CHANGES IN THE GASTROINTESTINAL TRACT IN BURN-INDUCED CACHEXIA DURING COMBINED TREATMENT INCLUDING CONTRYCAL

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Lesions of the gastrointestinal tract play an important role in the clinical picture of burn cachexia [1-7]. Burn specialists thus need to organize the rational feeding of their patients and to carry out appropriate therapeutic measures. However, this is difficult because of the lack of exact data on the state of the different parts of the gastrointestinal tract during this period and on the dynamics of functional and morphological changes in the gastrointestinal tract in the course of pathogenetic treatment.

An important component of such treatment is contrycal, an inhibitor of proteolytic enzymes. Its use seems indicated, in the authors' opinion, because of its threefold action: inhibition of kallikrein and other trypsin-like enzymes, inhibition of systems of kinins, and inhibition of activity of cellular and tissue proteases. The investigation described below is devoted to a study of its pathogenetic action.

EXPERIMENTAL METHOD

A dynamic functional and morphological investigation of the gastrointestinal tract was carried out on 36 dogs with experimental burn cachexia resulting from the infliction of thermal burns of the IIIB degree covering 12-15% of the body surface (dorsum), under ether anesthesia. The animals were killed at various times between the 35th and 60th days. Combined pathogenetic treatment included standard antishock infusion therapy, parenteral protein feeding (with the amino-peptide hydrolyzin), and antibiotics. Contrycal was given in courses of 20,000 activity units/day for 5 days at intervals of 7-8 days.

The development of burn cachexia in the animals was characterized in the control by reduction of body weight by 30-45%, the development of hypochromic anemia and leukopenia, raised ESR, marked hypoproteinemia with hypoalbuminemia and a fall in the level of α- and γ-globulins, and by delayed repair of the wound. There were three series of experiments. In series I (control, 10 dogs) the state of the gastrointestinal tract of untreated burned animals was studied. In series II and III (10 and 16 dogs respectively) changes in the gastrointestinal tract were studied in burned animals receiving combined treatment (series II) or combined treatment together with contrycal (series III).

EXPERIMENTAL RESULTS

Animals of the control series developed atrophy of the gastric mucosa of diffuse-focal type, sclerosis, and structural changes in the glands. The gastric pits were greatly widened, some glands of the fundus and body of the stomach were shortened, mainly through shortening of the basal part of the glands; the number of glands was reduced (Fig. 1). Some glands were dilated to form cysts. Mucus on the surface of the mucosa was irregularly distributed: In some places it covered the mucosa in a wide and thick layer, also filling the necks of the glands; in other places the amount of mucus was much smaller and the mucosa was "bare." In these areas degenerative changes and desquamation of the surface epithelium of the mucosa were observed. Some of the chief and parietal cells of the main glands showed degenerative changes. The content of RNP in the chief cells was appreciably reduced. In some groups of glands structural changes toward the pyloric type were observed. In four cases severe degenerative changes of the cells and necrosis of the mucosa were observed, with the formation of small multiple erosions and acute ulcers(usually not more than 0.8-0.9 cm in diameter). In the region of the erosions and ulcers, focal disturbances of the circulation and of permeability were observed in the submucosa and the deep layers of the mucosa: congestion of veins, arteries, and capillaries, prestasis and stasis, paralytic dilatation of capillaries and venules with deformation of their lumen, occasionally microthromboses and edema, and saturation of the mucosa and submucosa with plasma.

The mucosa of the small intestine showed focal atrophy with shortening of the crypts and widening and deformation of their lumen. In two cases necrosis of the mucosa of the intestine was found, with the formation of small erosions and

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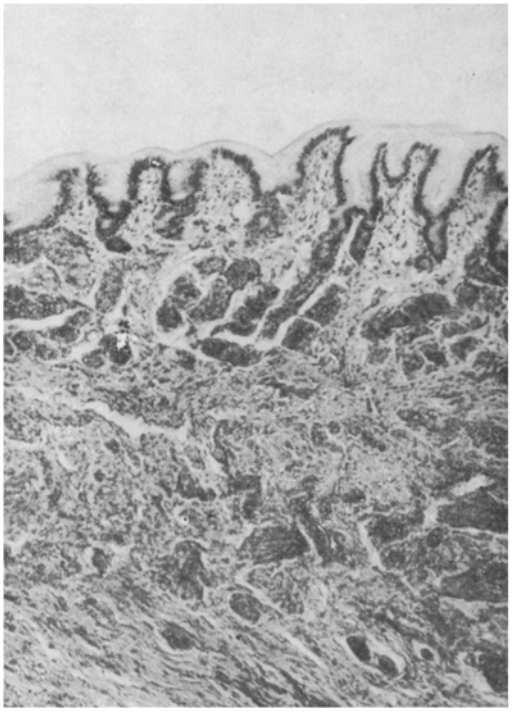

Fig. 1

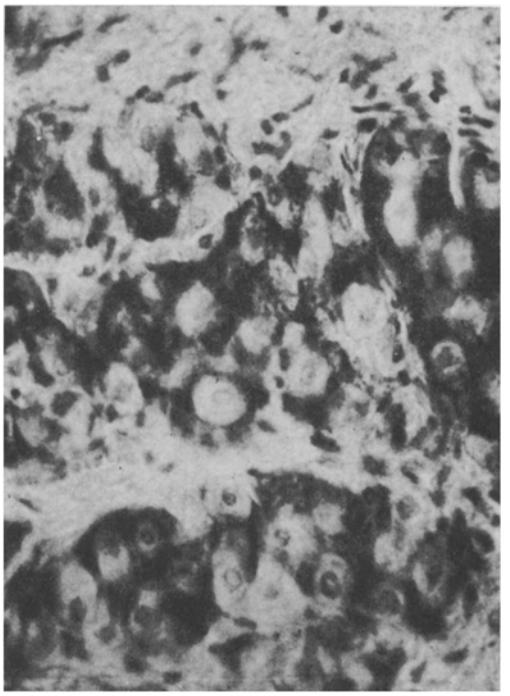

Fig. 2

Fig. 1. Experiment of series I. Dog No. 56, 50 days after burning. Irregular alternation of gastric pits. Marked atrophy and shortening of glands in body of stomach. Sclerosis of mucosa and submucosa. Hematoxylin and eosin, 160 X.

Fig. 2. Experiment of series II. Dog No. 86, 55 days after burning. Irregular distribution of RNP in chief cells of glands in body of stomach. Brachet's reaction, 650 X.

and ulcers. Their morphological structure and the picture of the vascular disturbances in the base and margins of the ulcers were identical with those observed in the stomach.

In the large intestine atrophy of the mucosa was observed. The glands were rather shortened, and in some places they were unevenly dilated. In the lumen of some glands and on the surface of the mucosa, the quantity of mucus was sharply reduced. Small erosions and ulcers were located mainly in these areas.

In the experiments of series II moderately severe focal atrophy of the gastric mucosa was observed; the gastric pits were irregularly arranged, thickened and apparently smoothed in some places, whereas in others they were deepened. The glands were of uneven length and diameter, but most were arranged parallel to each other (Fig. 2). The RNP content in the chief cells of the glands in the body and fundus of the stomach varied, but on the whole it was rather higher than in the control; cells with an increased RNP content were often seen. The intensity of the degenerative changes in cells of the principal glands, the signs of structural changes, and sclerosis of the mucosa and submucosa also were less marked than in the control group. The quantity of mucus on the surface of the mucosa and in the necks of the individual glands also was increased, mainly on account of an increase in the content of its PAS-positive components.

The small intestine showed moderately severe atrophy of the mucosa. Degenerative changes and desquamation of the enterocytes were found in some places. Production of PAS-positive mucins, filling the lumen of the glands and lying on the surface of the villi, was considerably increased compared with the control. Focal sclerosis of the mucosa and submucosa was observed. Moderate atrophy of the mucosa was present in the small intestine with shortening of the glands, and an increase in the number of goblet cells in the glands, together with a selective increase in the production of PAS-positive mucins. In the submucosa signs of sclerosis could be seen. Circulatory disturbances in the wall of the stomach and intestine were characterized by focal congestion of the vessels and capillaries and edema of the mucosa and submucosa.

In the experiments of series III the mucosa of the stomach and intestine was free from focal hemorrhages, ulcers, and erosions. On histological investigation, the signs of atrophy of the mucosa of the gastrointestinal tract were much less marked than in the experiments of series I and II. The gastric pits in the gastric mucosa were uniformly arranged and roughly all of the same shape and depth. Glands of the mucosa in most cases were arranged parallel to each other (Figs. 3a) and were equal in length (although a certain proportion of the glands were affected by atrophy). A thin uniform layer of mucus covered the surface epithelium and the necks of the glands. Cells of the surface epithelium contained large quantities of

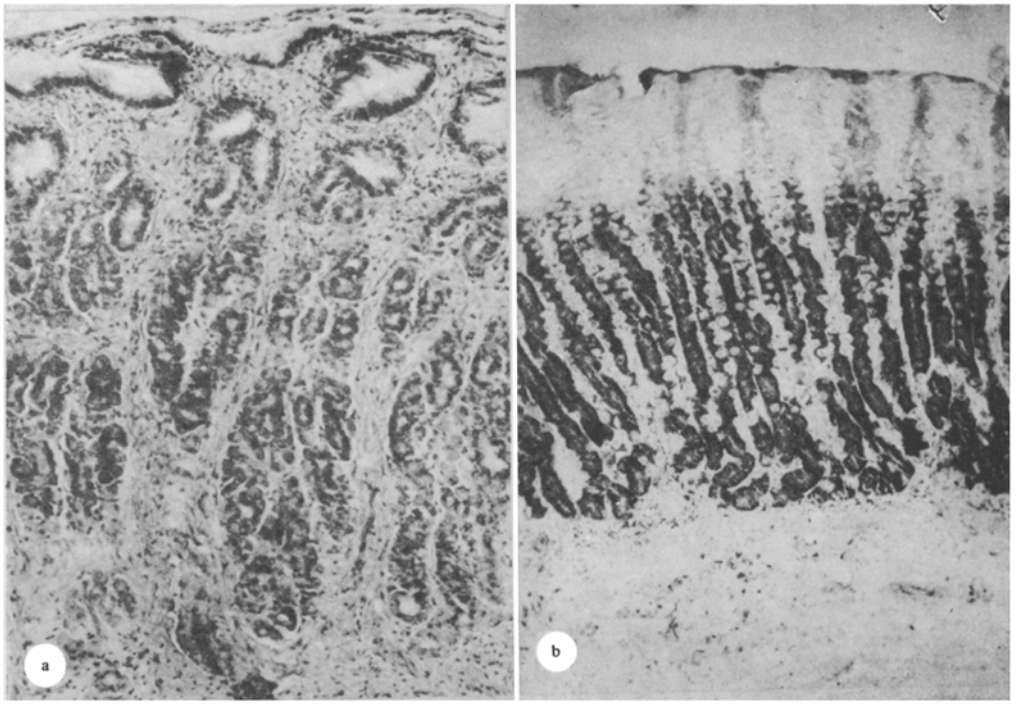

Fig. 3. Experiment of series III. Dog No. 92, 55 days after burning. Absence of atrophy of gastric mucosa. a) Glands in body of stomach wide, long, and separated by bands of connective tissue. Hematoxylin and eosin, 160 X; b) high RNP content in chief cells of glands in body of stomach. Brachet's reaction, 120 X.

mucins. The RNP content in the chief cells of the fundal glands was higher than in the preceding series (although the RNP distribution was definitely mosaic in character; Fig. 3b). No disturbances of the capillary circulation were found in the mucosa or submucosa.

The mucous membrane of the small and large intestine was characterized by absence of ulcers and erosions and also by minimal circulatory disturbances; it was covered by a thin layer of mucus. Atrophy of the mucosa was slight; small foci of sclerosis were present only in the submucosa.

The results are evidence that in burn cachexia atrophic changes develop in the gastrointestinal tract, with a component of ulceration and erosion, and with signs of focal structural changes in the glands. Combined treatment is to some extent effective. The addition of contrycal, an inhibitor of proteolytic enzymes, to the therapeutic program potentiated this action. The intensity of the microcirculatory disturbances and of the atrophic and dystrophic changes in the mucosa was reduced, with the result that there were fewer ulcers and erosions and less marked scar changes in the mucosa and submucosa. This can evidently be explained by the specific action of contrycal primarily on the kinin system, which causes disturbances of the normal microcirculation in the mucosa of the gastrointestinal tract, and also by its inactivating action on tissue proteases.

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