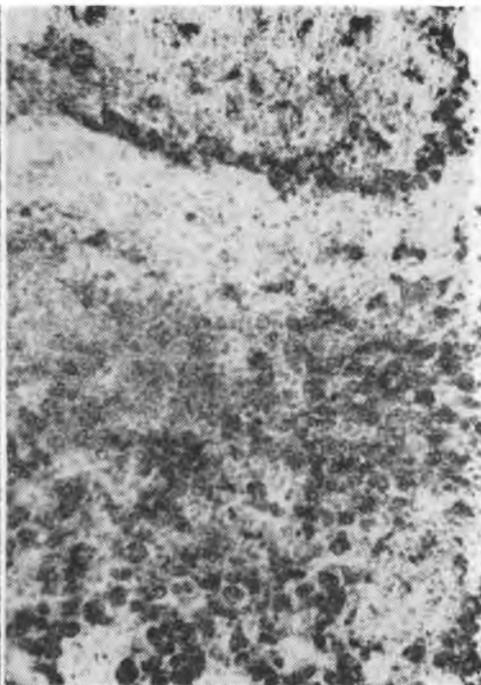


Fig. 6

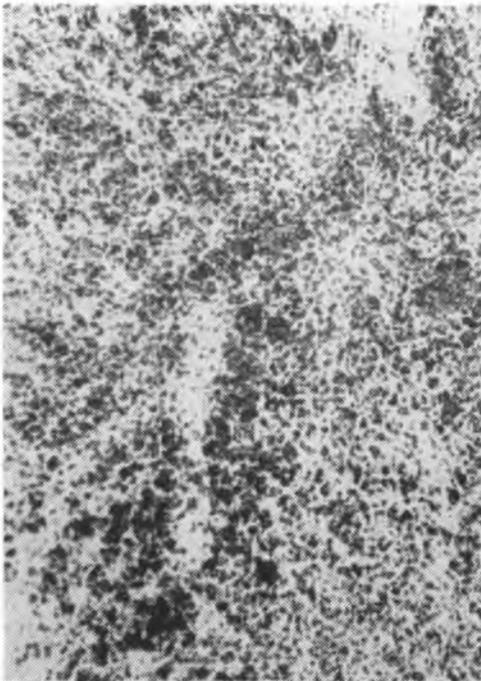


Fig. 7

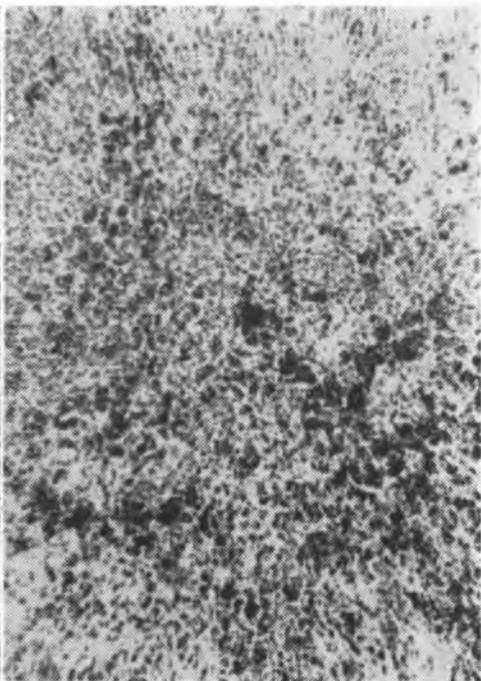


Fig. 8

the organism in this period. One of many spleen functions is the decreasing drug toxicity (5) which occurs also in case of torethane. This function seems to be less efficient in pregnant animals.

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EXPLANATION TO FIGURES

Fig. 1. The spleen of rat from control group II. Slide of organ is normal. Staining with hematoxylin and eosin. Magn. ca 200X.

Fig. 2. The spleen of rat from experimental group IV. Small nontypical lymphatic papules and lymphocyte concentrations are visible in red pulp. Staining with hematoxylin and eosin. Magn. ca 200X.

Fig. 3. The spleen of rat from control group II. Staining by Brachet's method. Magn. ca 200X.

Fig. 4. The spleen of rat from experimental group IV. The enlarged number of cells with big amount RNA is visible in the red pulp. Staining by Brachet's method. Magn. ca 200X.

Fig. 5. The spleen of rat from control group II. Reaction to acid phosphatase according to Gomori's method. Magn. ca 200X.

Fig. 6. The spleen of rat from experimental group IV. The moderate increase of acid phosphatase activity. Gomori's method. Magn. ca 200X.

Fig. 7. The spleen of rat from control group II. Reaction to alkaline phosphatase by Gomori's method. The enzyme activity is visible in the walls of sinuate vessels. Magn. ca 200X.

Fig. 8. The spleen of rat from experimental group IV. Reaction to alkaline phosphatase by Gomori's method. The moderate decrease of enzyme activity in the red pulp. Magn. ca 200X.

STRESZCZENIE

Samice ciężarne szczura białego otrzymywały torekana w iniekcji dootrzewnowej w dawce 0,5 mg/kg i 5 mg/kg masy ciała codziennie przez 3 dni przed ciążą i przez okres ciąży. Równolegle podawano lek zwierzętom nieciążarnym. Na podstawie otrzymanych wyników badań wyciągnięto wnioski: 1) śledziona ciężarnych szczurów jest bardziej wrażliwa na torekana niż śledziona szczurów nieciążarnych; 2) dawka torekana — 0,5 mg/kg masy ciała była dobrze tolerowana przez ciężarne szczury; 3) dawka — 5 mg/kg masy ciała wywołała zmiany, które można uważać za zjawisko czynnościowe, równoznaczne z przejściowym osłabieniem aktywności metabolicznej narządu.

РЕЗЮМЕ

Беременным самкам белой крысы внутрибрюшинно впрыскивали торекан в дозе 0,5 мг/кг и 5 мг/кг массы тела. Торекан впрыскивали ежедневно в течение 3 дней до беременности и в период беременности. Одновременно торекан впрыскивали небеременным животным. На основе полученных результатов определено, что: 1) селезенка беременных крыс более чувствительна к торекану, чем селезенка небеременных крыс; 2) дозу торекана 0,5 мг/кг массы тела животные хорошо сносили; 3) доза 5 мг/кг массы тела вызывала изменения, которые можно определить как функциональное явление, отвечающее временному понижению метаболической активности органа.