HISTOLOGICAL CHANGES IN THE DUODENAL MUCOSA DURING PANCREATIC ATROPHY

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The writers showed previously [1] that the development of atrophy of the pancreas is accompanied by a decrease in its secretory activity and by cessation of the arrival of pancreatic juice in the duodenum. Secretions of the digestive glands, on entering the duodenum, including pancreatic juice, are known to have a trophic action on its mucosa [2, 3]. It was accordingly decided to carry out a histological study of the duodenal mucosa during the development of pancreatic atrophy.

EXPERIMENTAL METHOD

Chronic experiments were carried out on dogs (three groups of animals). In all the animals the greater pancreatic duct was exteriorized by means of a cannula with a side tube, so that the secretory activity of the pancreas could be measured.

Group 1 consisted of four dogs with a normally functioning pancreas [1], group 2 of five dogs in which a model of gradual development of pancreatic atrophy was created. Atrophy developed as a result of artificially induced obstruction to the outflow of pancreatic juice [1, 4]. Group 3 consisted of three dogs into which boiled pancreatic juice was periodically injected subcutaneously during the development of pancreatic atrophy.

The pancreas was investigated histologically in autopsy material, and the duodenal mucosa on material obtained by aspiration biopsy. Sections 5-7 μ thick were fixed with 10% neutral formalin and embedded in paraffin wax. They were stained with hematoxylin and eosin, with Heidenhain's azan, and with alizarin blue by Hotchkiss' method.

EXPERIMENTAL RESULTS

In the dogs of group 1 (period of observation 8 years) the secretory activity of the pancreas was unchanged. The exocrine and endocrine parenchyma was normal in appearance. The efferent ducts were filled with secretion. The duodenal mucosa was indistinguishable from normal (Fig. 1a).

The development of pancreatic atrophy in the dogs of group 2 (period of observation 13 months) was accompanied by a decrease in the secretory activity of the pancreas. The volume of pancreatic juice fell during the 6 h after feeding from 67.99 ± 4.65 ml during the first months after the operation to 3.54 ± 1.01 ml toward the end of the period of observation. The bicarbonate concentration fell from 89.04 ± 3.2 meq/liter to 0, and its output from 4.05 ± 0.46 meq also to 0. The concentration of proteolytic activity fell from 3.12 ± 0.18 to 0.35 ± 0.1 μeq tyrosine/ml pancreatic juice/min of incubation and its output from 175.71 ± 16.35 to 3.11 ± 1.01 μeq tyrosine, the concentration of amylolytic activity fell from 0.43 ± 0.04 g hydrolyzed starch/ml pancreatic juice/min of incubation to 0, and its output from 21.35 ± 3.6 g hydrolyzed starch to 0.

During the first month after the operation leading to the development of pancreatic atrophy, when the level of secretory activity of the organ was still high, the villi and crypts of the duodenal mucosa were normal in appearance. The goblet cells were filled with secretion, containing acid and neutral mucopolysaccharides. During the subsequent months, with a decline in the secretory activity of the pancreas, inflammatory and atrophic changes began to develop in the duodenal mucosa, leading to gradual thinning of the mucosa, shortening

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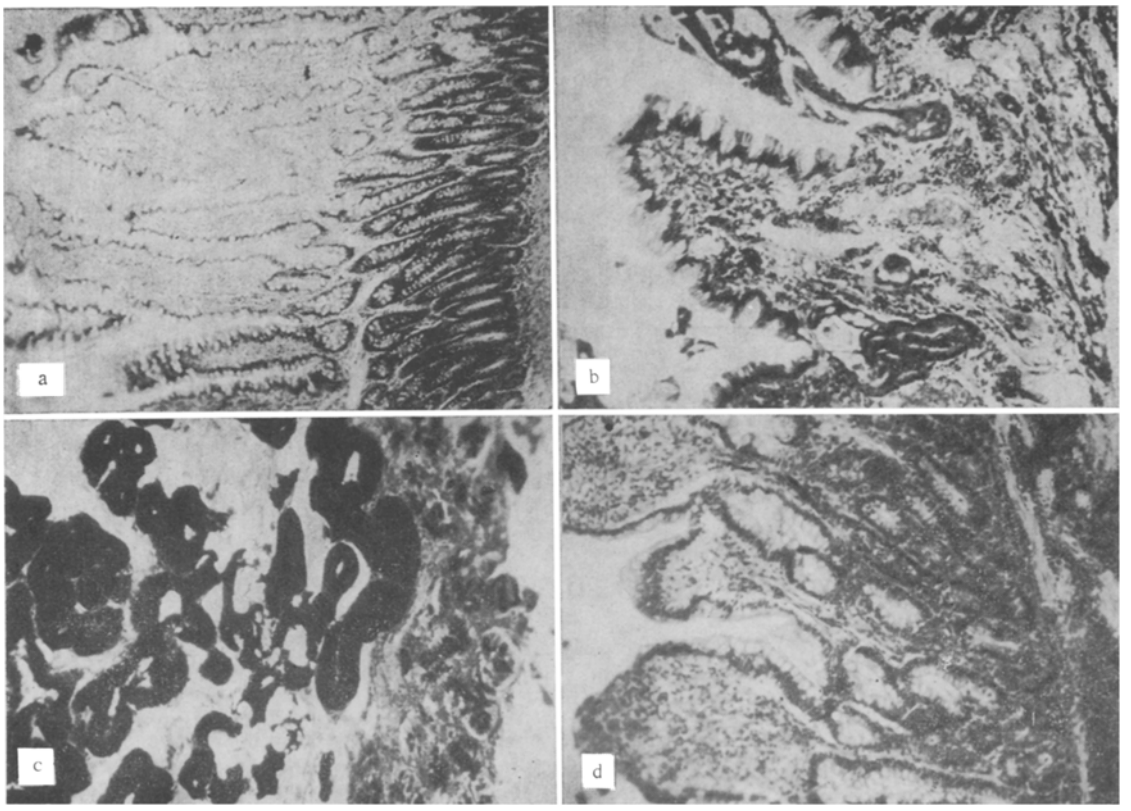

Fig. 1. Duodenal mucosa of dogs. a) Mucosa of dogs of group 1 is normal in appearance; b) in dogs of group 2 it is atrophied; d) in dogs of group 3 it preserves its normal appearance; c) hyperplasia of Brunner's glands in dogs of group 2. Formalin. a, b, d) Stained with hematoxylin and eosin; c) stained by Hotchkiss' method. Magnification: a) 63; b, c, d) 112.5×.

of the villi and, in some places, obliteration of the relief. A sharp decrease was observed in the number of crypts and connective tissue developed in their place (Fig. 1b); the number of goblet cells also was appreciably reduced. It is important to note that in dogs with pancreatic atrophy hyperplasia of Brunner's glands was observed. A high proportion of their terminal segments was found to be located not only in the submucosa, but also in the layer of the mucous membrane proper. In sections stained by Hotchkiss' method, neutral mucopolysaccharides filling their secretory portions appeared bright crimson in color (Fig. 1c). At autopsy marked atrophy of the pancreas was found macroscopically. Histologically, atrophy of the exocrine parenchyma and its replacement by connective and adipose tissues were observed. The efferent ducts were dilated and their epithelial lining disturbed in places.

In the dogs of group 3 (maximal period of observation 4 years), into which boiled pancreatic juice was injected subcutaneously during the development of pancreatic atrophy, the pancreas functioned longer and its atrophy developed more slowly. The duodenal mucosa in two dogs of this group remained unchanged for 2 years and its villi and crypts were normal in appearance. Only dilatation of the lymphatics and lymphoid infiltration were observed. At the beginning of the 3rd year both these dogs died from accidental causes. In the third dog 1.5 years after the operation a decrease in the number of crypts was observed, with their replacement by connective tissue and lymphoid infiltration. The goblet cells were normal in appearance. After 2.5-3 years the histological picture of the mucosa was somewhat restored to normal, but the lymphoid infiltration continued throughout the period of observation (Fig. 1d). Hyperplasia of Brunner's glands in the dogs of this group also was distinct. At autopsy, 4 years after the operation the pancreas was macroscopically close to normal in appearance. Histologically, the exocrine and endocrine parenchyma of the pancreas and the ducts showed no significant changes. The duodenal mucosa had no visible abnormality; hyperplasia of the Brunner's glands was preserved.

The results indicate that the development of atrophy of the pancreas and a decline in its secretory activity are accompanied by atrophic changes in the duodenal mucosa, which resemble the picture of chronic duo-

denitis [5]. Attention is drawn to the presence of hyperplasia of Brunner's glands, which is here described for the first time during the development of pancreatic atrophy. We know that secretion of Brunner's glands is alkaline in character, with a pH between 8.2 and 9.3 [8]. Mucoproteins are the chief component of their secretion. It is considered that the secretion of Brunner's glands protects the duodenal mucosa against ulceration which could arise on the arrival of acid gastric contents, with high peptic activity, in the duodenum [5, 8, 9]. Hyperplasia of Brunner's glands during the development of pancreatic atrophy can evidently be regarded as a compensatory and adaptive reaction aimed at maintaining the pH and mucoprotein concentration in the duodenum. Indirect confirmation of this suggestion, on the one hand, is given by maintenance of the basal concentration of motilin in the blood plasma, despite cessation of the arrival of pancreatic juice in the duodenum [10], for motilin is liberated in dogs only if the reaction in the intestine is alkaline [11]. On the other hand, with a considerable decrease in the number of goblet cells and, consequently, in the volume of their secretion, in the presence of normal acidity and peptic activity of the gastric juice [12] ulcers were never found in the duodenum.

Injection of boiled pancreatic juice delayed the development of pancreatic atrophy and the duodenal mucosa remained near to normal in appearance. We have no information as yet on the nature of the factor contained in boiled pancreatic juice which exerts a trophic action on the pancreas and duodenal mucosa. This is a topic for future research. All that can be asserted is that this factor is not a protein and that its action is evidently not confined to the digestive system [6, 7].

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