HISTOLOGICAL CHANGES IN THE SMALL INTESTINE TRANSPLANTED SUBCUTANEOUSLY

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The structure of the small intestine, transplanted subcutaneously on a vascular pedicle, and of a free graft consisting of the mucosa and submucosa only, was studied in experiments on dogs. The degree to which the graft tissues survived was directly dependent on their distance from the vascular pedicle. The free intestinal graft died and was replaced by scar tissue.

The small intestine is regarded as the best plastic material for the reconstructive surgery of the esophagus [7, 12-16]. However, a serious disadvantage of the small intestine for plastic purposes is the unsatisfactory blood supply of the graft. Various methods have been used to improve its blood supply: a Filatov's stalk [9, 11], transplantation of a segment of intestine subcutaneously [8], formation of a collateral circulation from the omentum [4, 5], and incisions in the intestinal wall [1].

This paper describes the results of a histological study of the small intestine in which different parts of the organs differed in their conditions of nutrition. Attempts were made to lengthen the small intestinal graft and to improve its blood supply by removal of the serous and muscular coats over a large area. Other experiments were carried out to study the fate of a free graft of a segment of small intestine from which the mesentery and serous and muscular coats had been removed.

EXPERIMENTAL METHOD

Three series of experiments were carried out on 23 dogs. In series I a segment of small intestine, 12-15 cm in length, was taken from 8 dogs on a vascular pedicle, consisting of one arteria recta and the homonymous vein, without removal of its outer membranes. The remaining mesenteric vessels of this segment of small intestine were ligated and divided close to the intestinal wall. Continuity of the intestine was restored by end-to-end anastomosis. A subcutaneous pouch was constructed on the right side of the abdominal incision, of the same length as the intestinal graft prepared for insertion into it. Both ends of the graft were exteriorized through skin incisions and sutured to the wound edges. The intestinal graft and surrounding tissues were taken for histological investigation 1, 3, 6, 10, and 15 days after transplantation.

In series II, a segment of small intestine 12-16 cm in length also was grafted on a vascular pedicle in 12 dogs. For a distance of 10-14 cm the mesenteric vessels were ligated and divided and the serous and muscular membranes removed to accelerate ingrowth of vessels from the surrounding tissues. These membranes were left in situ only at one end of the graft for a distance of 2 cm, and 1 arteria recta and the homonymous vein were preserved. This vascular pedicle was initially the only blood supply to the grafted segment of intestine. Material was fixed 1, 5, 8, 10, 15, 19, 24, 27, 35, and 40 days after transplantation.

In series III a segment of intestine 7-8 cm in length was transplanted into a pouch on the anterior abdominal wall. The mesentery with its vessels and the serous and muscular membranes were removed from the whole length of this segment of intestine, so that the free graft doubled its length and consisted of

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mucosa and submucosa only. Both ends of the graft were exteriorized and sutured to the wound edges. Material was fixed 10, 15, 19, 24, and 27 days after transplantation.

In all series of experiments material for histological investigation was taken from the sacrificed dogs, fixed with 10% neutral formalin, and embedded in paraffin wax. Sections 7-8 μ in thickness were stained with hematoxylin and eosin.

EXPERIMENTAL RESULTS

The experiments of series I showed that 24 h after grafting changes developed in the small intestine, and their severity was directly proportional to the distance of the part of the graft from its end with an intact blood supply. The veins of the intestinal wall were dilated and congested with blood, the connective tissue of all layers of the intestine was permeated with erythrocytes, and the epithelium of the villi had died. Small groups of viable epithelial cells still remained only here and there in the crypts. As the end of the graft with the vascular pedicle was approached, the number of hemorrhages and the degree of venous stasis diminished and the mucosa gradually regained a more normal appearance, but the villi in these areas were shortened. Necrobiotic changes were found in the mucous membrane where it was in contact with the skin. Macroscopically, during the first 2 days this end of the graft appeared cyanotic, but later it regained the usual pink color of the intestinal mucosa. The crypts bordering on this part of the mucosa were turned toward the junction between the intestine and skin, an early sign of regenerative changes in the intestinal mucosa [2, 3].

During the first 3 days the end of the intestinal graft which had lost its blood supply and was farthest from the opposite end still supplied with blood, died and sloughed away on the 4th-5th day, and the skin wound above it gradually epithelized. In the middle part of the graft, regeneration began to take place in the mucous membrane against the background of well-defined degenerative and necrobiotic changes. The cells of the crypts began to proliferate intensively. Bands of a single layer of flat, cubical, or prismatic cells, lining the cavities or covering the newly formed villi, began to appear. In areas with a high prismatic epithelium, in places this became pseudostratified in character. In every case the epithelium of the regenerating areas of intestine had no brush border, no did it contain goblet cells. The foci of enterodermal regeneration were separated from the persistent areas of necrotic mucosa by newly formed granulation tissue. The regenerative changes in the mucous membrane were focal in character.

Regeneration of the intestinal epithelium was more intensive still at the end of the graft retaining its vascular pedicle and lying next to the skin. Differentiated layers of intestinal epithelium, one cell in thickness, spread along the border with the necrotic end of the graft to form multiple tubes and gradually to cover the bare mucous membrane. The villi in these areas were shorter than normally. Considerable changes were observed during the first 3-5 days at the border between the skin and intestine. To begin with, the space between them was filled with fibrin, leukocytes, and fibroblasts. Gradually a layer of granulation tissue developed between the skin and intestine. After 6 days, goblet cells and cells with a brush border appeared in the foci of epithelial regeneration and in the newly formed covering of the villi, and crypts were formed. The outline of the mucous membrane of the graft after 10-15 days began to resemble that of the normal intestinal mucosa.

The experiments of series II showed that soon after grafting, differences between the structure of the mucosa in different parts of the small-intestinal graft, differing in their blood supply, began to appear and gradually became more definite. The mucous membrane in the middle third of the transplanted intestine remained intact. However, changes were seen in its relief, the villi were shortened, and the connective tissue permeated by erythrocytes. At the end of the intestinal graft farthest from the nutrient artery, the mucous membrane was dead on the 5th day. After 10 days the differences between the structure of parts of the graft with different conditions of nutrition were more marked still. The mucous membrane of the middle third of the grafted segment of intestine was now more normal in appearance, but at the end of the graft farthest from the nutrient artery it was replaced by granulation tissue.

The results of the experiments of series I and II showed that the length of graft still remaining viable was about equal, namely 5-6 cm. In the region of contact between the skin and end of the intestinal graft with a vascular pedicle, regeneration led after 10-15 days to the formation of union between the epithelia of the skin and intestine [2, 6, 10]. The importance of preservation of the blood supply, even at only one end of the segment of transplanted intestine, is clear when the results of the experiments of series I and II are compared with those of series III. The mucous membrane of the free graft (series III) died rapidly,

and by the end of the 2nd week was replaced by granulation tissue. Only a band consisting of connective scar tissue remained in its place.

Although removal of the serous and muscular membranes (series II) led to a valid improvement in the blood supply of the graft on a vascular pedicle, this was not the only condition for preservation of the histological features of the grafted mucous membrane. A more important factor, especially in the early stages after transplantation, was the integrity of the vascular pedicle, even though it supplied blood only to one end of the graft.

Roentgenograms of the intramural vessels of the small intestine of the dogs showed that they were 3.5-4 cm in length. It can be concluded from the results of the experiments in series I and II that the pedicle graft remained viable for a distance of 5-6 cm in that part of it which was without a mesenteric blood supply. The ischemia developing in the absence of an extramural blood supply probably gave rise to conditions favoring manifestation of the compensatory and adaptive reactions of the intramural vessels. Consequently, the length of the segment of small intestine remaining viable was 1.5 times greater than the length of the intramural vessels. A role of definite importance in the blood supply to the graft was also played by blood vessels growing in from the surrounding tissues [1]. Removal of the serous and muscular membranes did not improve the blood supply to the attached intestinal graft. The results of series III indicate that free grafting of the intestine is useless.

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