Experimental Repair of Tracheal Defects with Gallbladder Mucosa

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Surgical treatment of malignant and certain benign lesions of the trachea may require plastic reconstruction or segmental replacement. The ideal of a rigid yet elastic tube compatible with the tracheal environment remains a problem of great challenge. In spite of outstanding success with prosthetic materials in arterial replacement there has been no satisfactory solution to tracheal reconstruction with either prosthetics or host tissues. The most promising results have utilized inert materials for support of the lumen with or without the addition of covering tissue.

In an effort to use the prosthetics only as a temporary support, investigation was undertaken of the possible adaptation of host tissues with osteogenic properties. Early experimental work of Huggins demonstrated the specific ability of urinary tract epithelium to induce new bone formation in ectopic locations. Following the report of Rush, who employed portions of urinary bladder mucosa for tracheal reconstruction, our preliminary studies demonstrated the gallbladder to have similar osteogenic potential.

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FIGURE 1: Types of tracheal prosthesis: No. 1—Ivalon and stainless steel mesh, No. 2—Nylon springs, No. 3—Nylon rings in Silastic, Nos. 4 and 5—Nylon, No. 6—Teflon, Nos. 7, 8 and 9—Polyethylene.
Methods

Healthy adult mongrel dogs weighing between 11 and 25 kg. were anesthetized with pentobarbital. All operative procedures were performed on the cervical trachea under sterile conditions. In experiments using gallbladder mucosa a cholecystectomy was performed first. The seromuscular layer was stripped from the underlying biliary mucosa prior to its implantation in the neck. Following the insertion of the prosthesis the epithelium was then wrapped about it, placing the mucosa side out and suturing the edge of the autograft to the cut ends of the trachea with a running suture of fine catgut or wire.

In creating window defects a section one-third to two-thirds of the circumference and 5 cm. long (length of three cartilages) was excised. Segmental or sleeve resections were usually 5 to 7 cm. in length (three to four cartilages). In early experiments an attempt was made to anastomose the prosthesis end on to the cut ends of the trachea. As experience was gained and the prosthesis was improved (Fig. 1) endoluminal insertion was employed. Transfixion of the prosthesis, tracheal wall and adjacent tissues with mattress sutures of steel wire proved to be the best method for fixation.

Each experimental animal was bronchosoped at intervals of one month or whenever indicated by obstructive symptoms. Every tissue implant was examined histologically from biopsy or necropsy specimens.

Results and Observations

Series 1. Stainless Steel Wire Mesh and Ivalon Prosthesis With or Without Gallbladder Mucosa

FIGURE 2: Interior view of window defect with Ivalon and stainless steel wire mesh prosthesis prolapsed into lumen.
Nine dogs were used in this series. In four animals a window defect was produced in the cervical trachea. The defect was repaired with a patch of wire mesh and Ivalon and covered with gallbladder epithelium. In each instance the patch pulled loose from the margin of the defect (Fig. 2) and prolapsed into the lumen at intervals of three to five months. Attempts to remove the prosthesis via the bronchoscope were unsuccessful and reoperation was necessary. The gallbladder mucosa had formed a cartilagenous bony plate over the defect which maintained the conformity of the tracheal wall (Fig. 3 and 4). The luminal surface revealed satisfactory epithelization (Fig. 5).

The remaining five animals had sleeve resection of the trachea. Each animal subsequently expired from respiratory obstruction at intervals of six days to five and one half months.

In each instance the tracheal stenosis, whether acute or chronic was due to inadequate fixation of the prosthesis. There was no evidence of healing at the junction of the prosthesis and severed end of the trachea. The prosthesis was often found to have pulled away from one or both ends of the trachea in spite of careful suturing. In the animals surviving for longer periods a ring of granulation tissue usually developed at this junction and protruded into the lumen, contributing to the cicatricial stenosis (Fig. 6).

**Series II. Ivalon and Gallbladder Muscosa**

Four animals were used in this group. In two window defects were created and replaced with patches of compressed Ivalon (4 to 1) often supported with wire and overlaid with gallbladder mucosa. The neck in one animal was re-explored for biopsy at four weeks to determine how early osteoid or chondroid tissue would develop. This animal was subsequently sacrificed at six months. The implant area in the second dog was explored for biopsy at 60 days and the animal sacrificed at 62 days for study. The remaining two dogs with window defects survived periods of six weeks and two months respectively. In each instance the Ivalon and/or part of the autografted mucosa had sloughed or prolapsed into the tracheal lumen with subsequent local and pulmonary sepsis and obstructive death.

**Series III. Nylon Spring Prosthesis With Fascia or Gallbladder Muscosa**

Six dogs underwent segmental resection of the cervical trachea. Specially fabricated nylon springs varying from 3/8-inch to 3/4-inch in diameter were used as the prosthesis (Fig. 1). Difficulty was experienced with fixation of the springs. Although mobility of the prosthesis was excellent, there was a tendency for the spring to telescope on itself. Two springs became detached at their proximal end and a third was coughed out, resulting in an obstructive death as the residual fibrous tube collapsed. Fascia implanted about this prosthesis was slower to gain a blood supply and thus was more liable to necrosis than gallbladder mucosa. Survival in this group varied from six days to two months.

**Series IV. Silastic Prosthesis With or Without Gallbladder Muscosa**

The results in three dogs with a prosthesis fabricated of nylon rings embedded in Silastic* (Silicone rubber) were unsatisfactory. The longest surviving animal expired

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*Dow-Corning

![Figure 3A](https://example.com/figure3a.png)  ![Figure 3B](https://example.com/figure3b.png)

**FIGURE 3A:** Luminal view of window defect at three months. Gallbladder mucosa has formed osteoplastic roof. 3B—End-on view showing maintenance of lumen and paratracheal proliferation of fibrous tissue.
at two months. Failure again resulted from inadequate fixation of the prosthesis. Malposition of either end of the prosthesis resulted in a ring of infected granulation tissue which contributed to excessive secretions and the obstructive syndrome.

Series V. Polyethylene Prosthesis With Gallbladder Mucosa

Five animals in this group had implantation of a polyethylene prosthesis. In two, a straight tube 1/16 to 1/32-inch thick and 5 to 7 cm. long was used. More recently the tube has been fabricated to simulate the trachea. Crimping of the tube tends to increase its flexibility and decrease wall thickness. The posterior wall of the tube is flattened to correspond to the membranous trachea and avoid pressure on the esophagus. In several dogs partial esophageal obstruction resulted from too bulky a prosthesis. All of these animals have survived over six months and appear well, without stridor. Bronchoscopic examinations have revealed a clean lumen with epithelization.

Summary of Microscopic Findings

The first change of the gallbladder mucosa following this ectopic dis- position was cystic dysplasia. Microscopically, a biopsy at four weeks showed papillary mucosal remnants at the base of large cystic follicles. In many areas the cystic mucous glands had ruptured and coalesced into still larger cysts (Fig. 7). Scattered islands of pink staining chondroid or osteoid material appeared to be developing in proximity to the proliferating interstitial fibroblasts (Fig. 8). At six and 10 weeks the islands of chondroid or new cartilage were better developed at the base of the cystic spaces some of which were largely evacuated of mucin.

At seven months following repair of a window defect, a cross section revealed pink staining osteoid or chondroid material growing from the cut ends of the tracheal cartilage (Fig. 9). The gallbladder mucosa was still recognizable as papillary epithelium among the enormous cystic hyper-

![Figure 4](image_url)  
**Figure 4**: Large window defect at six months. Note excessive formation of fibrocartilagenous tissue in paratracheal area. Defect is completely filled with similar tissue.

![Figure 5](image_url)  
**Figure 5**: Luminal view of fenestra defect repaired with biliary epithelium showing complete epithelization at four months.
trophic of the mucous glands. Subacute and chronic inflammatory round
cells were present in the granulating tissue. New bone formation (endo-
chondral type) is also seen in areas distinctly removed from the margins
of proliferating tracheal tissue. On the luminal surface of the gallbladder
patch pseudostratified metaplastic squamous epithelium had regenerated
over the entire area (Fig. 10).

Discussion

Regardless of the type of tube used for the stent providing it is stable and of inert
material, a fibrous pseudotraheca forms from the cut ends. The tube thus formed
never gains a sufficient degree of rigidity to remain patent during respiration. The
hope in using implants of tissue with known osteogenic potential such as rib or in-
ter-costal pedicle for segmental tracheal replacement is the formation of a permanent
tube. With autografts capable of inducing bone formation by metaplasia of connective
tissue fibroblasts, urinary or gallbladder epithelium may offer the same possibility.

Many workers\textsuperscript{a-d} have used autografts for experimental or clinical replacement of a
tracheal or bronchial defect. Bronchial autografts are ideal but their use is limited
by their availability and unique clinical circumstances. Autografts of fascia, pleura
and periosteum have met with limited success. Wire-supported dural skin has proved
very satisfactory in the expert hands of Gebauer.\textsuperscript{e}

Although Rush\textsuperscript{f} in attempting to use the urinary bladder mucosa as a sheet around
a polyethylene stent noted new bone formation at 60 days, he was unable to gain
surviving animals when the stent was removed at three month intervals. The majority
of animals died of respiratory obstruction from marked edema in the submucosal
layers.

The possibility of using an autograft initially rigid such as cartilage, bone or a tissue
with osteogenic potential as periosteum has been explored by several investigators.
Pressman\textsuperscript{g} demonstrated healing of a section of decalcified bone implanted in an
anterior tracheal window. The same type of implant failed as a posterior window
due to lack of blood supply. Segmental replacement with a decalcified hollow bone
tube was also unsatisfactory as the fibrous tube which resulted from resorption of the
bone was non-rigid. Extending his earlier work,Pressman\textsuperscript{h} reported the success of
preserved dura mater and lyophilized homologous aorta in closing large tracheal de-
defects. Using these tissues about a polyethylene tube as a stent he obtained improved
healing and epithelialization of the mucosal surface.

The critical problem in maintaining the tracheal lumen following creation of a
large fenestration or ring defect is adequate fixation of the stent. Plastic tubes are
readily available and apparently present less of a mucous barrier than metallic

\textbf{FIGURE 6:} Malposition of a stainless steel wire mesh and Ivalon prosthesis. Ob-
structive granulations and stenosis at proximal end of implant site (2 1/2 months).
Whether a stent is used temporarily to permit healing of a non-rigid autograft or is allowed to remain as a permanent replacement, similar methods of fixation are required. The most frequent complication is migration of the stent to a subglottic position or local malposition. With excessive motion of the tube a ring of protuberant granulation tissue may form at either end. Pressman has noted that if the severed

![Figure 7](image1.png)  ![Figure 8](image2.png)

**FIGURE 7:** Photomicrograph of papillary hyperplasia and retention cysts of mucous glands of gallbladder mucosa. Island of new bone formation at four weeks. X 43

**FIGURE 8:** Photomicrograph of cystic dyplasia of mucosa. Island of osteoid or chondroid developing from subjacent fibroblasts in lamina propria at six weeks. X 400

![Figure 9](image3.png)  ![Figure 10](image4.png)

**FIGURE 9:** Photomicrograph of new cartilage regenerating from parent tracheal cartilage. Persistence of papillary hyperplasia and cysts of adjacent biliary mucosa at six months. X 43

**FIGURE 10:** Photomicrograph of regenerated pseudostratified squamous epithelium. Underlying the fibrous tissue layer is an island of metaplastic cartilage far removed from tracheal cartilage. Six months. X 43
ends of the trachea are allowed to heal to autografted tissue there is less tendency for
the proliferating granulation tissue to invade the lumen.

The survival of autografted tissue would appear to depend on the success of local
vascularization. With a large fenestra type defect in which it is possible to preserve
the posterior third of the tracheal circumference an intrinsic blood supply is possible.
In cylindrical replacement, survival of tissue implants appears to depend on establish-
ment of a blood supply from the adjacent strap muscles. Exposure of the ectopic
tissue to the bacterial flora of the tracheal lumen may jeopardize the implant sur-
vival. Although Rob and Bateman\(^16\) were moderately successful with the clinical use
of tantalum gauze covered on both sides by fascia lata, we have been unable to dupli-
cate these results in the laboratory. The margins of the splint show no evidence of
healing to the adjacent trachea and if the splint is semi-permeable the ingrowth of
granulation tissue contributes to ultimate stenosis. Our best results to date have been
with the straightly slightly modified polyethylene tube.

In agreement with the findings of Huggins and others, we were able to identify
new bone or cartilage after four weeks of implantation. Serial study up to six months
reveals a progressive increase in the amount and maturity of the endochondral bone.
Although these scattered islands lend support to the fibrous tube, it has not been
demonstrated that such a tube is capable of complete replacement of ring defects
beyond two cartilages in length. Window defects and short cylindrical defects may
be successfully replaced by a variety of tissue autografts providing there is temporary
support.

Perhaps the most promising application for chondrogenic autografts is the treat-
ment of congenital tracheobronchial anomalies. A further use would be in repairing
localized areas of chondromalacia resulting from pressure of adjacent vascular
anomalies or benign tumors.

**SUMMARY**

1. New cartilage and bone formation may be consistently induced in the paratracheal
area by implantation of gallbladder mucosa.

2. With the use of non-rigid tissue autografts, temporary support of the tracheal
lumen with inert plastic tube stents is necessary.

3. Window defects are satisfactorily repaired with autografts of osteogenic poten-
tial. The assumption of a cartilagenous type of rigidity by the autograft permits
removal of the endoluminal stent.

4. Tissue autografts with osteo or chondrogenic induction capacity offer the possi-
bility of permanent rigid tube replacement of cylindrical tracheal defects. Such re-
placement has not yet been satisfactory in the absence of the stent support.

**RESUMEN**

1. Se puede provocar la formación de cartílago nuevo y de hueso de manera con-
stante, mediante la implantación de mucosa de la vesícula bilar.

2. Por el uso de autoinjertos de tejidos no rígidos, se requiere soporte temporal de
la luz tráqueal con tubos plásticos inertes.

3. Las ventanas por defecto se reparan satisfactoriamente con autoinjertos de
potencial osteogénico. Se supone que al obtenerse una rigidez del conducto de tipo
cartilaginoso, se puede retirar el tubo de soporte como féryula interna.

4. Los autoinjertos con capacidad para desarrollar huesos o cartílago, ofrecen la
posibilidad de substitución de los tubos rígidos en caso de defectos cilíndricos tra-
queales.

Tal substitución no ha sido aún satisfactoria sin el uso de los soportes de apoyo.

**RESUMÉ**

1. La formation de nouveau cartilage et d’os peut être provoquée d’une façon valable
da la zone paratrachéale par implantation de muqueuse de vésicule biliaire.

2. Avec l’emploi d’autogreffes de tissu non rigide, un support temporaire de la
lumière trachéale est nécessaire, avec un tube en plastique inerte.

3. Les altérations de la fenêtre sont réparées de façon satisfaisante avec des auto-
greffes à pouvoir ostéogénique. L’apparition d’une rigidité cartilagineuse de l’auto-
greffe permet la suppression du support endotrachéal.

4. Les autogreffes de tissu ayant un pouvoir de production ostéo ou chondrogénique
offrent la possibilité de remplacer par un tube rigide permanent les altérations trach-
éales cylindriques. Un tel remplacement n’a pas encore été satisfaisant en l’absence
d’un support solide provisoire.
ZUSAMMENFASSUNG


REFERENCES


