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HYPERPRODUCTION AND INTRAVITAL REJECTION OF SURPLUS EPITHELIUM OF INTESTINAL VILLI

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UDC 612.335.2:612.6/-085.23

KEY WORDS: intestinal villi; intestinal epithelium; rejection of surplus epithelium; sources of epithelium in deposits on luminal surface of small intestine.

During the study of intestinal biopsy material from dogs [9, 11] accumulations of epithelial and villous cells were found in the surface layer of mucus and patterns of formation and rejection of surplus structures of the crypt epithelium and of pinching off and rejection of the villi and their distal fragments were described. Several membrane enzymes were discovered in the epithelium covering the rejected villi and in the mucus [1, 3, 4, 7, 12], suggesting that the phenomenon of rejection of structures of the small intestinal mucosa plays a definite role in premembrane contact digestion. The origin of some of the rejected structural elements has not been explained. Gaps in the data on surplus formations on the surface of the villi in dogs also required to be filled.

Since the facts on intravital loss of layers of eptihelium outside the "extrusion zone" are of fundamental importance, it was decided to study the sources of epithelium in deposits on the luminal surface of the small intestine in some other species of animals and in man.

EXPERIMENTAL METHOD

The small intestine was removed in its entirety or segments were taken from different parts of it from anesthetized animals (cats, albino rats and mice, guinea pigs, rabbits) for morphological investigation, cut lengthwise and, together with its contents, fixed with 12% neutral formalin solution. The mucosa was dissected after fixation. Additionally, 25 biopsy specimens of mucosa from various parts of the small intestine unaffected by disease were obtained from patients after resection of the stomach or small intestine (for ulcer or fistula). The biopsy material was obtained and fixed without any mechanical procedures on the surface of the mucosa. The native mucosa was studied under a binocular loupe, using only atraumatic micromanipulations with instruments. Serial microscopic sections were prepared by a special method [10] from the various forms of villi, cut off the mucosa or isolated from the layer of deposits.

Laboratory of Experimental Pathology, N. V. Sklifosovskii Emergency Aid Research Institute, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR A. P. Avtsyn.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 100, No. 11, pp. 620-622, November, 1985. Original article submitted April 20, 1984.

0007-4888/85/0011-1595$09.50

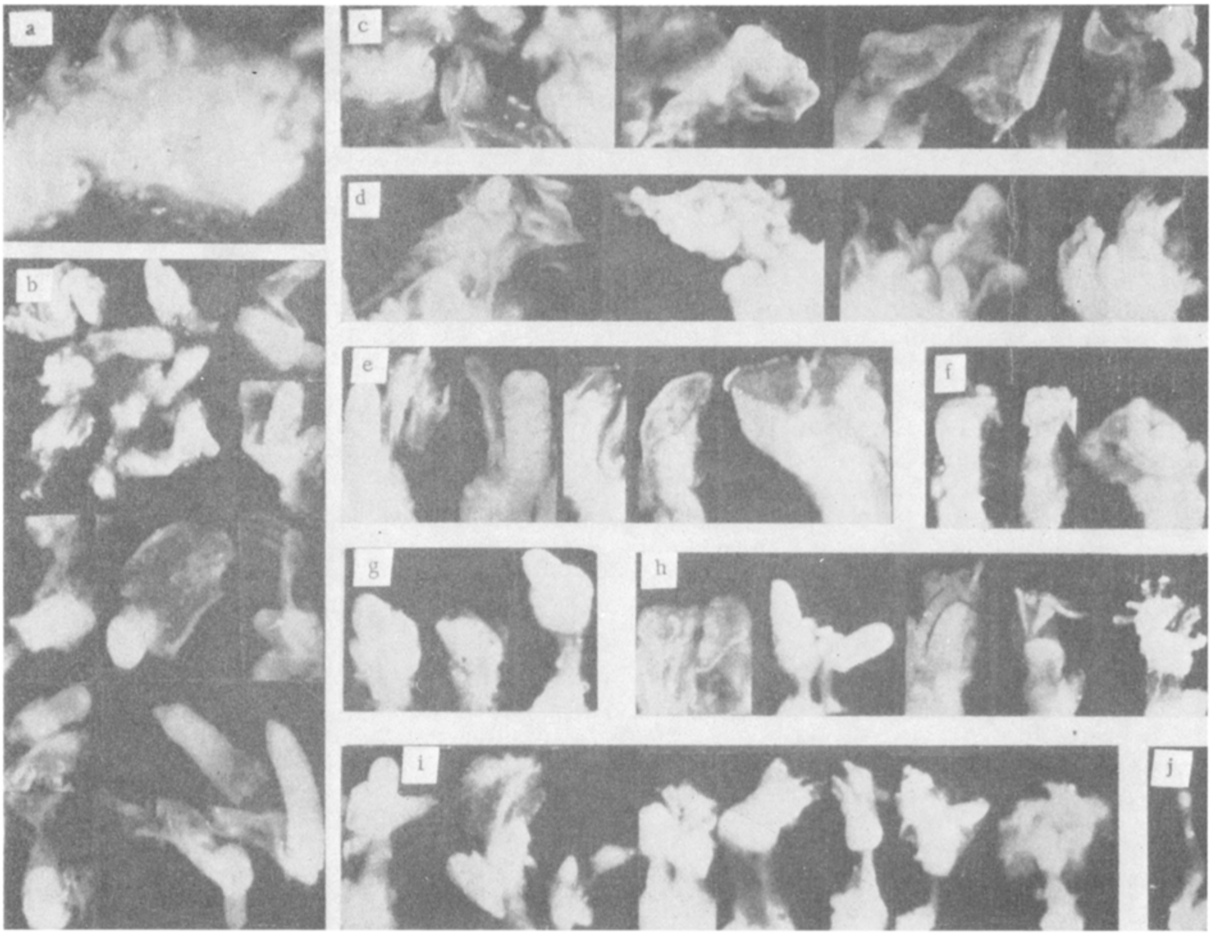

Fig. 1. Microscopic signs of the phenomenon: a) fragment of superficial mucous deposits with rejected structural elements (view from above); b, c) examples of structures rejected into deposit: whole villi and their distal fragments with surplus epithelium (b), accumulations of epithelial layers and structures (c); d) surplus epithelial structures in deposits, retaining their connection with the mucosa; e-i) forms of villi of mucosa with surplus epithelium in the form of layers (e), vertical folds and sheaths (f), encircling folds raised above the residual part of the epithelium (g), narrow tubules (h), and masses branching from the residual part of the epithelium, after loss of various amounts of epithelium (i); j) stromal stump of villus after rejection with surplus epithelium in areas which remained.

EXPERIMENTAL RESULTS

The layer of deposits on the luminal surface of the small intestine was compact, of considerable thickness, and free from structural inclusions only in the rabbit. In the other species of animals and in man, all that remained of it after fixation was a more or less thin film, due to loss of part of the deposits into the lumen of the intestine, or into the formalin, in which some of the mucus dissolved. An irregular and, in some places, macroscopically indistinct viscous film contained nests of rejected villous and epithelial structures and covered them externally (Fig. 1a). In the cat and occasionally in man, among the free-lying villous structures there were forms with a round basal end, typical of villi and their distal fragments after pinching off in dogs. Other forms of free-lying villous elements, which were rarely found in dogs, were observed in large numbers in cats, predominated in man, and characterized the deposits found in rodents (Fig. 1b). Their basal end terminated in a stromal column, and layers of different shapes and sizes usually branched from the residual part of the epithelial cover. Sometimes it was upturned, to form a sheath around the villi, or it was raised in a fold encircling the residual part of the cover. Epithelial structures of the mucous deposits (Fig. 1c) had the appearance of separate layers of different sizes and of indefinite shape, concentrations of interconnected layers, or narrow tu-

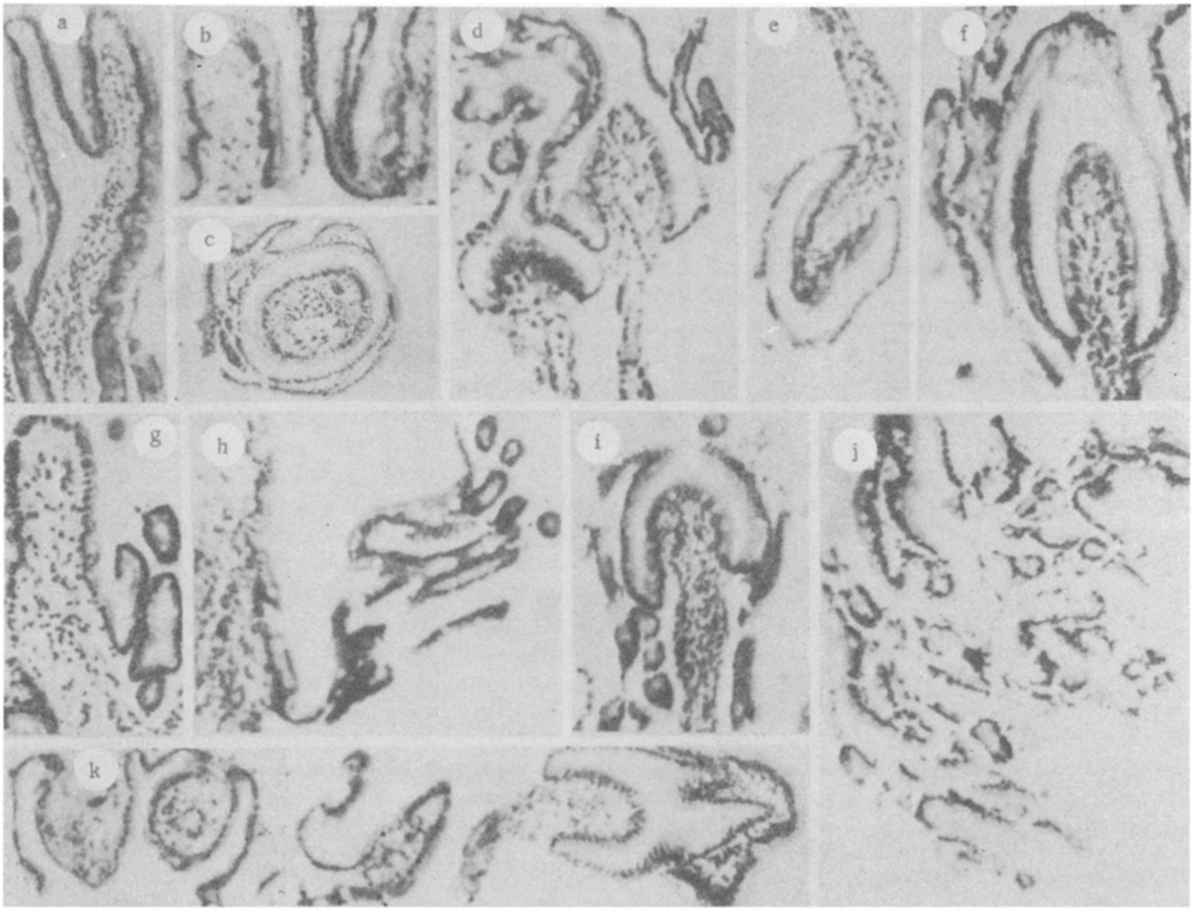

Fig. 2. Microscopic features of the phenomenon: a-i) serial microscopic sections through villi with surplus epithelium in the form of long folds (a), layers (b, d), sheaths (c, e, f), and narrow tubules (g-i); j) specimen of fragment of mucous deposits with sections through rejected epithelial layers and narrow tubules; k) serial sections through rejected villous structures with surplus epithelium. Hematoxylin and eosin. 70×.

bules, single or forming a group, and frequently arising from large layers. Villous structures were arranged chaotically in the thickness of the deposits and beneath them. However, whereas villi with a round basal end were easily removed from the epithelial accumulations, it was impossible to separate the remaining villous structures without injury. Many of the epithelial structures of the deposits also were connected with the epithelial cover of villi of various shapes (digitate, short, or wide) of the mucosa (Fig. 1d). Forms of native intestinal villi illustrated in Fig. 1e-i, are characterized by epithelial branches, varied in structure, degree of development, and localization, and also by partial absence of the epithelial cover. Villi without epithelium in the basal part or over a wider area differed from the corresponding rejected forms only in connection between the stromal column and the underlying tissue. Among them also were seen stumps of villi of altered shape, just as elsewhere in the mucosa, accreted villous formations, branched, villi, and crest-like structures with or without branches were often observed. Usually villi with changes in the epithelial cover were arranged in groups, unlike villi with signs of pinching off, which were observed as single phenomena in the cat and were found in only three cases in man. The surface area of such a site varied from 0.4 to 6 mm^2. There were from four to 15 such sites in one biopsy specimen, accounting for 1/7-1/2 of its total surface area.

Surplus structures branching from the normal epithelium of the villi, in serial sections through villi of different shapes with the macroscopic features mentioned above (Fig. 2a-i), were formed by simple flattened epithelium with small round nuclei, often bulging on the side of the base of the epitheliocytes, which were separated from the basement membrane. Such a layer of epithelium surround a villus with normal epithelial cover like a sheath, making contact with its apex but without a detectable junction. The surface of the villi in areas denuded of epithelium was outlined by the basement membrane. Signs of an inflammatory reaction in the stroma were absent. Sections through surplus epithelial layers and tubules in microscopic specimens of fragments of deposits (Fig. 2j) and of rejected villous structures (Fig. 2k) were absolutely identical with those of different kinds of villi (Fig. 2a-i).

Evidence of the formation of surplus epithelium on the surface of the villi was thus observed in healthy animals of various species and in human patients. By the character (simple, flattened epithelium with small round nuclei) and by the structures formed by it (layers, projecting folds, narrow tubules) it was indistinguishable from surplus crypt epithelium and from the surplus epithelium occasionally found on villi in dogs [9]. In all cases the villous epithelium, like that of the crypts, assumed the character described above after separation from the basement membrane, i.e., from the time lost its connection with the physiological connective-tissue substrate. While it remained in the mucus covering the intestinal epithelium, the separated area remained as a single layer of cells, which evidently was converted into surplus branching due to epitheliocytes reaching it from the crypt. The definite structural pattern of the branches can be explained by the property of intestinal epithelium of growing in unphysiological substrates and media (including mucus) as single-layered bands, outgrowths, and tubules [5, 6, 8, 13], whereas contact between the folds and layers at the apex of the sheaths around the villi and the formation of masses of anastomosing layers were probably due to its ability to form cell junctions between layers growing toward each other [2]. The fact that the signs of a surplus of epithelium differed in degree in different forms of villi in the biopsy material is proof of a trend of development of the branching formations into long folds, layers, and narrow tubules, into larger accumulations, and into complex structures of incomplete and closed sheaths. The evident injury to the basal end of the rejected villi, their close connection with accumulations of rejected epithelium, and the character of their arrangement in the mucus are evidence that rejection of surplus epithelium may be accompanied not only by partial or total loss of the epithelial cover of the villi, but also by detachment of the remnants, and their migration with the mass of epithelium into the layer of mucous deposits, and, moreover, regardless of whether the biopsy left the surface of the mucosa of the area of intestine from which it was removed intact. Information on the resistance of the basement membrane of the villi in the absence of epithelium [14], not only in the mucosa but also in the enteral medium [11], confirm that the structure of the villi may be preserved while partly or completely denuded of their epithelium. As regards their character and localization, signs of intravital formation and rejection of surplus epithelial structures of the villi differ significantly from signs of artificial loss of their surface epithelium under unphysiological conditions and after death, when, having become completely separated, it either comes away from the villus in a sheath or, after straightening out of the folds, it hangs from the apex of the villus in a wide, hollow tube or a compact double band.

On the basis of the above description the macroscopic and microscopic features of the patterns can be interpreted as signs of hyperproduction of the villous epithelium, and the phenomenon itself as one process in the physiological activity of the mucosa of the small intestine. The data presented add to information obtained previously by the writer on the various sources of the epithelium on the luminal surface of the small intestine and provide a basis for examination of the problem of the role of each source of structures detached from the mucosa as a supplier of certain enzymes and other substances of endogenous nature for luminal and contact membrane predigestion in mucosal deposits.

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PATHOMORPHOLOGY OF EXPERIMENTAL PANCREATIC NECROSIS AFTER ENDOLYMPHATIC INJECTION OF CONTRYKAL

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UDC 616.37-002.4-092.9-091/-092-07

KEY WORDS: experimental pancreatic necrosis; contrykal; electron microscopy.

Antienzyme treatment of acute pancreatitis (AP) is regarded as pathogenetically one of the soundest ways of combined treatment of this disease. Practical experience of the use of antienzymes in the treatment of AP has shown that their intravenous and intra-arterial administration do not arrest the course of pancreatic necrosis (PN) [6, 11]. Antienzyme treatment has proved to be most effective in the edematous form of AP [2, 5, 9]. However, mortality from destructive pancreatitis still remains high — from 30 to 86% [1, 3, 4].

The lymphatic system is a powerful collector of activated pancreatic enzymes and toxic breakdown products in AP [10]. The use of the lymphatic system, not only for the removal of toxic waste products by external drainage of the thoracic duct (TD), but also for endolymphatic administration of protease inhibitors in order to inactivate enzymes in the lymph, and thereby delay proteolysis in the pancreas, is a promising approach at the present time [7, 9].

The aim of this investigation was to study the trend of the morphological changes in the pancreas in experimental PN, treated by endolymphatic injection of contrykal, with simultaneous monitoring of pancreatic enzyme activity in the blood and lymph.

EXPERIMENTAL METHOD

Experimental PN was produced in mongrel dogs under general anesthesia by injection of infected bile under pressure into the pancreatic duct in a dose of 0.5 ml/kg body weight, with stimulation of pancreatic secretion by secretin (1 clinical unit/kg body weight, from Boots, England). Lymph for enzyme investigation was obtained by external drainage of TD. There were two series of experiments: I) control (five dogs), II) experimental (16 dogs). Every hour for 4 h, 10,000 antitrypsin units of contrykal was injected through a catheter into a lymphatic vessel of the hind limb of animals of the experimental series 2 h after production of experimental PN. The animals were withdrawn from the experiment by the usual method 9-10 h after its beginning. Pancreatic enzymes in the blood serum and lymph from TD were studied every hour (2 h after production of AP) in dogs of both series. Amylase activ-

Laboratory of Pathomorphology with Electron Microscopy Group, N. V. Sklifosovskii Moscow Emergency Aid Research Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR D. S. Sarkisov.) Translated from Bylleten' Éksperimental'noi Biologii i Meditsiny, Vol. 100, No. 11, pp. 622-626, November, 1985. Original article submitted January 18, 1985.

0007-4888/85/0011-1599$09.50