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REGENERATION OF THE MUCOSAL LINING OF THE ESOPHAGUS

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In the human embryo the esophagus is initially lined with stratified columnar epithelium which later becomes ciliated. The columnar epithelium is replaced by squamous epithelium in process which begins in the middle third of the esophagus and spreads proximally and distally to cover the entire esophageal lumen.¹ The presence of columnar epithelium in an adult esophagus is an unusual finding. In all of the clinical cases with which we are familiar, it has been associated with hiatus hernia, reflux esophagitis and stricture formation, as in the cases described by Allison and Johnstone.²

It has been suggested by some writers, notably Hayward,³ that the columnar epithelium in these patients is the result of metaplasia in response to the erosive effect of gastric secretions entering the esophagus because of a faulty esophagogastric sphincter mechanism. Barrett,⁴ on the other hand, holds that the columnar lined esophagus is a congenital abnormality. He states, “If the squamous epithelium be removed from the esophagus of a dog, the raw surface is soon covered by squamous epithelium again”. Because of our interest in the cause of the columnar-lined esophagus, this study was undertaken.

MATERIAL AND METHODS

Ten dogs were used in the study. Under general anesthesia, the esophagus and stomach were mobilized through a left intercostal incision. The esophagus was opened longitudinally and a circumferential piece of mucosa and submucosa 2 centimeters long was taken out by sharp dissection. The resection was made just proximal to the mucosal junction of the esophagus and stomach, the lower edge of the excision being in juxtaposition to the gastric mucosa. The esophageal wall incision was closed with interrupted silk sutures and the esophagus and stomach restored to their normal anatomical position. The animals were given a diet of milk and soft food postoperatively.

RESULTS AND OBSERVATIONS

Two of the dogs were sacrificed electively at the end of the first postoperative week. One was sacrificed at the end of the second week. Five died during the third postoperative week of esophageal obstruction from stricture formation. Two animals survived without developing stricture and were sacrificed 4 weeks after operation.

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Figure 1
Esophageal wall immediately after mucosal excision. The submucosa with its mucus glands is removed along with the squamous lining leaving only the circular and longitudinal muscle layers.

Figure 2
Regeneration of the squamos epithelium 2 weeks after resection. The submucosal glands terminate to the right of the slide, marking the upper limit of the resection. There is no regeneration of the submucosal glands or the muscularis mucosae. There is a thin layer of regenerating epithelium projecting down from the proximal cell margin.
Figure 3a
Completely regenerated mucosa 4 weeks after resection. The regenerated surface is entirely squamous.

Figure 3b
Section from proximal part of the specimen. Note junction of normal and regenerated mucosa.
Distal or gastric side of same specimen. Resection was carried down to gastric mucosa as indicated by mucus gland pattern. There is no proximal growth of gastric epithelium.

Since the resection was carried out in the natural tissue plane between the submucosa and the circular muscle layer, the esophageal wall in the area of resection consisted only of the muscle layers as shown in Figure 1. As healing occurred, the squamous cell layer migrated over the denuded surface, but the submucous glands, which are numerous in the dog, did not regenerate (Figure 2). Therefore, the area of regenerated mucosa could be measured as that surface with a thin squamous cell covering, but no mucus gland substrate. The rate of growth of the squamous epithelium was approximately 4 millimeters per week. The 2 centimeter resected area was completely covered at the end of the fourth week, the remaining distance being taken up by contracture. At two weeks a thin layer of epithelium could be seen coming down from the squamous side, but there was no corresponding upward migration from the gastric side (Figure 3). The specimens with complete mucosal regeneration showed the entire process to consist of squamous epithelium.

A process of fibrous contracture occurring simultaneously with mucosal regeneration caused obstruction of the esophagus and death in 50 per cent of the animals in the third postoperative week. The 2 centimeter gap between the upper and lower limits of the mucosal resection was reduced by about one-half in these specimens (Figure 4).
Animal which died of stricture 3 weeks after resection. Considerable regeneration is present in some areas and downward extensions of squamous epithelium are grossly visible. Note the decrease in the length and width of the resected area.

**COMMENT**

The process of mucosal regeneration exhibited no columnar cell component in spite of the proximity of the gastric mucosa to the lower border of the resected area. As the submucosa was removed along with the mucosa, the possibility of upward growth of columnar cells from the submucosal glands to cover the defect was obviated. This has been suggested as a possible method of formation of a columnar lined esophagus. In addition, as the esophagogastric sphincter mechanism was probably not affected by the mucosal resection, the factor of gastric reflux was not involved in these experiments. The process of mucosal regeneration was relatively rapid and efficient enough to cover a sizeable raw surface providing the caliber of the esophageal lumen was not critically reduced in the meantime.

**CONCLUSIONS**

1. After resection of the mucosa of the normal canine esophagus, there was a rapid regeneration of squamous cells in an attempt to cover the defect.

2. There was no regeneration of the glands of the submucosa which was removed along with the epithelium.
3. The rate of regeneration of the squamous cell layer was about 4 millimeters per week.

4. Although the gastric mucosa formed the lower border of the resected area, no upward growth of gastric cells took place to cover the defect.

5. In 50 percent of the animals simultaneous with cell regeneration on the mucosal surface, a process of fibrous contracture took place causing death in the third postoperative week from esophageal obstruction.

REFERENCES


