FUNCTIONAL AND MORPHOLOGICAL CHANGES IN THE GASTROINTESTINAL TRACT IN EXPERIMENTAL BURN SHOCK

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KEY WORDS: burns; shock; gastrointestinal tract.

Severe burn shock, characterized by widespread marked microcirculatory disturbances and degenerative changes, naturally is bound to affect the mucous membranes of the different parts of the gastrointestinal tract. Information on the character of functional and morphological changes in the stomach and intestine in patients with severe burns, however, is somewhat contradictory. Some workers [4, 5, 9] have shown that during this period the secretory, acid-forming, motor, and evacuatory functions of the gastrointestinal tract are depressed. Conversely, other workers [1, 2, 4, 5, 8, 10, 12] found that acid formation is increased at this time, and this is combined with increased peristalsis. Morphological investigations [3, 6, 7, 11] have shown that the mucoid activity of the epithelial glands in the mucosa of the gastrointestinal tract is increased during the period of shock, the circulation in the mucosa and submucosa is profoundly disturbed, and signs of acute gastroenteritis may arise. However, this information is based on the study mainly of autopsy material. Changes due to autolysis make it generally impossible to interpret the data reliably.

EXPERIMENTAL METHOD

The gastrointestinal tract of 56 dogs was studied during the period of burn shock (72 h after trauma). In the experiments of group 1 (control) a flame burn of the IIIB degree, covering 15-18% of the body surface was inflicted on 22 dogs under ether anesthesia. The animals of group 2 (34 dogs) were burned in the same way, and then divided into three series. Ten dogs (series 1) received antishock infusion treatment (polyglucin, rheopolyglucin, neuroplegic mixture, 5% solution of glucose, cardiac drugs). Twelve dogs (series II) received contrycal by intravenous drop in a dose of 20,000 activity units daily throughout the experiment. Twelve dogs (series III) received antishock treatment as described above together with contrycal. The animals were killed in the course of 3 days. During the experiment the arterial pressure (BP), pulse rate, respiration rate, and rectal temperature of the animals, the hemoglobin concentration, and hematocrit index were recorded.

For morphological investigation fragments of the wall of the organ were excised from the region of the cardia, fundus, and body of the stomach, the greater and lesser curvature, the pyloro-antral region, and different parts of the small and large intestines, fixed in 10% neutral formalin or Carnoy's fluid, and embedded in paraffin wax; sections were stained with hematoxylin and eosin, picrofuchsin by van Gieson's method, the PAS reaction with amylase control, with alcian blue at different pH values, and with methyl green and pyronine by Brachet's method. Some sections were cut on a cryostat and stained by Goldman's method.

EXPERIMENTAL RESULTS

In the experiments of group I a significant change was found in the various parameters (BP fell to 50/0 mm Hg and the pulse rate rose to 180-170 beats/min. The body temperature rose to 39°C.

Morphological investigation showed swelling, edema, and petechial hemorrhages in the mucosa of the stomach and small and large intestine. The gastric pits in the gastric mucosa were smoothed because of edema of the surface layer of the mucosa. The covering epithelium contained a moderate quantity of mucoids. The layer of mucus covering the epithelium varied in thickness. In some places it was very thin or completely absent. In these areas marked degenerative changes were seen in the covering epithelium, with desquamation and small foci of necrosis and superficial ulceration of the mucosa. A varied degree of dilatation was characteristic of the lumen of some of the principal glands of the body and fundus of the stomach, and individual parietal cells showed degenerative changes and necrobiosis. In some of the chief cells the RNP content was reduced, and some of the cells were undergoing destruction. Marked congestion of the capillaries and venules,

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statis and prestasis, perivascular edema, and focal hemorrhages were observed in the submucosa (Fig. 1). In some parts of the mucosa of the stomach and small and large intestines tiny erosions and small (not more than 0.7 cm in diameter) ulcers penetrating throughout the depth of the mucosa, and in some places also into the submucosa, were observed. In the region of the base and margins of the erosions and ulcers massive signs of capillary stasis and multiple microthrombi were observed (Fig. 2). Sometimes the edges of an ulcer were formed by a zone of necrosis of the mucosa. The glands of the gastric mucosa in the region of the edges of ulcers showed degenerative changes in the chief and parietal cells. They were irregularly widened and shortened.

In the small intestine the villi in some places were a little swollen and the crypts unequally dilated. The mucosa of the large intestine was covered by a layer of mucus of variable thickness. Goblet cells contained large quantities of mucus, rich in glycosaminoglycans (GAG) and neutral mucopolysaccharides (NMPS), which also filled the lumen of the glands.

Among the animals of the second group in the first experimental series the results of functional analysis indicated a rise in arterial pressure to 100/60 torr and a decrease in respiration frequency to 38/mm. The mucus membrane of the stomach is nonuniformally plethoric, and displays a focus of edema and ulcerations of various radi and depths. The mucus membranes have small erosion surfaces. Uniform, rich GAG and NMPs with rather thick mucus layers cover the epithelium of the mucus membrane. The glands are undeformed and dystrophic changes in the coating and major cells are poorly expressed. There is a moderate plethora of venula and capillaries of mucus and submucus membranes, edema foci, stomach mucus membranes and of the small intestine. In the region of low surface erosion there is a decrease in the content of GAG on the mucus membrane surface. In the opening of the duct at the large intestine there is a significant quantity of PAS-positive mucilage and a little GAG.

The glands were not deformed and the degenerative changes in the parietal and chief cells were less marked. Moderate congestion of venule: and capillaries in the mucosa and submucosa and focal edema of the mucosa of the stomach and small intestine were noted. In a region of infrequent surface erosions the GAG content on the surface of the mucosa was reduced. Large quantities of PAS-positive mucus and small quantities of GAG were present in the lumen of the glands of the large intestine.

In the experiments of series II in animals of group 2 the rectal temperature was lowered to 37.2°C, and the respira-

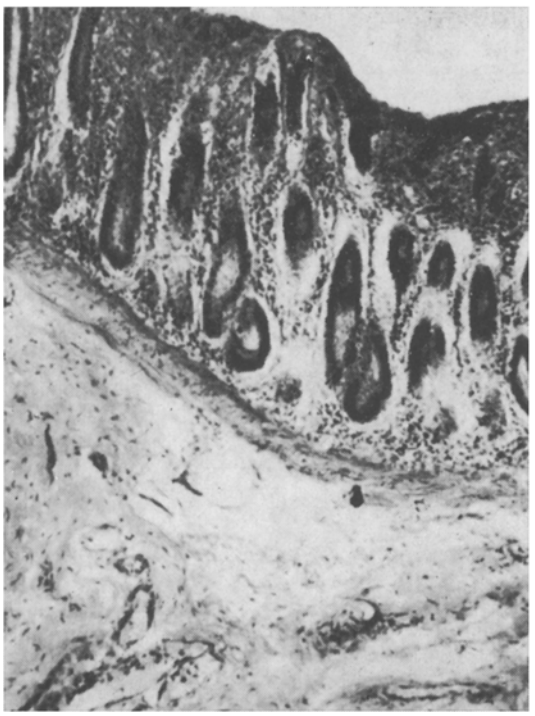

Fig. 1

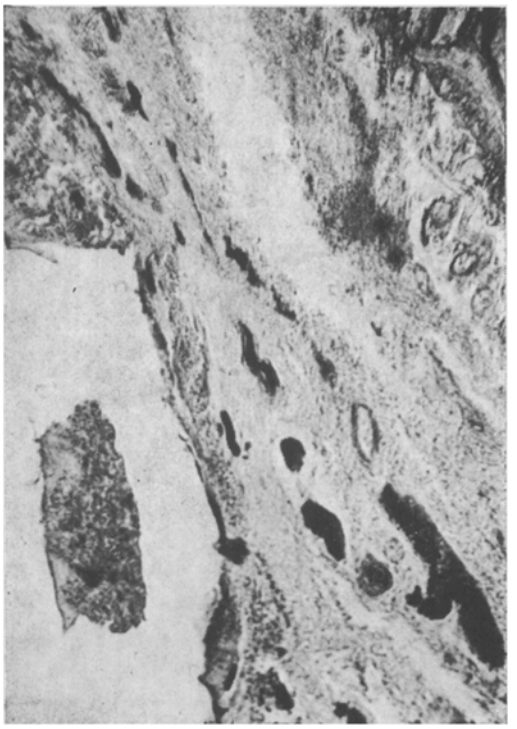

Fig. 2

Fig. 1. Dog No. 8. First day after trauma. Burn of IIIB-IV degree covering 18% of body surface, untreated. Marked disturbances of microcirculation in submucosa of stomach. Paralytic dilatation of vessels and capillaries in submucosa, with congestion, stasis, and prestasis. Hematoxylin–eosin, 50 ×.

Fig. 2. Dog No. 11. First day after trauma. Burn of IIIB-IV degree covering 18% of body surface, untreated. Ulcer of mucosa on greater curvature of stomach. Marked circulatory disturbances, massive areas of capillary stasis and microthromboses. Hematoxylin – eosin, 48 ×.

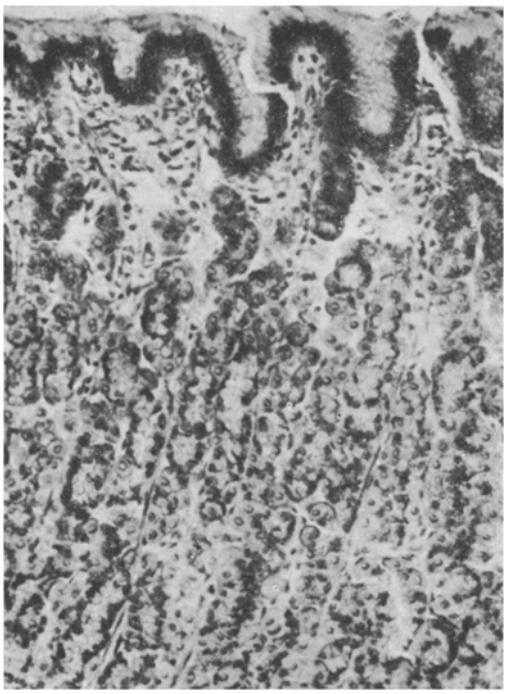

Fig. 3. Dog No. 41. Third day after trauma. Burn of IIIB-IV degree covering 18% of body surface; combined treatment including with contrycal. Surface of gastric mucosa is well folded. Gastric pits are deep and filled with mucus. Glands of uniform diameter. Stained with alcian blue, 180 X.

tion rate returned to normal (to 28/min) after administration of contrycal; the Hb concentration was raised slightly (to 16 g%), BP to 40 mm Hg, and the heart rate to 100 beats/min (tachycardia).

The mucosa of the stomach and small and large intestines was slightly congested in some places, but with no visible hemorrhages or erosions, and it was covered with a thin but uniform layer of mucus rich in GAG and NMPS. The epithelium lining the mucosa of the stomach and small and large intestines showed no particular features. Degenerative changes in the parietal and chief cells of the glands of the body and fundal part of the stomach were slight and the RNP content in the chief cells was high. Moderate focal congestion of the vessels and capillaries and focal edema of the submucosa were observed in the stomach and, to a lesser degree, in the intestine.

In the animals of group 2 in the experiments of series III rapid normalization of all the functional parameters was observed: BP (to 100/70 mm Hg), respiration rate to (22/min), and temperature (to 37.1°C).

The mucosa of the stomach and intestine was covered by a uniform and fairly wide layer of mucus rich in GAG and NMPS. The epithelium lining the gastric mucosa and the villi and crypts of the small intestine and glands of the large intestine was free from degenerative changes (or they were very slight; Fig. 3). Absence of erosions and ulcers was characteristic. Glands of the fundal portion and body of the stomach were of equal length and diameter and were regularly oriented. No degenerative changes were present in the parietal and chief cells and the RNP content in the chief cells was high. Villi of the small intestine were regular and formed a regular "palisade." The enterocytes showed no signs of degenerative changes. The glands of the large intestine were normal. The almost complete absence of circulatory disturbances and of capillary permeability in the mucosa and submucosa of the different parts of the gastrointestinal tract was characteristic.

In burn shock the GAG content in the epithelium lining the mucosa of the stomach and intestine is thus reduced. According to McAlhany et al. [11] sulfated mucopolysaccharides contained in cells of the epithelium of the stomach and intestine protect the mucosa against the action of the digestive juices. A fall in the GAG content facilitates the ulcerogenic effect. The possibility cannot be ruled out that this is an important factor in the development of ulcers in burned subjects during the period of shock. Combined treatment, aimed at normalizing primarily the state of the circulation and the content of protective mucus on the mucosa, lowers the intensity of the processes mentioned above in the wall of the gastrointestinal tract and largely prevents the development of erosive and ulcerative lesions.

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A MODEL OF DESTRUCTIVE TUBERCULOSIS IN GUINEA PIGS

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The destructive process in the lung tissue of experimental animals has been shown to depend on the method of sensitization. A model of experimental cavernous tuberculosis of the lungs was formed in two series of experiments on 124 guinea pigs. It was shown that in order to undertake long-term experiments with cavernous changes in the lungs of guinea pigs a model with preliminary injection of BCG, followed by a course of treatment with sulfadimethoxine to prevent the nonspecific pneumonia which frequently arises, is the optimal choice. By this method cavernous tuberculosis, with the formation of three-layered cavities and multiplication of the bacterial population which resembles human tuberculosis more closely than other types of experimental model of this disease, can be obtained.

The most convenient model for cavity production was found to be injection of *Mycobacterium tuberculosis* into the substance of the lung by thoracic puncture. The first reports on this method were published in 1954 [3] . Later the method was improved and modified: Killed mycobacteria, their fractions, or even mycobacteria of BCG were injected into the lung [4, 5]. It was also suggested that a strongly depot-forming preparation consisting of a mixture of paraffin and lanolin or rat fat be used in order to reduce the dose of injected agent by 100 times, for a relationship has been found between the dose of a virulent infecting agent and the survival rate of animals sensitive to tuberculosis [1]. Mainly dogs have been used as experimental animals.

Meanwhile tuberculosis obtained in experiments on dogs has little in common with the process found in other experimental animals and is very far removed in pathogenesis and, in particular, in its course from the destructive changes in human lung tissue. For these reasons many workers have used small laboratory animals in their experimental studies.

To investigate problems connected with the study of the dynamics of the bacterial population and of healing processes, especially when antibacterial therapy was used, the creation of an adequate experimental model was necessary.

EXPERIMENTAL METHOD

Altogether 124 animals were used. In the animals of the control group (64 guinea pigs) a model of experimental tuberculosis was produced by the usual method, according to which Freund's adjuvant was injected intradermally 5 times at intervals of 1 week. *M. tuberculosis* cells of human type $H_{37}Rv$ were killed by autoclaving, after which they were suspended in a mixture of petrolatum and lanolin. If skin sensitivity to tuberculin was present (the mean area of hyperemia of the skin was 20 × 30 mm), an injection of *M. tuberculosis* of human type $H_{37}Rv$ was given into the diaphragmatic lobe of the right lung in a dose of 2 mg/kg in 0.2 ml of petrolatum-lanolin suspension. The puncture was carried out by means of a syringe in the 6th intercostal space 1 cm to the right of the spine; the length of the needle was 2 cm and the syringe was perpendicular to the animals' trunk. The needle was inserted throughout its length and the weight of each animal was at least 400 g.

Animals of the experimental group (60 guinea pigs) received a subcutaneous injection of BCG vaccine in a dose of 0.2 mg/kg in 0.5 ml physiological saline instead of Freund's adjuvant. The sensitivity of the skin to tuberculin was determined

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