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**The Influence of Biseptol 480 on Histochemical Reactions in the Testicles
of a Rat After Surgical Removal of a Kidney or a Liver Lobe**

**Wpływ Biseptolu 480 na histochemiczne odczyny w jądrach szczura po chirurgicznym
usunięciu nerki lub płata wątroby**

**Влияние Бисептола 480 на гистохимические реакции в ядрах крысы
после хирургического удаления почки или доли печени**

Metabolism of medicines in an organism depends on genetic and enzymatic conditions, but about 30% of enzymes reveals specific and heterogeneous activity which is conspicuous by different reaction to compounds which are included in them (5).

So the principle of controlled pharmacotherapy which takes into account both the pathophysiological and individual features of a patient is necessary.

Bisteptol 480, which contains sulfamethoxyl (SMZ) and trimetaprim (TMP) is widely used in therapeutics, e.g. in urinary tracts infections, inflammations of a prostate gland or of testicles (1—4, 6). But yet cases when administration of the medicine made activity of kidneys worse, or caused occlusion of ureters or even serious liver necrosis (2) were described.

Since one could not find complete explanation of mechanism of activity of Biseptol 480 in available literature, it has been decided to investigate in this work the effect of this compound on man's testicles in conditions of liver injury or removal of one kidney.

MATERIAL AND METHODS

An experiment was carried out on white male-rats of Wistar race weighting 300—350 g. They were divided into six groups, five of which were experimental and one — control.

Animals of the first experimental group underwent surgical removal of the right liver lobe. Two weeks after the manipulation 2 cm³ of Biseptol 480 in aqueous suspension was given by a stomach-tube to the rats during seven successive days after morning feeding. This dose was 10 times greater (reducing to kg of the body weight) than it was used for a man. So each rat was given 560 mg. of the medicine. Animals from the second experimental group underwent a similar operation but they were not given Biseptol 480. Rats of the third experimental group had the left kidney removed and two weeks after the manipulation they were given Biseptol 480 just as the animals of the first group. Rats of the fourth experimental group did not receive the medicine after removal of the left kidney. Animals from the fifth experimental group were not operated but they received Biseptol 480 under the same conditions as those described above. The sixth group (a control one) consisted of the animals which received distilled water instead of the medicine but under the same conditions as the experimental animals.

Twenty-four hours after the last dose of the medicine or solvent was given, animals were decapitated and male gonads for histological (staining with hematoxylin and eosin) and histochemic examinations (detection of acid phosphatases and alcalic phosphatases by means of Gomori's method, of nucleic acids by Brachet's method and of polysaccharides by means of a PAS method according to McManus) were taken.

RESULTS

Staining with hematoxylin and eosin

One could observe a proper view of spermatogenic ducts and Leydig's cells of an interstitial gland (Fig. 1) in the control group of animals.

In spermatogenic ducts of rats from the first experimental group abortive cells appeared and relaxation of ties between spermatocytes and atrophy of spermiogenesis took place (Fig. 2). The similar changes appeared also in testicles of animals from the second experimental group (Fig. 3).

Spermatogenic ducts of the third and the fourth experimental groups resembled a control view (Figs. 4 and 5). However, in gonads of rats from the fifth experimental group, one could find some ducts with spermatogenesis disturbances and with abortive cells (Fig. 6) between proper spermatogenic ducts.

The histological view of Leydig's cells was similar as far as all animals are concerned.

Acid phosphatases

Male testicles of control animals revealed a positive reaction to an enzyme under examination first of all in Leydig's cells. Faint activity was observed in spermatogoniums and Sertoli's cells. Slightly increased reaction in Sertoli's cells was in the first and the second experimental groups (Fig. 7); but in the third experimental group — in Leydig's cells (Fig. 8). Testicles of rats from the fourth and the fifth experimental groups reacted to a test in a similar manner as the testicles of animals from the control group.

Alkaline phosphatases

Activity of enzyme in gonads of control animals was located in a basic membrane of spermatogenic ducts, in blood vessels, and in cellular membranes of respective generations of cells. A view similar to a control one was also observed in the first and the third experimental groups (Fig. 9), but in gonads of experimental groups: II, IV, V the activity of alkaline phosphatase in blood vessels and in spermatogoniums increased (Fig. 10).

Nucleic acids

Positive reaction to nucleic acids as far as the animals of the control group are concerned was located in spermatogoniums, much weaker — in spermatocytes and spermatids. In some spermatogenic ducts one could observe characteristic, pyrominabsorptive grains which corresponded with residual bodies Regaud which were made while transforming spermatids into spermatozoons. In testicles of experimental rats of groups: I, II residual bodies were seen in ducts which contained few abortive cells (Fig. 11). A view which was similar to a control one was observed in spermatogenic ducts of experimental groups: II and IV. But one could find only faint and homogeneous reaction which betokened distempers in the spermatogenesis process and abortive cells in some ducts as far as animals of the fifth experimental group were concerned.

Polysaccharides

As far as control rats were concerned — PAS-positive substance stained in a basic membrane of spermatogenic ducts, in Leydig's cells, walls of blood vessels and in acrosomes. A view similar to a control one was observed in experimental groups IV and V. In groups, I, II and III activi-

ty of polysaccharides increased a little. In groups I and II one could observe the enlargement of reaction in Sertoli's cells (Fig. 12), and in group III — in Leydig's cells.

DISCUSSION

Many years' studies have proved that combined usage of TMP and SMZ intensifies antibacterial effect of each of these compounds (2, 6). Biseptol 480 is often adhibited with protracted infection of urinary tracts but with patients with insufficiency of kidneys it can worsen their activity (1—4). It is excreted almos entirely with urine and even with heavy insufficiency of kidneys its rigidity n urine is high. It was also recorded the excretion of the medicine to a bile 24 hours after administering reaches value nearing rigidity of the medicine in plasma (2).

Thus it seems that administration of Biseptol 480 to animals after hepatectomy or nephrectomy has an effect on internal organs that is also on gonads of experimental rats. Histological staining revealed, however, that male testicles reacted to removal of the liver lobe much more than to administration of the medicine.

The similar changes were in spermatogenic ducts (disturbances of spermatogenesis and spermiogenesis, abortive cells) of groups I and II. Removal of a kidney and administration of the medicine did not reveal any visible changes in gonads of experimental rats of groups III and IV. Histochemical tests revealed also inconsiderable effect of Biseptol 480 on a gonad. After removal of a liver lobe, in male testicles of the animals which received the medicine as well as the animals which did not receive it only activity of acid phosphatases and polysaccharides in Sertoli's cells was greater; however, reaction to alkcalic phosphatases was greater in gonads of the animals which were operated but were not administrated Biseptol 480.

Greater reaction to acid phosphatases and polysaccharides was observed first of all in an interstitial gland of group III (animals which were given the medicine and had a kidney removed).

In literature dealing with effect of chemical compounds on morphology of male gonads, authors also noticed increment of activity of acid phosphatases in Sertoli's and Leydig's cells that may prove intensification of lytic processes. Increment of reaction of polysaccharides can betoken accelerated transmutation of carbohydrates, to (7—9). Brachet's test dealing with nucleic acids proved the view obtained after staining with hematoxylin and eosin.

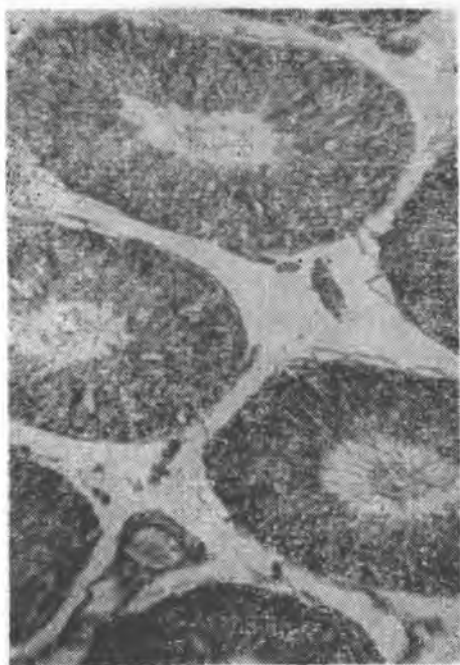


Fig. 1

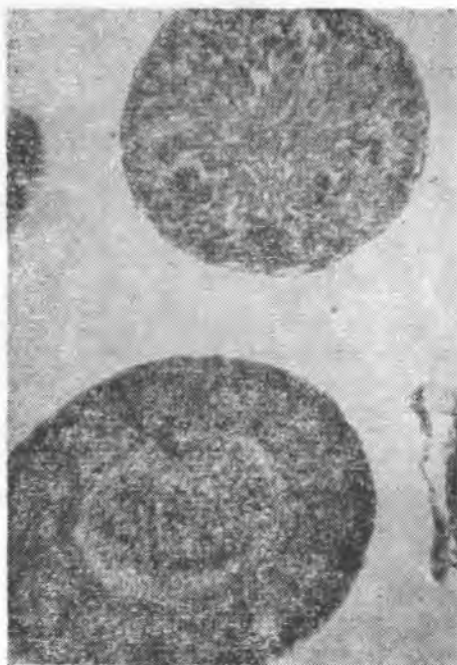


Fig. 2

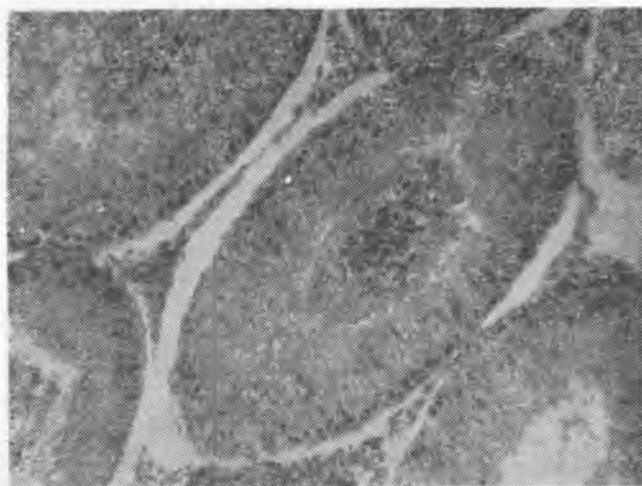


Fig. 3

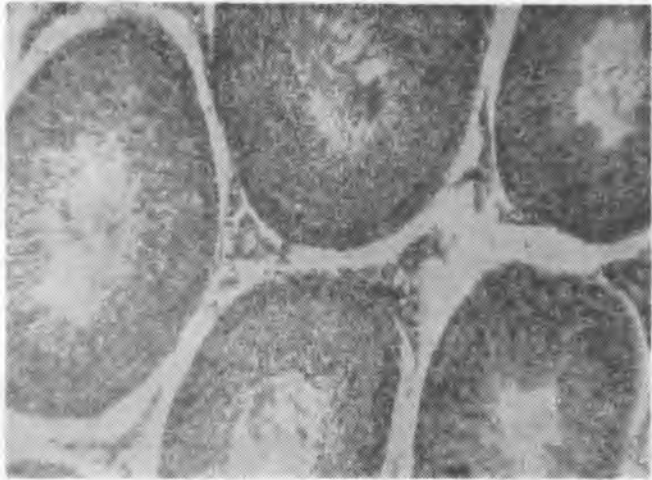


Fig. 4

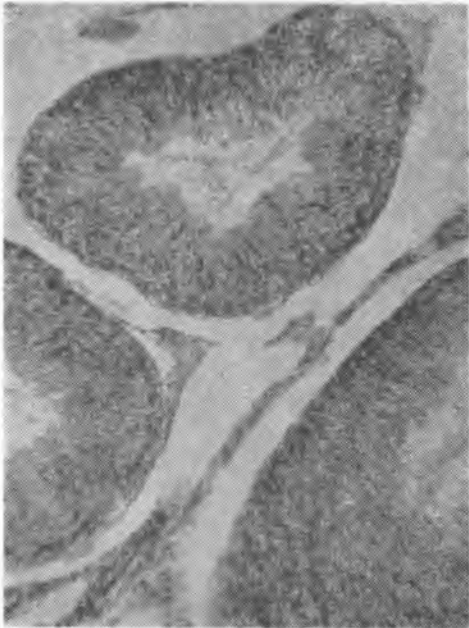


Fig. 5

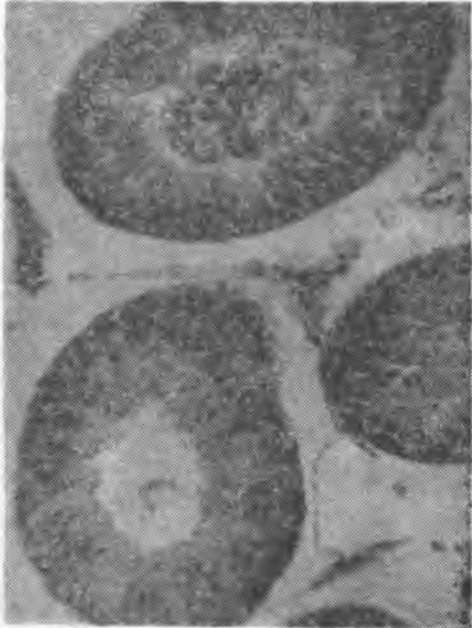


Fig. 6

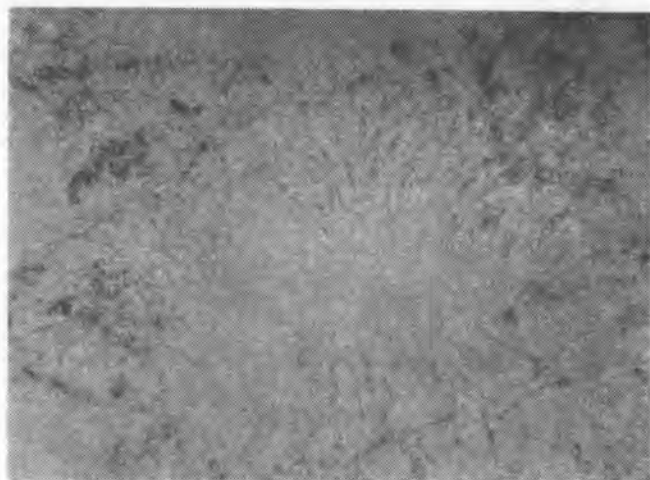


Fig. 7

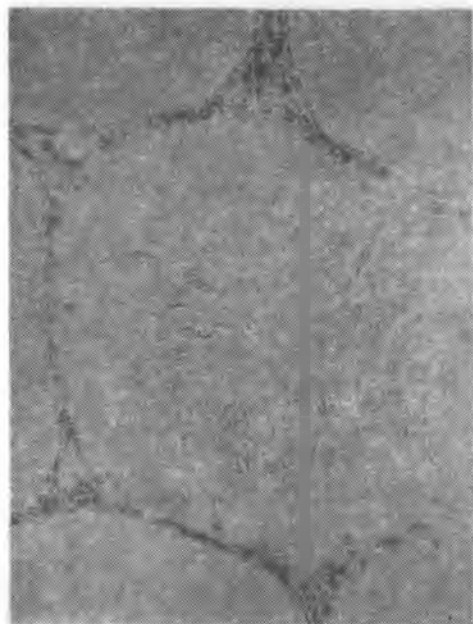


Fig. 8

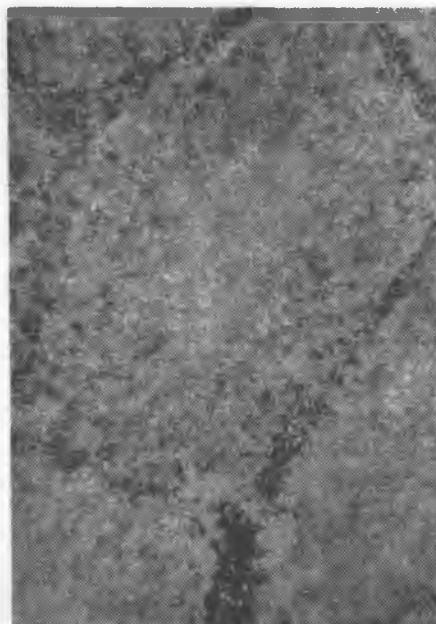


Fig. 9

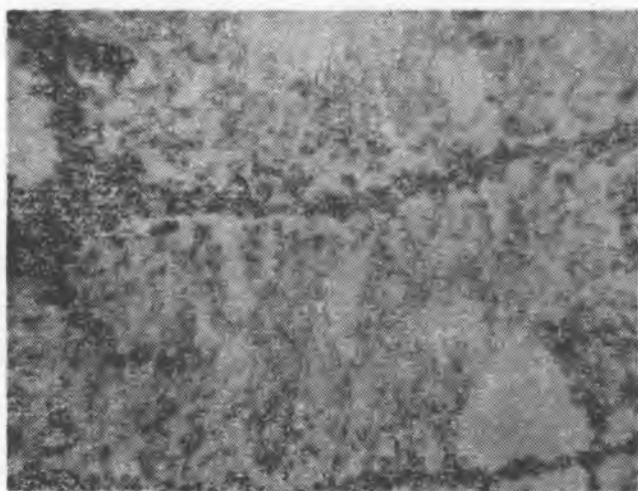


Fig. 10

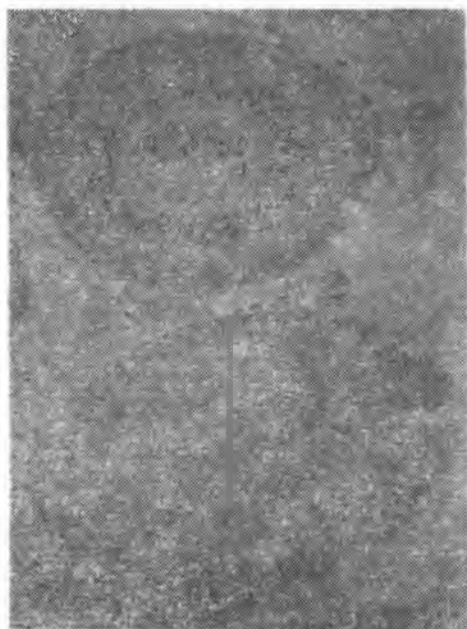


Fig. 11



Fig. 12

On the grounds of the results of this work one could think that Biseptol 480 while administered in curative aims to individuals with insufficiency of a liver or an excretory system did not cause any important morphochemical symptoms in a male gonad of a white rat.

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EXPLANATION TO FIGURES

Fig. 1. The rat's testicle of the control group. Hematoxylin and eosin. Magn. 200 X.

Fig. 2. The rat's testicle of the I experimental group. Hematoxylin and eosin. Magn. 200 X.

Fig. 3. The rat's testicle of the II experimental group. Hematoxylin and eosin. Magn. 200 X.

Fig. 4. The rat's testicle of the III experimental group. Hematoxylin and eosin. Magn. 200 X.

Fig. 5. The rat's testicle of the IV experimental group. Hematoxylin and eosin. Magn. 200 X.

Fig. 6. The rat's testicle of the V experimental group. Hematoxylin and eosin. Magn. 200 X.

Fig. 7. The rat's testicle of the I experimental group. Acid phosphatase by Gomori method. Magn. 200 X.

Fig. 8. The rat's testicle of the III experimental group. Acid phosphatase by Gomori method. Magn. 200 X.

Fig. 9. The rat's testicle of the III experimental group. Alkaline phosphatase by Gomori method. Magn. 200 X.

Fig. 10. The rat's testicle of the II experimental group. Alkaline phosphatase by Gomori method. Magn. 200 X.

Fig. 11. The rat's testicle of the I experimental group. Brachet's method. Magn. 200 X.

Fig. 12. The rat's testicle of the II experimental group. PAS method by McManus. Magn. 200 X.

STRESZCZENIE

Jądra męskie badano histologicznie (barwienie hematoksyliną i eozyną) oraz histochemicznie (wykrywanie fosfatazy kwaśnej i fosfatazy zasadowej według metody Gomoriego, kwasów nukleinowych według metody Bracheta oraz wielocukrów metodą PAS według McManusa). Wykazano, że Biseptol 480 nie powodował istotnych zmian morfologicznych w gonadach szczura. Reagowały one bardziej na usunięcie płata wątroby bądź usunięcie nerki.

РЕЗЮМЕ

Мужскую семенную железу исследовано гистологически (окрашено гематоксилином и эозином) и гистохимически (выявление кислой и щелочной фосфатазы методом Gomori, нуклеиновой кислоты методом Brachet и полисахаридов методом PAS по McManus). Показано, что Бисептол 480 не вызывал существенных морфологических изменений в гонадах крысы. Они более реагировали на удаление доли печени или почки.