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Necrosis of Gastric Mucosa Following Orthostatic Collapse in Rabbits*

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Summary. Twenty-five rabbits were submitted to orthostatic collapse, divided into 6 groups and sacrificed about 4, 24 and 48 hours, 8, 15 and 30 days following collapse; two animals died during collapse and another 72 hours later. Seven animals were used as controls.

Necrotic changes involving small areas of the gastric mucosa in the fundic and body portions were seen in successive stages up to regeneration. Such changes were present in all animals submitted to collapse, except three with no lesion. The necrosis is related to a nutritive disturbance of the gastric mucosa, mainly anoxic in nature.

Grossly, the necrotic areas were similar to the acute erosions of the gastric mucosa seen in man.

Acute changes in gastric mucosa occur in man following shock of different causes (Woldman, 1952; Fletcher and Harkins, 1954; Risholm, 1956; Provana, 1963; Kaem and Kozina, 1965). Similar changes were seen in dogs (Lillehei, Dixon and Wangensteen, 1948), pigs (Simon, 1969) and rabbits (Harjola and Sivula, 1966) following hemorrhagic shock, and in guinea pigs (Ludwig and Lipkin, 1962) and rats (Brodie and Hanson, 1960; Guth and Hall, 1966; Hübner, Klein and Eder, 1970) following restraint shock. Parenchymatous changes in the myocardium as well as in the wall of small arteries were observed by Meessen (1937, 1939) in rabbits following orthostatic collapse. In the latter, necrosis was described in the media of arteries (de Faria, 1955, 1958, 1962) and in the liver (Korb, Müller, Gedigk and Hellwig, 1969).

Material and Methods

The experiment was carried out on 17 adult male rabbits and 15 females, 25 being submitted to orthostatic collapse and 7 serving as controls. The animals were New Zealand White and mixed of Chinchilla and New Zealand White, ranging in weight from 2450 g to 5650 g. A single collapse was induced as previously described (de Faria, 1958). The animals were restrained on a holder and then put in a vertical position. The collapse appeared about 20 to 30 minutes later. The signs of collapse were superficial respiration, tachycardia, disappearance of both corneal reflex and muscle tone in the limbs, cyanosis of ears and lips. The collapse could be interrupted immediately by putting the animal in the horizontal position. The rabbits were killed at varying times after collapse: 24 hours (5 animals), 48 up to 72 hours (4 animals), 8 days (4 animals), 15 days (4 animals) and 30 days (5 animals). Two animals died spontaneously during shock and another about 4 hours afterwards. The remaining rabbits were killed by a blow on the neck followed by cutting of the neck vessels. Gross examination of the stomach immediately after killing; then fixation in 20% neutral formalin with 0,7% sodium chloride (Birge and Tibbits, 1961) and occasionaly in Gendre's fluid. Staining methods used were hematoxylin and eosin, Gomori for reticulum, PAS, Mayer's intestinal mucus stain (Masson, 1968) and Van Gieson for collagen.

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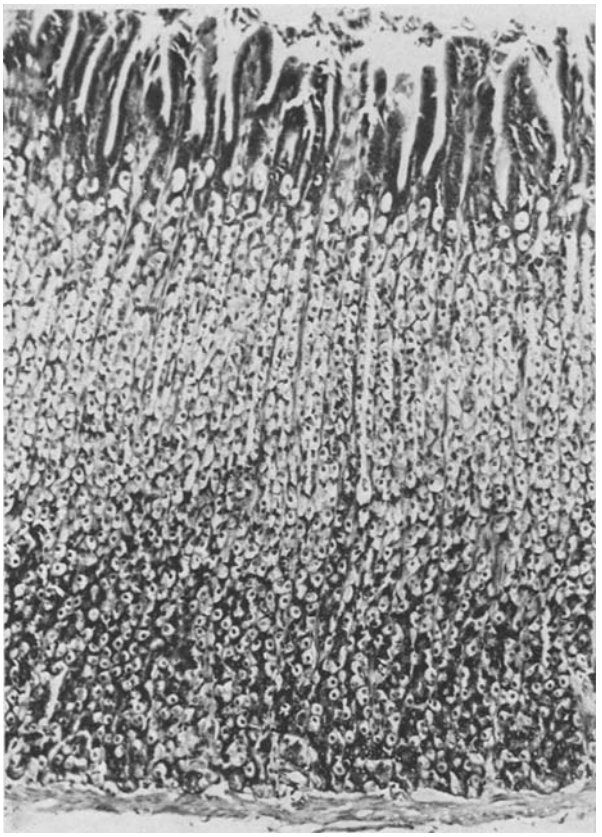

Fig. 1. Control rabbit C-13/70. Normal fundic gastric mucosa seen in its whole thickness: above is seen the surface epithelium, then a lighter area due to numerous parietal cells. Hematoxylin and eosin stain. ×100

Results

a) Control Animals

The gastric mucosa in the control animals was pink at the fundus and body, whitish at the piloric portion and presented conspicuous folds. Microscopically the mucosa showed glands with zymogenic, parietal and mucous neck cells in the fundus and body. A few lymphocytes, occasional plasma cells and eosinophil leukocytes were seen in the superficial part of the mucosa, just below the surface epithelium. The latter was tall and formed short papilla-like projections (Fig. 1).

b) Test Animals

Group 1, rabbits dying during orthostatic collapse (2 animals) and about 4 hours following collapse (1 animal). Grossly, the gastric mucosa at the fundus and body presented hyperemia in one animal; hyperemia and small petecchiae in another, and a third animal, dying in shock, showed three small erosive areas, the largest one 3 mm in diameter. Microscopically, the mucosa in the fundus and

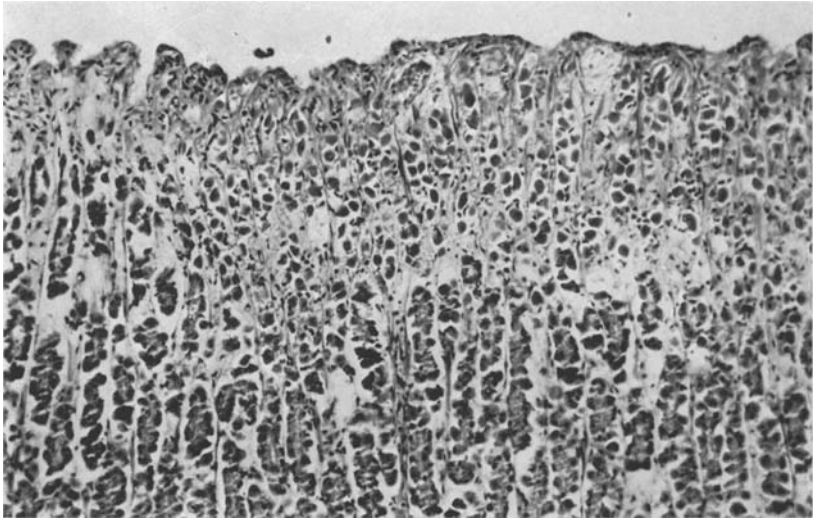

Fig. 2. Rabbit C-16/70, 4 hours following collapse. The superficial part of the gastric mucosa is necrotic. Hematoxylin and eosin stain. ×100

body region presented cell necrosis, characterized by nuclear pyknosis, karyorrhexis, homogeneous and very acidophilic cytoplasm, as well cellular detritus. Both surface epithelium and glandular cells were necrotic. These changes damaged single cells or band-like areas in the superficial part of the mucosa (Fig. 2). These areas were seen in the animal dying 4 hours following collapse, and involved about one third of the mucosa height. A few neutrophil leukocytes were observed in these necrotic areas.

Group 2, 24 hours after collapse (5 animals). Grossly, one animal with mild shock did not present any change at the gastric mucosa. The remaining animals showed a few small linear or rounded erosive areas at the mucosa of the fundus and body, changing between pin-head size and 3 mm in diameter; one animal presented a larger erosive area, 15 mm long. Two animals revealed a large highly hyperemic erosive areas (about 2 × 1 cm) at the body mucosa near the pyloric portion (Fig. 3). Microscopically necrotic changes in the gastric mucosa were found in all animals, but one animal with mild shock. The necrosis was in areas, moderate or severe, and involved the superficial portion of the mucosa (about two thirds). The necrotic area was poorly delineated at the moderate necrosis and sharp at the severe one, due to a few preserved cells in the former, which failed to be observed in the latter. The necrotic areas presented nuclear and cytoplasmic debris. These areas were hyperemic and presented a few neutrophil leukocytes; hemorrhage was seen in the areas with severe necrosis. The latter were erosive due to elimination of the necrotic tissue (Fig. 4). A few mitotic figures were seen in the surface epithelium and glandular cells neighbouring the necrotic areas.

Group 3, 48 up to 72 hours after collapse (4 animals). Grossly and microscopically the gastric mucosa presented about the same changes as observed in Group 2. Erosive areas were seen in all animals, but one. The latter with mild shock showed only hyperemic mucosa. The necrosis involved up to the whole thickness of the

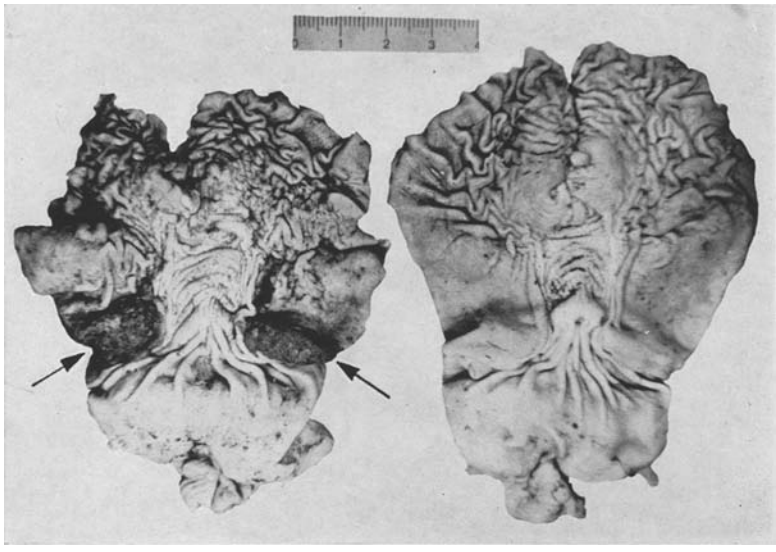

Fig. 3. Rabbit C-14/70, 24 hours following orthostatic collapse. At left, large erosive highly hyperemic areas (arrows) near the pyloric portion (to be compared with the normal stomach of control rabbit, C-13/70, at right)

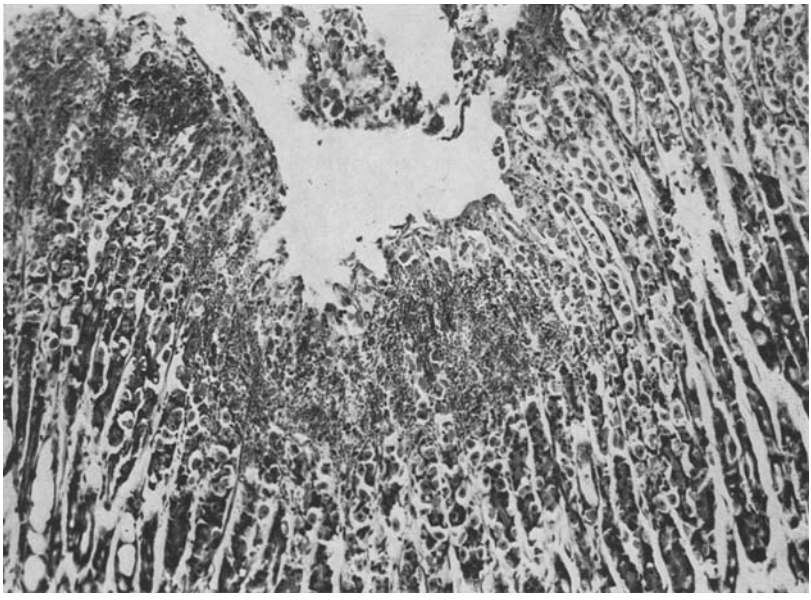

Fig. 4. Rabbit C-14/70, 24 hours following collapse. More conspicuous (advanced) necrosis in the gastric mucosa than in Fig. 2, with cellular lysis and sloughing of the necrotic tissues. Hematoxylin and eosin stain. ×100

mucosa (Fig. 5). There were more neutrophil leukocytes in the necrotic areas, specially in the rabbit dying 72 hours after collapse. In addition, there was also a greater number of mitotic figures in the surface epithelium and glandular cells.

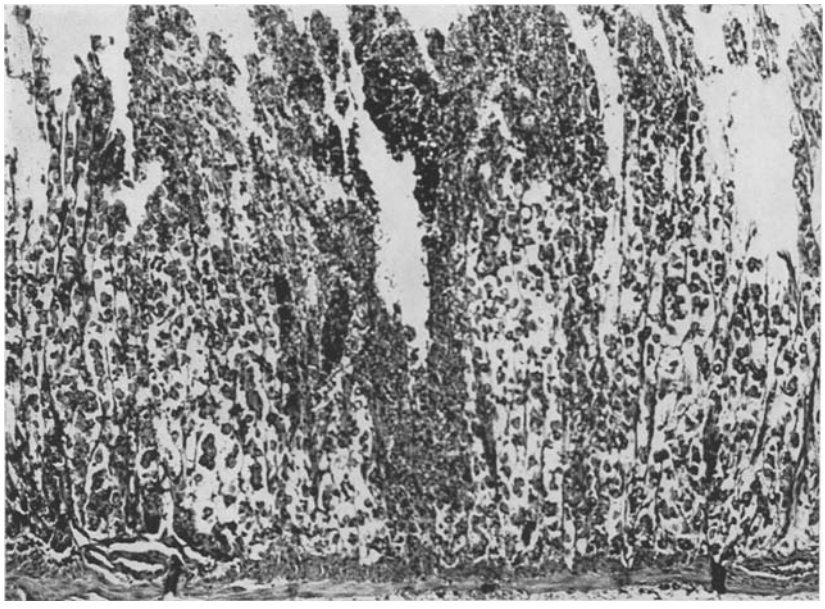

Fig. 5. Rabbit C-6/70, 72 hours following collapse. A necrotic, darkly stained area involving the whole thickness of the mucosa. (The muscularis mucosae is seen at the bottom.) Hematoxylin and eosin stain. ×100

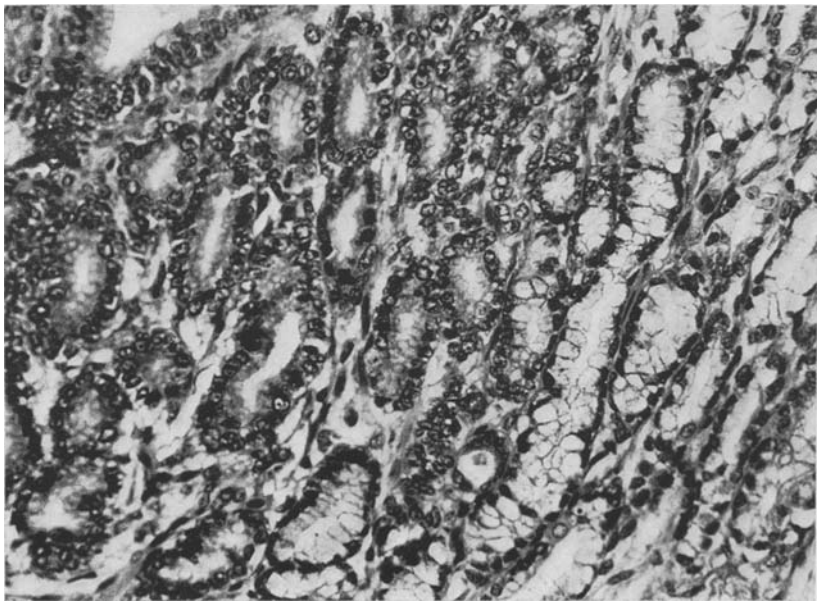

Fig. 6. Rabbit C-13/70B, 8 days following collapse. Regenerative changes in the gastric mucosa at the body region: both immature and mucous glands are to be seen. (The surface epithelium seen at the left upper corner.) Hematoxylin and eosin stain. ×250

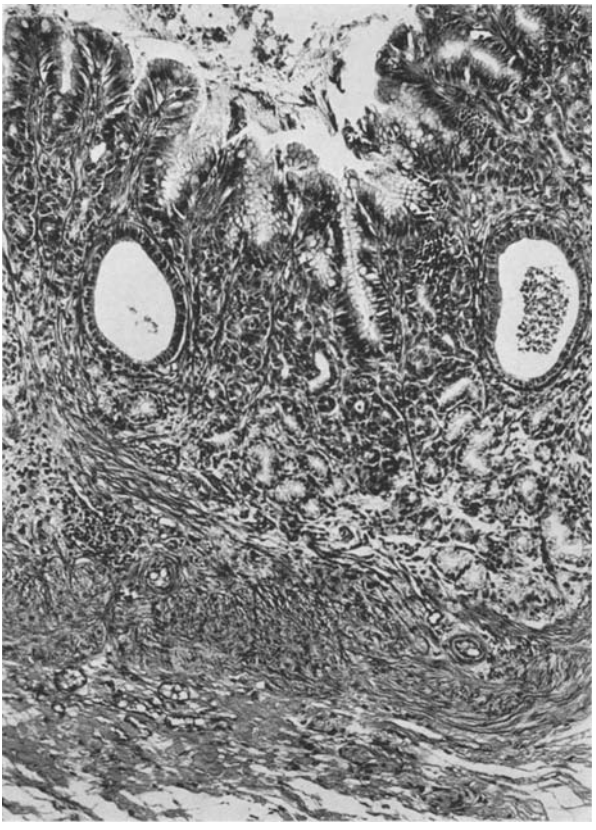

Fig. 7. Rabbit C-SN/71, 15 days following collapse. Regenerated atrophic mucosa of the body region with dilated glands. (To be compared with the normal mucosa of the Fig. 1.) Hematoxylin and eosin stain. ×100

Group 4, 8 days after collapse (4 animals). Grossly, two animals presented only hyperemia in the gastric mucosa. Another animal (C-15/69B) presented a conspicous granular aspect in the body, near the pyloric portion. A fourth rabbit (C-13/70B) had a smooth or slightly granular mucosa. Microscopically, the body gastric mucosa of the latter animal showed thinner regenerated areas with glands consisting mainly of indifferenciated cells, a few mucous secreting cells similar to those of the intestine and rare parietal cells (Fig. 6). Rare regenerated glands presented wide, dilated, lumina. Between the glands there were few inflammatory cells (lymphocytes and plasma cells) and thin strands of proliferated fibroblasts. Fibrosis was more severe immediately below the surface epithelium. Frequent mitotic figures were seen. The changes in the gastric mucosa of the other animal (C-15/69B) were similar but with thicker strands of proliferated fibrous tissue. The latter divides the gastric mucosa in areas, corresponding to the granulous aspect seen grossly. In another rabbit the regenerative changes of the glands were less conspicuous, and in the remainder animal no changes were observed in the mucosa.

Group 5, 15 days after collapse (4 animals). Grossly there was a granular appearance in the gastric mucosa of the body in 3 animals and a smooth aspect in another one (C-18/70). Microscopically the changes were essentially similar to those observed in Group 4, with disorganization of the mucosa structure, fibrosis, immature regenerated glands and new conspicuous mucous glands in the body mucosa (Fig. 7). These changes were severe in 2 animals, moderate in one and slight in another animal (C-18/70). The regenerated mucosa in both former animals did not present the glands peculiar of the body region. In the latter animal the more conspicuous changes was flattening of the surface epithelium with no papilla-like projections, as seen in controls, and slight connective tissue proliferation separating the body glands. In one animal with mucous glands in the mucosa there were many eosinophil leucocytes.

Group 6, 30 days after collapse (5 animals). Grossly, only two animals presented a smooth appearance of the gastric mucosa in the body, near the pyloric portion. The other animals had no changes. Microscopically, a few areas in the body portion mucosa were thinner, edematous and with more connective tissue between the glands; such appearance of the mucosa was observed in all animals but one with a normal mucosa.

Discussion

The acute changes in the gastric mucosa following orthostatic collapse were similar to those seen in man and animals after shock (see Introduction). The most conspicuous changes was necrosis involving in general the superficial part of the mucosa in the body region. The evolutive stages of necrosis were followed up to regeneration. The latter began at 48 hours following collapse with the presence of mitotic figures and was complete after 8 days. The sequelae were only hypotrophy of the mucosa, seen 30 days after the collapse.

The cause of the necrosis could not be determined. Surely it was due to a nutritive disturbance, mainly anoxic in nature. The anoxia might be produced by several mechanisms, such as oligemia (de Faria, 1955; Harjola and Sivula, 1966), vasoconstrictions of small arteries in the gastric wall (Berg, 1942; Crane, 1954), venous stasis (Guth and Hall, 1966), ischemia and stasis (Watt, 1959; Hübner *et al.*, 1970; Klein *et al.*, 1971) or shunt in arteriovenous anastomoses (Sherman and Newman, 1954; Palmer and Sherman, 1958). All these phenomena could occur during collapse or shock. Other mechanisms have been invocated to explain the necrosis of the gastric mucosa, such as liberation of ulcerogenic substances by the kidney (Aron and Sabassier, 1954), increase of free acidity (Brodie, Marshall and Moreno, 1962), histamine action (Watt, 1959; Sing, Sharma and Kar, 1967) or mechanisms related to the general adaptation syndrome (Selye, 1946).

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