Thorax (1975), **30**, 152.

Local ablative procedures designed to destroy squamous-cell carcinoma[1]

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Lee, J. M., Stitik, F. P., Carter, D., and Robinson Baker, R. (1975). *Thorax*, **30**, 152–157. **Local ablative procedures designed to destroy squamous-cell carcinoma.** In a series of experiments in dogs, the bronchial mucosa was either excised or destroyed prior to closure of a bronchial stump following a lobectomy or the reanastomosis of a divided bronchus. The experiments were designed to simulate the clinical situation in which focal areas of squamous-cell carcinoma in situ in the bronchial margin would be managed by local ablation of the mucosa rather than by excision of additional bronchus. The experiments demonstrated that the bronchial mucosa is not necessary for bronchial healing. They also demonstrated that functionally and morphologically normal bronchial epithelium regenerates across the denuded bronchus. The source of this regenerated epithelium appears to be the submucosal glands which remain in the bronchial wall after a variety of local ablative procedures. Since our clinical experience has demonstrated that these submucosal glands frequently contain small foci of squamous-cell carcinoma in situ, we have concluded that either excision or thermal destruction of the bronchial mucosa has very limited clinical application and should be considered only in patients who cannot tolerate excision of more than one lobe of the lung.

Our experience with a small series of early lung cancers has recently been reported (Baker *et al.*, 1974). Four patients with normal chest radiographs were found to have cells shed from a squamous-cell carcinoma in their sputum. The source of these cells was localized by fiberoptic bronchoscopy to a specific lobar bronchus. These microinvasive carcinomas were excised by an initial lobectomy in all four cases. However, in three of these four cases the initial lobectomy had to be extended to a bilobectomy, pneumonectomy, and sleeve resection in order to excise persistent foci of squamous-cell carcinoma in situ in the bronchial margin. This clinical experience has stimulated us to investigate the possibility of developing local ablative procedures which would destroy the squamous-cell carcinoma in situ in the bronchial mucosa and thus permit conservation of large areas of distal lung parenchyma.

METHOD

The initial experiments (group I) were designed to determine if the bronchial mucosa is necessary for healing of a bronchial stump following a lobectomy. These experiments were designed to simulate the clinical situation in which squamous-cell carcinoma in situ is found in the bronchial margin following excision of a squamous-cell carcinoma arising in a segmental bronchus or lower lobe bronchus. The second group of experiments (group II) were designed to determine the feasibility of excising the bronchial mucosa from a main stem bronchus and then reanastomosing the denuded bronchus. This second group of experiments simulated the clinical situation in which squamous-cell carcinoma in situ is found in the bronchial margin following an upper lobectomy.

In both groups of animals, bronchial healing was evaluated by clinical observation and tantalum bronchography. Tantalum is an inert powder that is cleared by the tracheobronchial tree solely by mucociliary action. Tantalum bronchography thus provides a means of assessing the function of regenerated bronchial epithelium as well as a means of assessing bronchial healing. The tantalum bronchograms were performed through an endotracheal tube, and tantalum powder was

[1]Supported by National Cancer Institute Contract NIH 69-2172

insufflated into the bronchial tree with a controllable Medi-Teck catheter. After adequate deposition, anterior–posterior, lateral, and both oblique radiographs of the chest were obtained.

GROUP 1 The first series of experiments were carried out in 15 dogs. A left lower lobectomy was performed in all 15 animals leaving a 2-cm bronchial stump (Fig. 1). In five of these dogs, the distal 2 cm of bronchial mucosa was destroyed by electrocoagulation. In another five animals, the distal bronchial mucosa was destroyed with the cryosurgical probe set at −160°C and applied to the mucosa for four minutes. In the remaining five animals, the bronchial mucosa was excised. A specimen of the excised or destroyed mucosa and one cartilage ring of the denuded bronchus were submitted for histological study immediately following these procedures. The remaining denuded bronchus was closed with interrupted sutures of 4-0 Tevdek. Tantalum bronchograms were performed one month postoperatively. All animals were followed for six months and then necropsied.

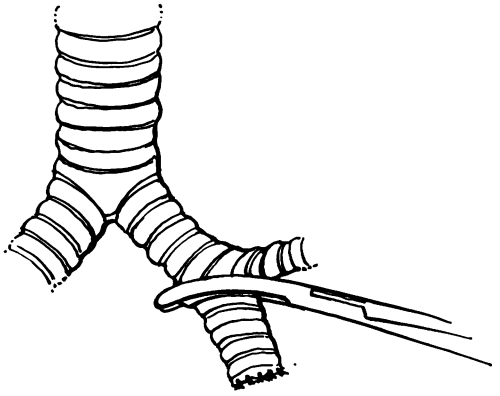

FIG. 1. *The left lower lobe bronchus was occluded with a bronchial clamp, and following a left lobectomy the distal 2 cm of bronchial mucosa was either excised or destroyed prior to closure of the bronchial stump.*

GROUP II In another group of five dogs, the left main stem bronchus was occluded just distal to the carina and divided proximal to the origin of the left upper lobe bronchus (Fig. 2). The bronchial mucosa of the left main bronchus was circumferentially excised from the bronchial clamp to the edge of the divided bronchus. The excised specimen of bronchus plus one cartilage ring were submitted for histological section. The left main stem bronchus was then reanastomosed with interrupted sutures of 4-0 Tevdek. Tantalum bronchograms were performed six months postoperatively and the animals were necropsied ten days after bronchography.

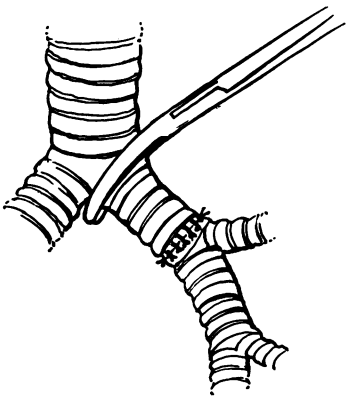

FIG. 2. *The left main stem bronchus was occluded with a bronchial clamp and divided proximal to the origin of the left upper lobe bronchus. Prior to reanastomosis, the bronchial mucosa was excised from the entire main stem bronchus.*

RESULTS

GROUP I All 15 animals recovered without complication. Tantalum bronchograms performed one month postoperatively revealed no evidence of disruption of the bronchial suture line. The tantalum was promptly cleared from the bronchial stump. Histological sections of the remaining bronchus after stripping, electrocoagulation, and cryosurgical destruction immediately after surgery demonstrated that all of the techniques used to destroy the bronchial mucosa, whether surgical or thermal, destroyed most but not all of the submucosal glands (Fig. 3). Histological sections of the necropsy material revealed that these bronchial glands extended to the bronchial cartilage so that total excision of the glands would require excision of the cartilage (Fig. 4).

GROUP II These five animals recovered from the operative procedure without complication. Tantalum bronchograms performed six months postoperatively demonstrated healing in all instances. The fine mucosal detail afforded by tantalum bronchography demonstrated minimal nodularity at the site of the anastomosis in four animals and only minimal stricture formation. The tantalum powder was promptly cleared from the main stem

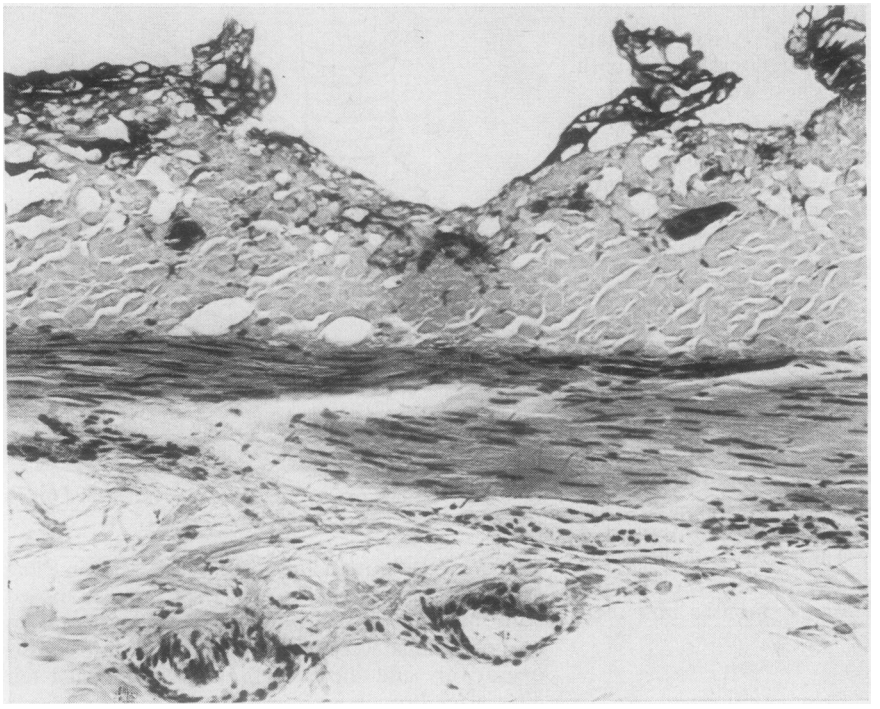

FIG. 3. *Bronchial biopsy from a group I dog obtained immediately following electrocoagulation of the bronchial mucosa. Note destruction of surface epithelium at the top but two intact submucosal glands in the submucosa. Haematoxylin and eosin* ×195.

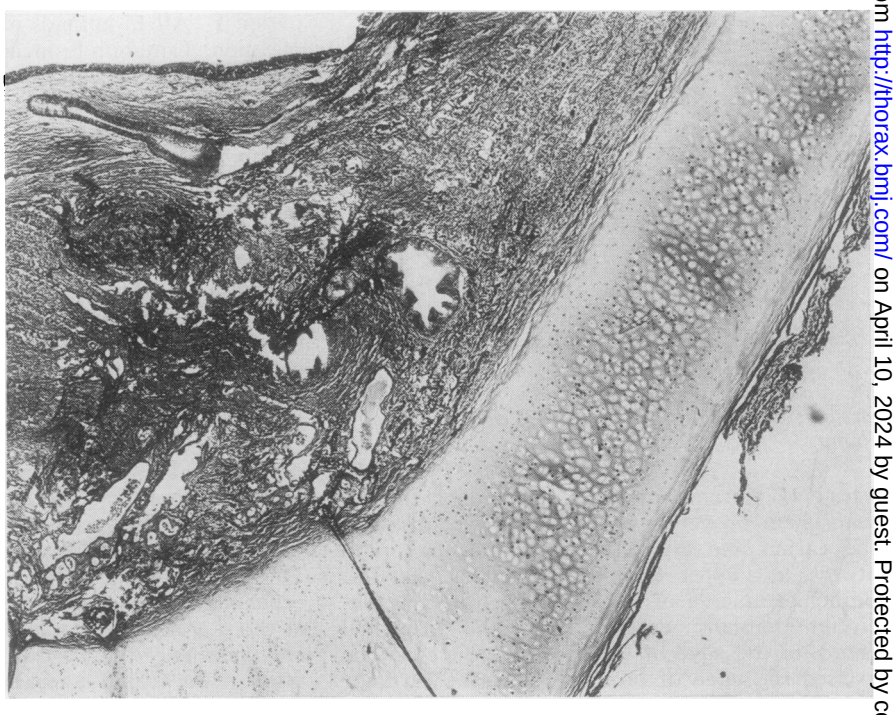

FIG. 4. *Dog bronchus examined at necropsy from a group I animal. Bronchial mucosa has been surgically removed and healing has occurred. Note scar overlaying distorted submucosal glands which lie adjacent to bronchial cartilage. H and E* ×25.

bronchus, indicating that the regenerated bronchial mucosa had a normal mucociliary action (Fig. 5). In one dog a severe bronchial stricture was demonstrated at the site of the anastomosis. Tantalum appeared to pool in the bronchus immediately distal to the anastomosis but eventually the tantalum was completely cleared across the anastomosis (Fig. 6).

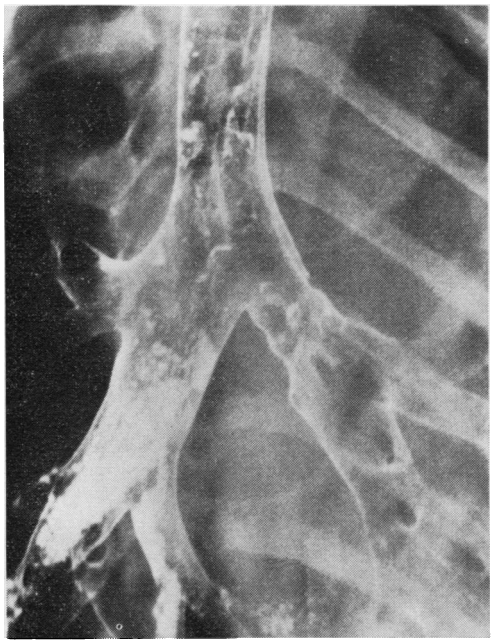

FIG. 5. *Tantalum bronchogram. Oblique radiograph demonstrating minimal nodularity in the left main stem bronchus at the site of anastomosis.*

Histological sections of the excised mucosa and of the cartilage rings immediately following the operative procedure again revealed that histologically normal submucosal glands were present adjacent to the bronchial cartilage and also in focal areas between the bronchial cartilage rings. Histological sections of the healed bronchus obtained at necropsy revealed that the surface was covered by a layer of epithelium which varied from low cuboidal epithelium to an epithelium which was indistinguishable from normal ciliated columnar respiratory epithelium. This ciliated epithelium was in continuity in some areas with that of the submucosal glands (Fig. 7).

DISCUSSION

The first group of experiments demonstrated that

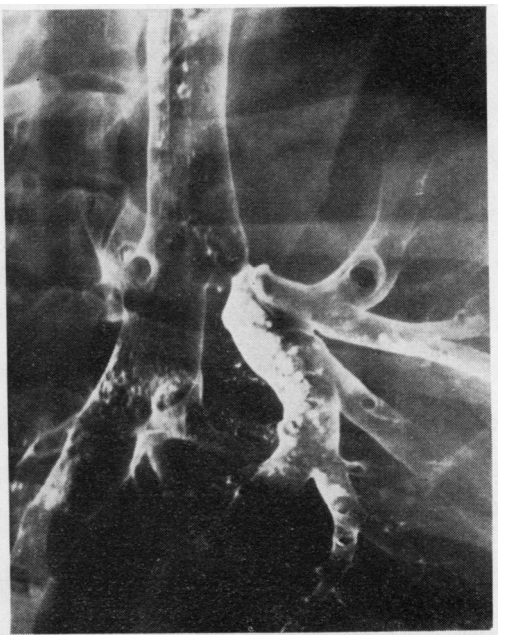

FIG. 6. *Tantalum bronchogram. Oblique radiograph showing severe stenosis in the left main stem bronchus at the site of anastomosis. A moderate amount of tantalum-coated mucus is pooled distal to the anastomosis.*

bronchial closure can be obtained in the absence of bronchial mucosa in the bronchial stump. Bronchial stripping or local thermal ablation of the mucosa in the bronchial stump removed or destroyed all of the surface epithelium. These procedures also removed or destroyed almost but clearly not all of the submucosal glands. Clinical application of this technique would be hazardous therefore, because in our clinical material these submucosal glands frequently contain foci of squamous-cell carcinoma in situ (Fig. 8).

The second group of experiments demonstrate that the bronchial mucosa of a main stem bronchus can be circumferentially excised and the bronchus subsequently successfully reanastomosed. If the mucosal excision is accomplished without damage to the underlying cartilage, the anastomosis heals without stricture formation. Damage to the cartilage in the course of the bronchial stripping resulted in stricture formation at the site of the anastomosis. The regenerated bronchial epithelium has a normal mucociliary action and is capable of clearing tantalum. The source of the regenerated epithelium appears to be the epithelium in the residual foci of deep

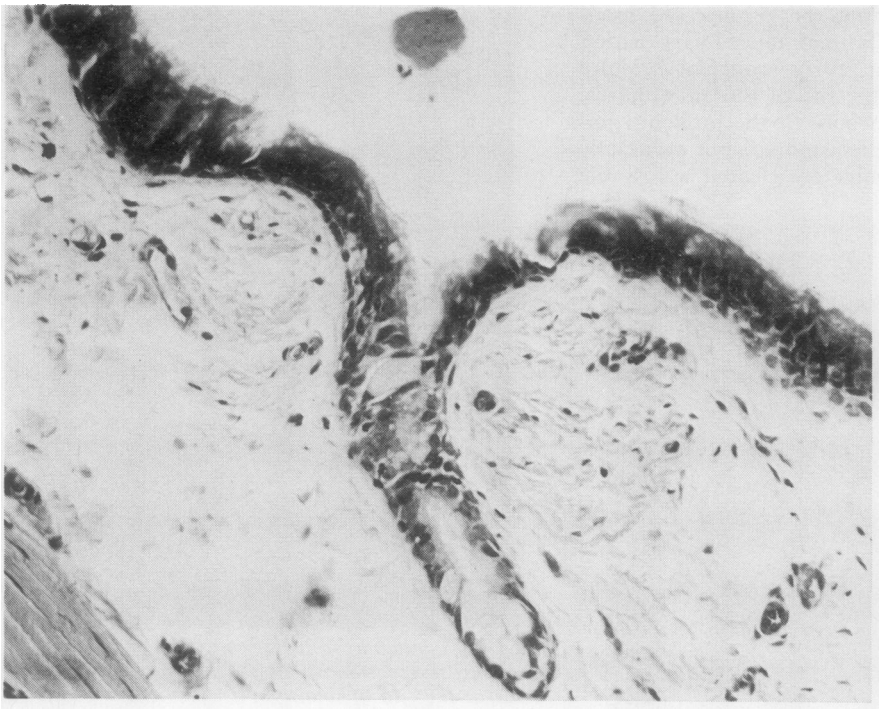

FIG. 7. *Healed bronchus from a group II animal. Note respiratory epithelium on the surface in continuity with a submucosal gland. H and E* ×275.

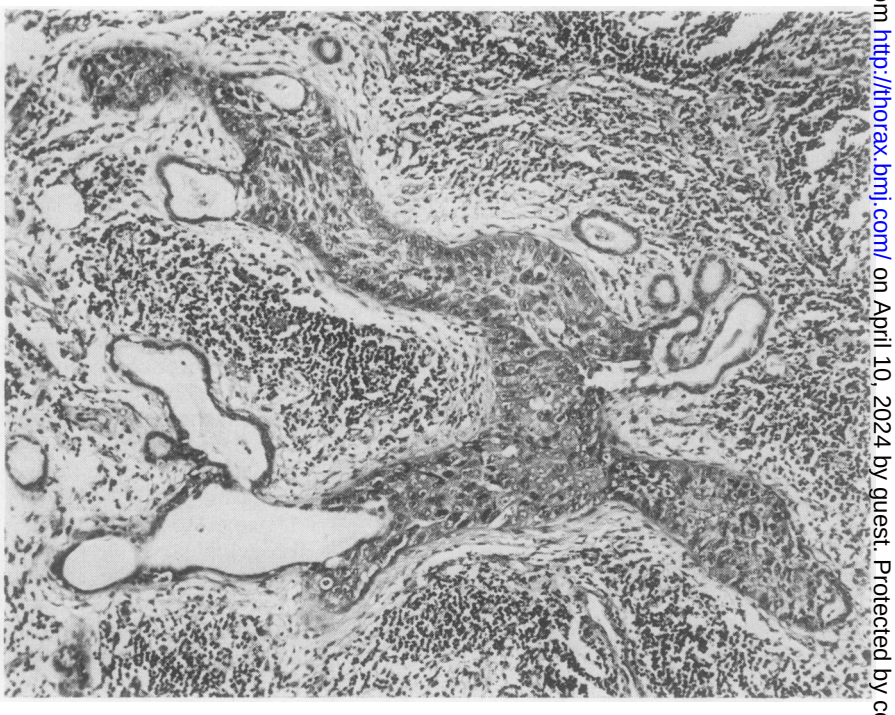

FIG. 8. *In situ squamous-cell carcinoma partially filling bronchial glands in the submucosa of a lobar bronchus. These sections were obtained from a patient with malignant cells in the sputum and a normal chest radiograph. A microinvasive squamous-cell carcinoma was present in the lobar bronchus distal to the in situ lesion in the bronchial glands. H and E* ×100.

submucosal glands which remian following the stripping procedure. Unfortunately, in the clinical situation the submucosal glands may also be the site of residual squamous-cell carcinoma in situ. In view of the results of these experiments we have concluded that excision of focal areas of squamous-cell carcinoma in situ in the bronchial stump or stripping of segmental areas of the bronchial mucosa in a major bronchus has very limited clinical application. These procedures should be considered only in patients with poor pulmonary function who could not tolerate excision of more than one lobe of their lung. In this specific situation local ablative procedures may have some clinical application.

REFERENCE

Baker, R. R., Marsh, B. R., Frost, J. K., Stitik, F. P., Carter, D., and Lee, J. L. (1974). The detection and treatment of early lung cancer. *Annals of Surgery*, **179**, 813.

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