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*Histological changes in the pancreas of white rats
after administering cephalixin and ethanol*

Most studies that aim at demonstrating the influence of cephalosporins on the living organism concern the kidneys as they play a crucial role in the process of eliminating the antibiotics from the body (4, 22).

Despite its relatively low toxicity, cephalixin may become more toxic after interacting with alcohol. In view of the fact that the pancreas produces most of the digestive enzymes it seemed necessary to investigate whether ethanol, cephalixin, and ethanol and cephalixin administered together would cause changes in the tissues of the exocrine part of the gland.

MATERIAL AND METHODS

The research was conducted on male Wistar rats weighing approximately 200 g. The animals were divided into 3 experimental groups and 1 control group, each consisting of 5 rats. The animals in the control group were fed standard granulated feed and had unlimited access to drinking water. Experimental group I were given standard feed and 20% ethyl alcohol instead of water. The animals in experimental group II were administered 42 mg of cephalixin (Lilly, Florence, Italy) which corresponds to 10 times the minimum daily therapeutic dose for humans. The drug was given for 10 days, in the mornings, in the form of suspension in physiological saline. Experimental group III were given cephalixin in an identical way to that of group II; additionally, instead of water the animals received 20% alcohol.

On average, each animal in group I had about 20 ml of ethanol/day, while in group III about 15 ml. After the experiment the animals were guillotined.

Biopsy specimens were preserved in neutral 10% formalin, dehydrated in alcohols, soaked in xylen and immersed in paraffin.

Hematoxylin and eosin stain, as well as PAS reaction aimed at discovering neutral mucopolysaccharides were carried out on paraffin sections $7\ \mu$ thick. The sections were photographed by microscope with a Carl Zeiss Jena photographic camera.

RESULTS AND DISCUSSION

In the pancreas of group I of animals there was discovered a decrease or lack of affinity of the base part of the cells to hematoxylin. The whole cytoplasm was of acidophilous character and could be stained with eosin. Inside some lobules, between the serous follicles there were found clusters of adipose cells (Fig. 1), while in some pancreatic islets clusters of spindle-shaped cells resembling fibroblasts were discovered (Fig. 2). However, neutral mucopolysaccharides reaction in vascular walls and basement membranes in the epithelium of the pancreatic ducts was not different from that of the control group. Only in the basement membranes of serous follicles was it slightly weaker.

All the observed changes result from the decrease in the dynamics of cellular secretion and are identical to those recorded by other authors, who point out that ethyl alco-

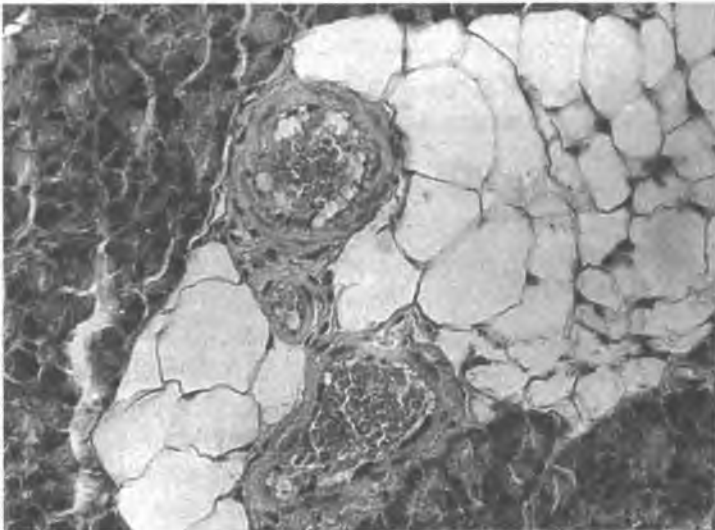


Fig. 1 The pancreas of a rat from experimental group I. In the exocrine part large clusters of adipose cells are visible. Stained with hematoxylin and eosin. Magn. ca 400x

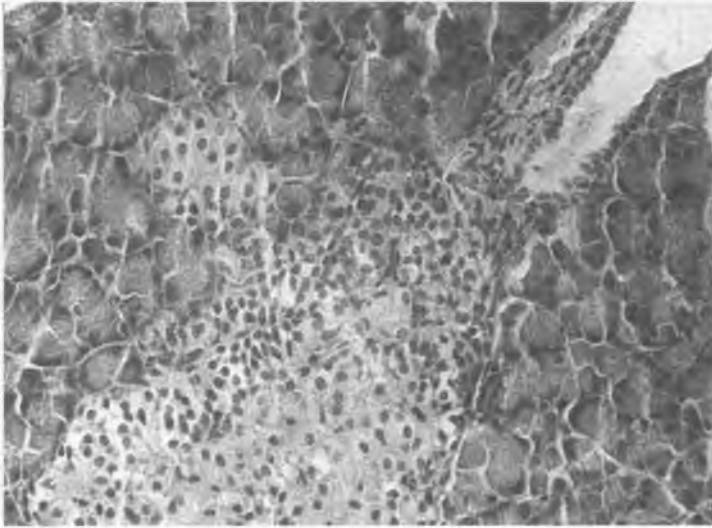


Fig. 2. The pancreas of a rat from experimental group I. Around a pancreatic islet clusters of fibroblasts are visible. Stained with hematoxylin and eosin. Magn. ca 400x

hol inhibits RNA synthesis and depresses the processes of protein synthesis (7, 8). The decrease in the number of ribosomes could be connected with the appearance of the smooth reticulum involved in detoxication processes (9, 10, 11).

After administering cephalixin there was observed an increase in the basophilia of the base parts of the exocrine cells, which could point to an increase in the number of ribosomes. At the same time, compared with the control group, the apical parts of the cells showed considerably less affinity to eosin staining prozymogen granules (Fig. 3).

It can be concluded, then, that a 10-day administration of cephalixin stimulates the proliferation of membranes in the rough reticulum. The increase in the number of ribosomes as well as the enlargement of nuclei and nucleoli in the exocrine cells of the pancreas was observed in rats after a partial hepatectomy and administration of Biseptol 480 (13). This fact would point to an increased activity of cells and the stimulation of the gland to intense excretion caused by the administration of the drug. Also Tune et al. (12) have observed a slight stimulation of mitochondrial respiration in the epithelium cells of the main part of nephrons caused by cephalosporins. This considerably weaker reaction to neutral mucopolysaccharides in some basal membranes of the follicles after administering cephalixin may be connected with biochemical changes in these membranes.

The changes caused by cephalixin are typical functional changes and do not point to any damage of cells. Other authors have not found any morphological changes in the pancreas of rats after administering Bencylina-1. Only after very large doses of the drug (in subacute poisoning) have they observed a slight decrease in the activity of succinate

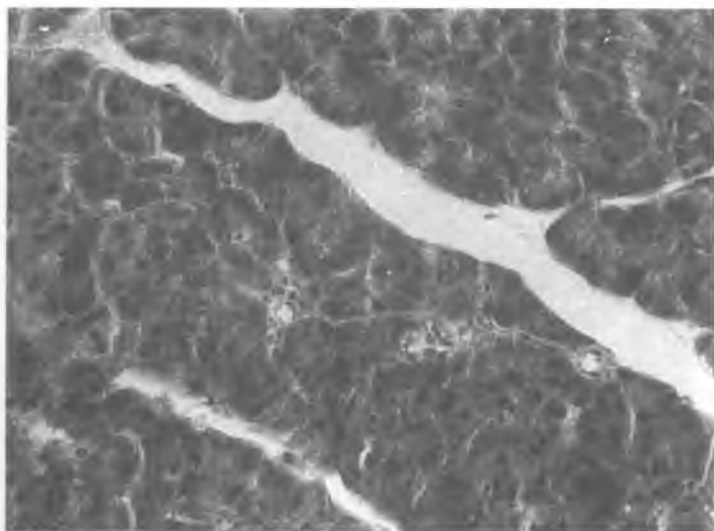


Fig. 3. The pancreas of a rat from experimental group II. The exocrine cells show a strong affinity to hematoxylin. Stained with hematoxylin and eosin. Magn. ca 400x.

dehydrogenase and an increase in the activity of lipase (6). Also Donaubaue r et al. (4), who used cefpirome in 100 mg/kg of body weight/day in the dose administered for 90 days did not observe any changes in the epithelium of nephrons. Only after administering very large doses of the drug – 400 and 1,600 mg/kg of body weight/day did they notice an increase in the number and size of lysosomes and pigment deposits in the thyroid gland.

The exocrine cells of the pancreas seem to be highly resistant to metabolites, which have to be administered in very large doses to have any toxic influence.

After simultaneous administration of cephalexin and ethanol there has been observed a strong affinity of follicular cells to eosin and a very weak affinity to hematoxylin. These changes are similar to those observed after administering only ethanol, however, they are stronger and point to a decrease in the secretory activity of cells as well as the presence of processes connected with ethanol metabolism. At the same time, a strong hyperaemia of the organ has been observed. Bario et al. (1) have observed that a 2-month administration of 15% ethanol drunk *ad libitum* lowers both the absorption of cephalexin and cephadroxil from the intestine and elimination of cephalexin in urine. It is thought that for various antibiotics ethanol modifies their transportation through the membranes to various degrees (3, 5).

The decrease in the secretory activity of cells in group III was accompanied by distinct morphological changes. Apart from typical follicles there were found clusters or cords of small basophilous cells that formed irregular lobules (Fig. 4) which most probably resulted from the trophic changes caused by the organ's attempt at adapting to the metabolic stress.

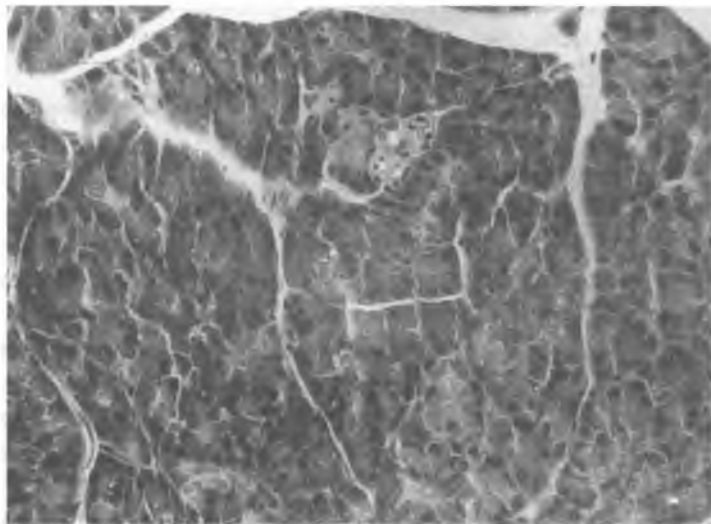


Fig. 4. The pancreas of a rat from experimental group III. Small irregular lobules with basophilous cells are visible. Stained with hematoxylin and eosin. Magn. ca 400x

The obtained data suggest that cephalexin alone administered for a short time (10 days) had no toxic influence on exocrine cells of the pancreas and only causes functional changes in the organ. However, simultaneous administration of cephalexin and ethanol for 10 days increases the toxicity of both of these substances and leads to degenerative changes connected with the activation of the connective tissue making up the stroma of the gland.

CONCLUSIONS

1. A 10-day administration of 20% ethyl alcohol *ad libitum* leads to a decrease in the secretory activity in the exocrine cells of the pancreas of rats.
2. A 10-day administration of cephalexin in the dose of 42 mg daily has no toxic influence on the exocrine cells of the pancreas of rats.
3. A simultaneous administration of cephalexin and ethyl alcohol in the above mentioned doses causes degenerative changes in the exocrine cells of the pancreas of rats; at this stage the changes are reversible.

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SUMMARY

The research was conducted on male Wistar rats weighing approximately 200 g. Animals of experimental group I were administered 20% ethyl alcohol for drinking, animals of experimental group II – cephalixin in the dose of 42 mg daily, animals of experimental group III – simultaneously alcohol and cephalixin in the mentioned doses.

After 10 days the animals were guillotined and pancreas was taken for research. On paraffin sections 7 μ thick there were carried out H + E stain and PAS reaction aimed at discovering neutral mucopolysaccharides.

After administering alcohol there was stated a decrease in the activity of exocrine cells and after administering of cephalixin – an increase in this activity. A simultaneous administration of ethyl alcohol and antibiotic causes trophic changes, which can be noticed as introductory, but at this stage – reversible, degenerative changes.

Histologiczne zmiany trzustki szczurów białych po doświadczalnym
podawaniu cefaleksyny i etanolu

Badania wykonano na szczurach – samcach rasy Wistar o masie ciała około 200 g. Zwierzęta I grupy doświadczalnej otrzymywały 20% alkohol etylowy do picia *ad libitum*, zwierzęta II grupy doświadczalnej – cefaleksynę w dawce 42 mg dziennie, zwierzęta III grupy doświadczalnej – alkohol i cefaloksynę łącznie w wymienionych dawkach.

Po 10 dniach zwierzęta usypiano eterem i pobierano trzustkę do badań. Na skrawkach o grubości 7 μ wykonano barwienie H + E i reakcję PAS na obecność mukopolisacharydów obojętnych.

Po podawaniu alkoholu stwierdzono zmniejszenie aktywności wydzielniczej komórek egzokrynowych, a po podawaniu cefaleksyny – zwiększenie tej aktywności. Natomiast łączne podawanie alkoholu i antybiotyku powodowało zmiany troficzne, które można uważać za wstępne, ale jeszcze na tym etapie odwracalne, zmiany degeneracyjne.