EXPERIMENTAL STUDY OF POSTTRAUMATIC REGENERATION OF THE EPITHELIUM OF THE GASTRIC AND INTESTINAL MUCOSA IN DOGS

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Sources of repetitive regeneration of the epithelium of the gastric and intestinal mucosa were studied. To do this, several operations were performed on the stomach and intestine of 16 dogs. The investigations showed that a leading role in the regeneration of the epithelium of the gastric and intestinal mucosa under experimental conditions is played by the intact epithlium surrounding the zone of the operation. This is confirmed by the fact that an intestinal graft on a vascular pedicle, stripped of its mucosa and sutured into a defect in the stomach wall, is covered by gastric mucosa, whereas a stomach graft, stripped of its mucosa, is covered by intestinal mucosa if it is transplanted as a cylindrical "insert" into the intestinal tube; a small gastric pouch, if stripped of its mucosa, is obliterated, as is completely explained by the absence of the main source of regeneration, namely intact epithelium of the mucosa at the periphery of the defect. Regeneration of the epithelium of the gastric mucosa from implanted cells could not be demonstrated; consequently, regeneration under the experimental conditions used took place as a result of sliding of epithelial cells surrounding the zone of the operation over the denuded surface.

KEY WORDS: gastric and intestinal mucosa; regeneration of the mucosa; sliding of epithelium over the wound.

The study of regeneration of the mucosa of the gastrointestinal tract is of clinical as well as purely biological importance, for mucosectomy has been used as a method of treatment of gastric and duodenal ulcer, polyps, and polyposis [2, 4, 7].

The problem of the sources of reparative regeneration of the gastric and intestinal epithelium has not been adequately discussed in the literature and the data are contradictory. For instance, observations on regeneration of the gastric mucosa in dogs [5] and the rectal mucosa in man have shown that the epithelium is restored from epithelial cells remaining behind after removal of the mucosa. Using repeated burning of the gastric mucosa with 96% alcohol, 10% silver nitrate solution, and 1% hydrochloric acid, Lazovskii [3] observed that the epithelium of this gastric mucosa can regenerate from cells left behind in the depth of the gastric pits. Meanwhile, Galeone et al. [7] consider that the epithelium of the gastric mucosa regenerates entirely by sliding from the periphery of the defect. A similar conclusion has been reached by other workers [6, 10] who have studied regeneration of the mucosa of the large intestine. Our own preliminary observations [1] showed that the epithelium of the gastric mucosa starts to regenerate after mucosectomy from undamaged mucous membrane.

Meanwhile that investigation [1] showed an accumulation of epithelial cells among granulation tissue a considerable distance from the undamaged border of the mucosa. It was suggested that after mucosectomy regeneration can take place through implantation of the epithelium. Desquamated epithelial cells, implanted in the denuded zone, were shown to be able to form islands of regeneration of the mucosa. However, these accumulations could have been left behind accidentally after mucrosectomy.

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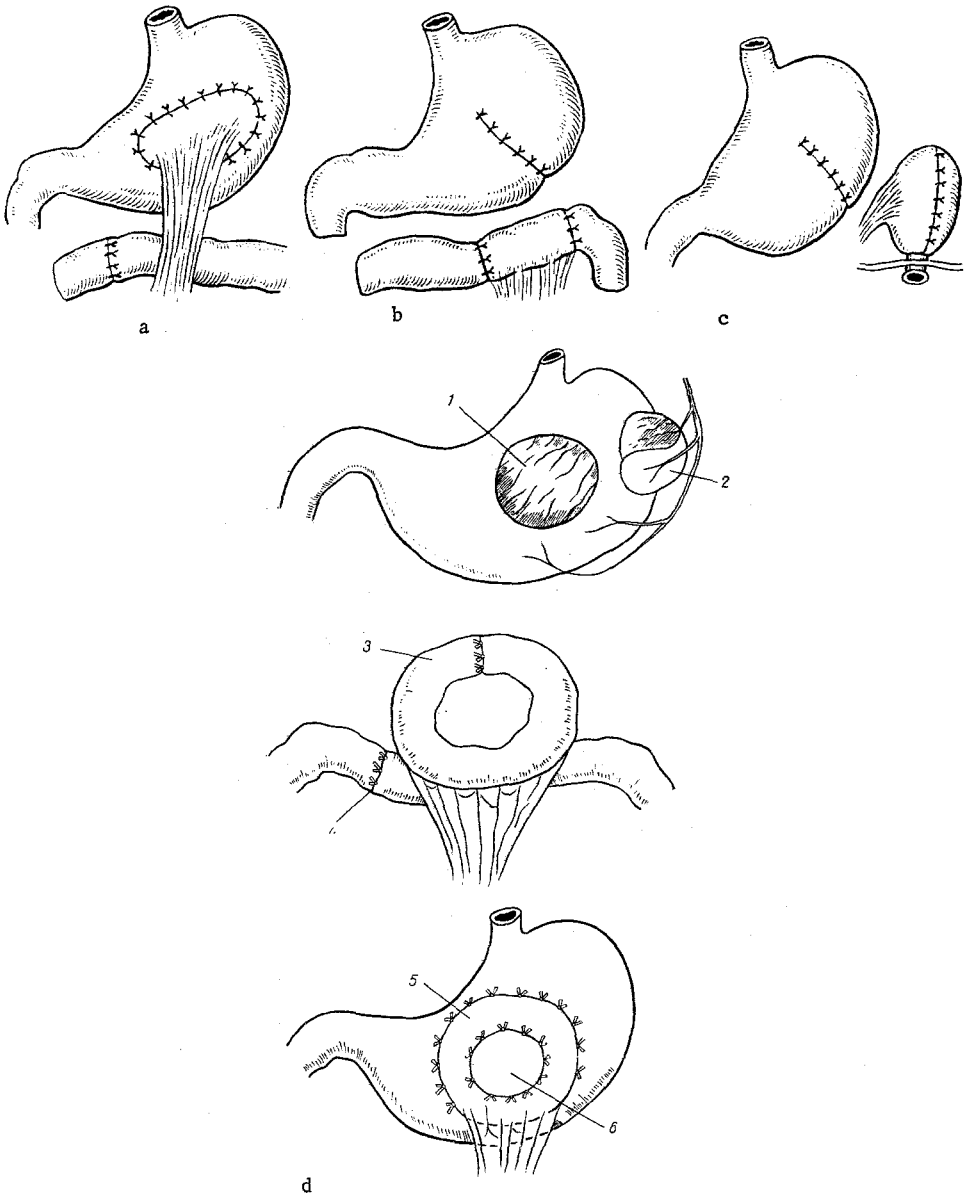

Fig. 1. Four types of operations on the stomach and intestine of dogs. a) Graft of small intestine on vascular pedicle sutured into defect in stomach wall; b) tube formed from denuded gastric graft sutured between ends of divided jejunum; c) "gastric pouch" formed from denuded gastric graft; d) stages of formation of ring made from piece of jejunum around denuded gastric graft: 1) defect in anterior wall of stomach, 2) denuded gastric graft, 3) ring of jejunum divided along its antimesenteric border, 4) anastomosis restoring continuity of small intestine, 5) ring of jejunum sutured into defect of stomach wall, 6) denuded gastric graft.

The object of this investigation was to study the sources of reparative regeneration of the epithelium of the gastric and intestinal mucosa, assuming that these sources could be: 1) epithelial cells of the intact mucosa – sliding regeneration, 2) epithelial cells left behind in the zone of denudation, and 3) epithelial cells implanted into the zone of denudation.

EXPERIMENTAL METHOD

Four different operations were performed on the stomach and intestine of 16 dogs.

The First Type of Operation (Fig. 1a). An oval defect measuring 5 × 6 cm was produced in the anterior wall of the stomach. A segment of the proximal portion of the jejunum, 5-6 cm, on a vascular pedicle was excised, divided along the antimesenteric border, stripped of its mucosa, completely, and sutured into the defect in the stomach wall. Continuity of the intestine was restored by means of an enterojejunostomy.

Type 2 (Fig. 1b). A flap measuring 6 × 8 cm was excised from the greater curvature of the stomach and adjacent areas of the anterior and posterior walls. It was supplied with blood by branches of the left and right gastro-epiploic arteries. The wound was sutured perpendicularly to the greater curvature of the stomach, thus preventing its deformation. Mucosectomy was performed on the graft and it was formed into a tube. The denuded tube of stomach was sutured between the ends of the divided jejunum. The denuded tube of stomach wall thus restored the continuity of the intestine.

Type 3 (Fig. 1c). A flap was excised from the stomach by the method described for type 2. The defect in the stomach was sutured. The flap was denuded of its mucosa and formed into a "gastric pouch," to which a Basov's fistula was formed.

Type 4 (Fig. 1d). The mucosa was removed from a piece of stomach wall, and a piece of jejunum excised from the antimesenteric border was introduced as a closed ring, with its mucosa facing the lumen of the stomach, between the edges of the stomach flap and the edges of the defect in the stomach wall. The jejunal graft obtained its blood supply from its intact vascular pedicle. Continuity of the intestine was restored by anastomosis.

Microscopic investigation was carried out 1.5 months after the operations of types 1, 2, and 3 and five months after the type 4 operation. Histological preparations were stained with hematoxylin–eosin and by the methods of Van Gieson, Dominici–Kedrovskii, and Mallory.

EXPERIMENTAL RESULTS

Investigation of the intestinal graft (type 1) showed complete restoration of the mucosa covered with a single layer of cylindrical glandular epithelium typical of the gastric mucosa. In the tunica propria of the mucosa there were many simple tubular glands, lying parallel to each other and containing chief, accessory, and parietal cells. In some area of the submucosa and in the muscular coat of the mucosa there were single foci of lymphoid infiltration and scar tissue.

Investigation of the gastric autograft (type 2) showed that the regenerated mucosa contained low villi and shallow crypts, lined with simple cylindrical epithelium and containing border cells and goblet cells. The tunica propria of the mucosa consisted of delicately fibered connective tissue and contained many lymphocytes, histiocytes, eosinophils, and plasma cells. In some areas of the muscle coat of the mucosa scar tissue was found.

After the type 3 operation complete obliteration of the "gastric pouches" was observed. After type 4, mucosa of intestinal character with a few ill-defined villi and shallow crypts, lined with cylindrical epithelium, consisting of border and goblet cells, was observed. Scar tissue was present in some parts of the submucosa.

Regeneration of the epithelium of the gastric and intestinal mucosa after mucosectomy thus takes place on account of intact mucosa surrounding the defect, i.e., by sliding from the periphery; this is particularly clear from the results of the experiments with the types 1 and 2 operations. At the same time, the possibility of implantation of epithelial cells cannot be ruled out, for the end result of regeneration would probably be the same after both sliding and implantation of epithelial cells on the denuded surface.

After the type 3 operation regeneration of the epithelium did not take place from the remaining cells and, since no epithelium was present at the periphery of the denuded area, the "gastric pouch" was obliterated.

The type 4 operation was carried out in order to discover whether regeneration can take place from implanted cells. If the mucosa had regenerated within the area of the denuded gastric graft, that would have proved that regeneration takes place from implanted cells capable of "stepping across" the circular jejunal autograft. However, the regenerating mucosa was intestinal. Further proof was thus obtained that regeneration under these experimental conditions takes place entirely through sliding of epithelial cells surrounding the zone of the operation over the denuded surface.

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DISTRIBUTION OF LYSOSOMAL ENZYME ACTIVITY IN CORTICAL CELLS OF THE KIDNEY AFTER SUBCAPSULAR TRANSPLANTATION OF ALLOGENEIC SPLEEN CELLS

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Following injection of allogeneic spleen cells beneath the renal capsule of mice irradiated in a dose of 650 R structures of the renal cortex were damaged. This effect was closely connected with the function of macrophages and activation of the lysosomal enzymes.

KEY WORDS: macrophages; lysosomes; renal cortex; local graft versus host reaction; acid phosphatase.

In recent years considerable attention has been paid to the study of reactions of cellular immunity, which play an important role in widespread pathological processes such as allergic states [1, 2, 17], autoimmune diseases [3, 12], and phenomena of tissue incompatibility [6, 11]. In some context new models have been developed in order to study these reactions in greater detail and depth. One such model is the recently suggested local renal graft versus host reaction [13, 14].

Considering the important role of lysosomal enzymes in the formation of reactions of cellular immunity [4, 8, 9], and also the fact that the histochemical distribution of the enzymes and the degree of their activity can provide an indication of the various functional states of the cell, including injury to it [5, 10], it was decided to study the distribution of activity of the lysosomal marker enzyme acid phosphatase (AcP) in the kidney cells during the local graft versus host reaction.

EXPERIMENTAL METHOD

Adult C57 Bl mice (H-2^b histocompatibility locus) were used as donors and adult CBA mice (H-2^k) as recipients. The recipients were irradiated on the RUM-11 apparatus under the following conditions: voltage 180 kV, current 10 mA, filters 0.5 mm Cu and 1 mm Al, skin-focus distance 60 cm, dose rate 10 R/min. The total dose of irradiation was 650 R. An extraperitoneal (lumber) approach was made to the left kidney under ether anesthesia 24-36 h after irradiation and 35×10^6–45×10^6 allogeneic donors' spleen cells in 0.1-0.2 ml medium No. 199 were injected beneath its capsule.

The cell suspension from the donor mouse was obtained by pressing spleen tissue (after first incising the capsule) through a Kapron filter in medium No. 199 at 0-4°C. The number of viable cells was determined by the trypan blue test (80%).

Animals undergoing a mock operation and mice into which syngeneic or disintegrated allogeneic spleen cells were transplanted were used as the control. Sections through the kidneys of the control and experimental animals were stained with hematoxylin–eosin, with Methyl Green and pyronine by Brachet's method, and for AcP by Gomori's method.

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