

MORPHOLOGICAL AND HISTOCHEMICAL CHANGES IN THE DUODENUM AND PANCREAS OF RABBITS AFTER ADMINISTRATION OF HETEROLOGOUS DUODENAL CONTENTS

A. I. Tyukov and E. R. Cherkezova-Kinova

The response and the degree of the morphological changes in the duodenum and pancreas of rabbits following administration of heterologous duodenal contents were studied in 40 animals. Pieces of duodenum and pancreas of the control and experimental rabbits were studied by histological and histochemical methods. Introduction of "pathological" duodenal contents taken from dogs with proven pancreatic necrosis into the duodenum of rabbits was shown to be a reliable experimental model of duodenitis and acute serous pancreatitis.

Previous investigations [7, 8] have shown that the duodenal contents obtained from dogs with experimental pancreatic necrosis and introduced into the duodenum of healthy dogs give rise to a definite pathological action. When similar investigations were carried out on rabbits, it was found that introduction of the duodenal contents of dogs into their duodenum induces a clinical picture of acute pancreatitis, confirmed by biochemical tests.

The object of the present investigation was to study the response and to determine the degree of the morphological changes in the duodenum and pancreas of rabbits after administration of heterologous duodenal contents.

EXPERIMENTAL METHOD

A permanent duodenal fistula was produced in 40 rabbits. Daily for 4 days a single injection of 4-5 ml of "normal" or "pathological" duodenal juice was given into the fistula of these animals. The "normal" duodenal juice was obtained from dogs with a chronic duodenal fistula. Pancreatic necrosis was then produced in these dogs by injecting bile (0.5 ml/kg body weight) under pressure into the pancreatic duct, after which "pathological" duodenal contents were obtained. The material for morphological investigation was divided into two main groups: animals receiving "normal" duodenal secretion and animals receiving the "pathological" duodenal contents. Material obtained from intact rabbits, from rabbits with a fistula, and from rabbits receiving physiological saline through the fistula was used as the control. The animals were killed by air embolism. Six rabbits died after 2 to 4 injections of 4-5 ml of the "pathological" duodenal contents from dogs.

Pieces of duodenum and pancreas were fixed in 10% formalin and 70° ethanol and embedded in paraffin wax; sections 5-6 μ in thickness were investigated by the following histological and histochemical methods: staining with hematoxylin and eosin, with Heidenhain's hematoxylin, by Mallory's method, with Heidenhain's azocarmine, with fuchselin and counterstaining by Van Gieson's method, silver impregnation by the methods

Central Laboratory of Morbid Anatomy, Institute of Human Morphology, Academy of Medical Sciences of the USSR, Moscow. Laboratory of Physiology and Pathology of Digestion, Institute of Normal and Pathological Physiology, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR A. M. Chernukh.) Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 75, No. 6, pp. 115-118, June, 1973. Original article submitted November 14, 1972.

© 1971 Consultants Bureau, a division of Plenum Publishing Corporation, 227 West 17th Street, New York, N. Y. 10011. All rights reserved. This article cannot be reproduced for any purpose whatsoever without permission of the publisher. A copy of this article is available from the publisher for \$15.00.

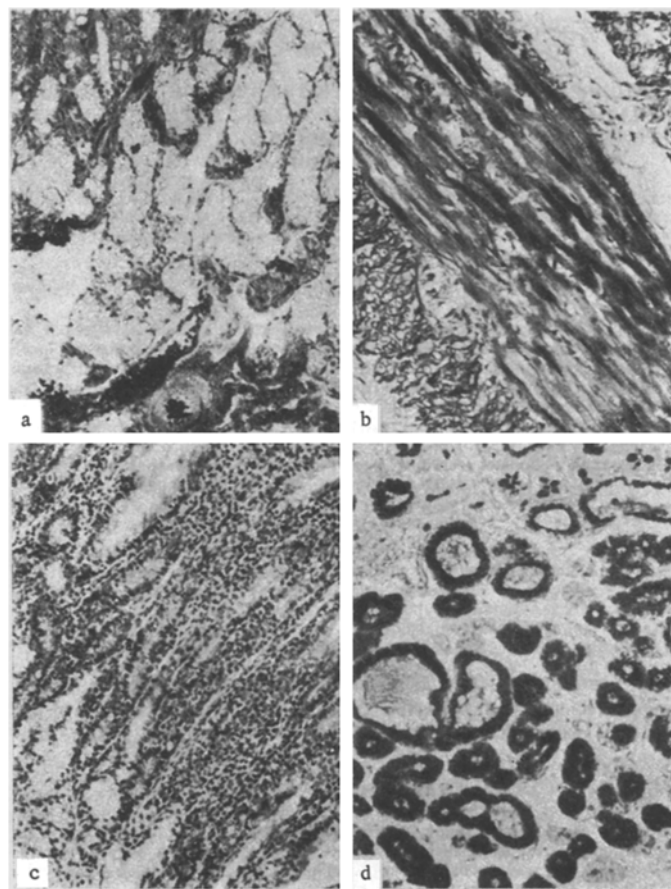


Fig. 1. Morphological changes in the duodenum of rabbits after introduction of pathological duodenal contents from dogs: a) vessels of all layers of the duodenal wall are dilated and congested (staining by Mallory's method, 125 \times); b) marked edema of duodenal wall and, in particular, of submucosa and muscular coat (hematoxylin-eosin, 250 \times); c) marked infiltration of mucous membrane with lymphocytes, plasma cells, and leukocytes (hematoxylin-eosin, 125 \times); d) hyperplasia and focal response of Brunner's glands (combined reaction for mucopolysaccharides with alcian blue + PAS reaction, 250 \times).

of Gomori and Foot, the reactions of Brachet and Feulgen for nucleoproteins, and a combined reaction for mucopolysaccharides (alcian blue + the PAS reaction).

EXPERIMENTAL RESULTS

After administration of "normal" duodenal contents obtained from healthy dogs the changes in the duodenum and pancreas correspond to the response to ordinary stimuli and consisted of congestion of the vessels and a slight increase in the level of digestive lympho-leukocytic infiltration [4, 5].

Macroscopic examination of the animals receiving "pathological" duodenal contents revealed swelling and dilatation of the loops of small intestine accompanied by edema, with marked dilatation and congestion of the blood vessels of the mesentery and intestinal wall. In three rabbits which died, loose deposits of fibrin were found on the serous membrane in the region of the duodenum. The small intestine was grossly dilated, its wall was edematous and congested, the serous membrane was dull, and solitary petechial hemorrhages were visible on it. Up to 100 ml of a purulent fibrinous effusion was found in the peritoneal cavity.

On microscopic examination of the duodenum and pancreas of the animals of this group the vessels in all layers of the duodenum were severely dilated and congested (Fig. 1a), the capillaries of the villi were

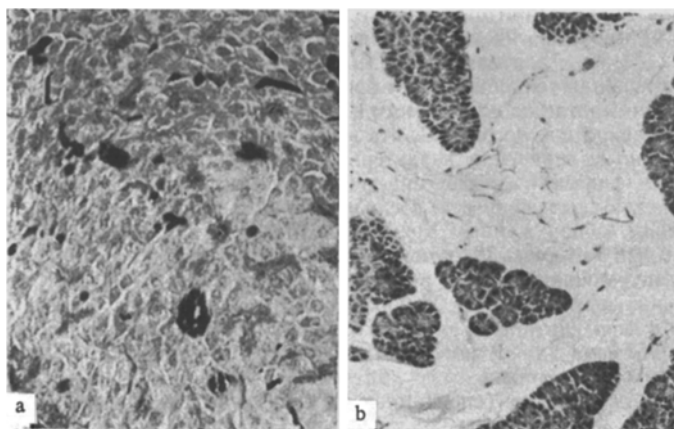


Fig. 2. Morphological changes in the pancreas of rabbits after administration of "pathological" duodenal contents from dogs: a) dilatation and congestion of vessels with perivascular hemorrhages (staining by Mallory's method, 125 \times); b) edema of pancreatic stroma with separation of fibers in connective-tissue bands (hematoxylin-eosin, 75 \times).

dilated, their lumen was irregular, and foci of erythrostatics were visible. In the submucous layer, the fibers of which were separated by the marked edema, perivascular petechial hemorrhages were seen. The duodenal wall was thickened by edema (Fig. 1b). The intestinal villi were most affected by edema, their appearance was polymorphic, and some parts were thickened and shortened. The muscular layer also was edematous. The lymphatics were dilated. Well marked infiltration of the mucous membrane with lymphocytes, plasma cells, and leukocytes was present in these animals both in the region of the villi and also in the crypts (Fig. 1c), where in places the cells formed foci of infiltration resembling "pseudofollicles" with the addition of a few eosinophils. There was also a marked increase in the number of goblet cells. Brunner's glands showed a focal reaction of hyperplasia (Fig. 1d). Examination of material from the rabbits which died revealed, besides the changes described above, a picture of focal necrotic duodenitis and of suppurative-fibrinous periduodenitis with deposits of fibrin on the serous membrane of the duodenum infiltrated with leukocytes.

Marked congestion of the dilated vessels and perivascular petechial hemorrhages (Fig. 2a), edema of the stroma of the gland, and separation of the fibers in the connective-tissue bands (Fig. 2b) were found in the pancreatic tissue of all the animals of this group. Tiny foci of lymphoid infiltration were seen in the stroma of the gland, both in its acinar part and in the islets of Langerhans. The capillaries of the islets were dilated and showed evidence of erythrostatics. The islets were a little enlarged. The ducts of the gland were dilated and distended with secretion. This morphological picture is characteristic of the acute serous pancreatitis described earlier by Rössle [9], and the similarity was confirmed by pathophysiological and biochemical tests. The reaction for nucleoproteins in the epithelium of the villi and, in particular, in the cells of the intestinal glands, and also in the cells of the acinar part of the pancreas revealed an increase in the RNA content as well as a general increase in the number of RNA-rich cells and cells giving a positive PAS reaction. The reaction for mucopolysaccharides showed a varied picture in the Brunner's glands, both in the same and in different glands.

The changes thus consisted chiefly of gross dilatation of the vessels, edema of the villi and the submucous layer, and increased cellular infiltration of the duodenal mucous membrane with lymphocytes, plasma cells, leukocytes, and a few eosinophils and macrophages. The morphological picture thus revealed corresponded to the first and second forms of jejunitis [10]. Prolonged exposure to the "pathological" juice led to the appearance of intensive leukocytic infiltration, marked hyperemia and lymphostasis, and tiny erosions on the surface of the villi, while some of the dying rabbits developed necrotic duodenitis and suppurative-fibrinous periduodenitis.

The changes described above are characteristic of the pathological picture of nonspecific atrophic degeneration in the intestine with a severe inflammatory response, corresponding to the changes found after

denervation of the small intestine [6], as a result of the action of aminopterin [3], and in other pathological states [1, 2].

The pancreas responds secondarily with focal degeneration and with functional disturbances, while the morphological changes are less marked than in the duodenum, although the structural changes in the gland are characteristic of acute pancreatitis, as clinical laboratory tests confirmed.

The results of this combined investigation thus show agreement between the pathophysiological, biochemical, and morbid anatomical findings, and they give evidence from which the morphofunctional state of the duodenum and pancreas can be assessed when they are exposed to a pathological agent, namely, the duodenal contents of dogs with experimental pancreatic necrosis. Introduction of heterologous "pathological" duodenal contents taken from dogs with proven pancreatic necrosis into the duodenum of rabbits provides a reliable experimental model of duodenitis and of acute serous pancreatitis.

LITERATURE CITED

1. L. I. Aruin, Arkh. Pat., No. 9, 3 (1967).
2. L. I. Aruin, Arkh. Pat., No. 10, 63 (1968).
3. N. P. Bochkov, Byull. Éksperim. Biol. i Med., No. 5, 114 (1960).
4. S. S. Vail' and L. B. Sheinina, in: Neurohumoral Regulation in the Activity of the Digestive Apparatus of the Stomach [in Russian], Leningrad (1935), p. 169.
5. Yu. M. Lazovskii, The Functional Morphology of the Stomach under Normal and Pathological Conditions [in Russian], Moscow (1947).
6. V. A. Titkova, Arkh. Pat., No. 8, 42 (1964).
7. E. R. Cherkezova-Kinova, Pat. Fiziol., No. 5, 52 (1962).
8. E. R. Cherkezova-Kinova, Z. inn. Med., No. 23, 1083 (1963).
9. R. Rössle, Beitr. Z. path. Anat., 69, 163 (1921).
10. C. E. Rubin, L. L. Brandborg, A. L. Flik, et al., Gastroenterology, 43, 621 (1962).