Management of Adult Benign Laryngotracheal Stenosis

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For the Degree MD (Res)

‘I Gurpreet Singh SANDHU confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.'

signed
Abstract

Upper airway stenosis has a significant impact on the quality of life and sometimes on life itself. The incidence of this condition is likely to be increasing as survival rates following periods of ventilation on Intensive Care Units (ICUs) improve (1, 2).

Paediatric laryngotracheal stenosis is a well researched discipline and treatment includes airway augmentation with rib grafts and tracheal or cricotracheal resection with end-to-end anastomosis. At the start of my research, in 2005, adult laryngotracheal stenosis was poorly researched and the treatment options were tracheostomy, tracheal resection or cricotracheal resection, each with associated morbidity and mortality.

This thesis investigates the aetiology, incidence, screening and alternative treatment options, which include endoscopic techniques, for the management of acquired adult benign laryngotracheal stenosis. The commonest causes for this condition are ventilation on intensive care units and inflammatory disorders such as Wegener’s granulomatosis, idiopathic subglottic stenosis and sarcoidosis.

In January 2004 a prospective database was set up in the busiest airway reconstruction unit in the United Kingdom. Data was collected on all new adult patients with upper airways stenosis. At the completion of this research in January 2010, 400 patients had been entered on this database. Due to the rarity of this condition, it was not possible to design randomised trials to compare different treatment options.

This thesis is an integrated series of prospective cohort studies, with the aim of developing a greater understanding of adult airway stenosis, with a particular emphasis on minimally invasive endoscopic techniques.
This research has shown that 72% of patients with post-intubation airway stenosis can be treated with these minimally invasive endoscopic techniques. Effective new treatments have been devised for the management of inflammatory stenoses when the results of previous treatments had not been effective. New tools for assessing the airway and outcome measures have also been proposed.
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<th>Description</th>
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<tbody>
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<td>ABLS</td>
<td>Adult Benign Laryngotracheal Stenosis</td>
</tr>
<tr>
<td>ACA</td>
<td>Angiotensin Converting Enzyme</td>
</tr>
<tr>
<td>ADVS</td>
<td>Airway, Dyspnoea, Voice, Swallowing</td>
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<td>AEF</td>
<td>Aryepiglottic Folds</td>
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<td>ANA</td>
<td>Antinuclear Antibody</td>
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<td>ANCA</td>
<td>Anti-Neutrophil Cytoplasmic Antibody</td>
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<tr>
<td>ASA</td>
<td>American Society of Anesthesiologists</td>
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<tr>
<td>BMI</td>
<td>Body Mass Index</td>
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<tr>
<td>BVAS</td>
<td>Birmingham Vasculitis Activity Scale</td>
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<tr>
<td>BVCMI</td>
<td>Bilateral Vocal Cord Mobility Impairment</td>
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<td>BVFI</td>
<td>Bilateral Vocal Fold Immobility</td>
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<tr>
<td>BVFP</td>
<td>Bilateral Vocal Fold Palsy</td>
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<tr>
<td>CAJ</td>
<td>Cricoarytenoid Joint</td>
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<tr>
<td>cANCA</td>
<td>Cytoplasmic-pattern Anti-Neutrophil Cytoplasmic Antibody</td>
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<tr>
<td>CCQ</td>
<td>Clinical COPD Questionnaire</td>
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<tr>
<td>CO2</td>
<td>Carbon Dioxide</td>
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<td>COPD</td>
<td>Chronic Obstructive Pulmonary Disease</td>
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<td>CPET</td>
<td>Cardiopulmonary Exercise Testing</td>
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<td>CT</td>
<td>Computed Tomography</td>
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<tr>
<td>D</td>
<td>Dyspnoea</td>
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<td>D&amp;D</td>
<td>Dyspnoea and Dysphonia</td>
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<td>Decan</td>
<td>Decannulation performed</td>
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<tr>
<td>E</td>
<td>Epiglottis</td>
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<tr>
<td>EAT-10</td>
<td>Eating Assessment Tool</td>
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<td>ECG</td>
<td>Electrocardiogram</td>
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<td>EDI</td>
<td>Expiratory Disproportion Index</td>
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<tr>
<td>ENT</td>
<td>Ear, Nose, Throat</td>
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<tr>
<td>FC</td>
<td>False Cord</td>
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<tr>
<td>FEES</td>
<td>Fibroptic Endoscopic Evaluation of Swallowing</td>
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<tr>
<td>Abbreviation</td>
<td>Full Form</td>
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<tr>
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<tr>
<td>FEV₁</td>
<td>Forced Expiratory Volume in One second</td>
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<td>FOV</td>
<td>Field of View</td>
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<tr>
<td>FVC</td>
<td>Forced Vital Capacity</td>
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<td>G</td>
<td>Glottis</td>
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<tr>
<td>GI-L-D</td>
<td>Glottic to Lesion Distance</td>
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<td>GORD</td>
<td>Gastro-Oesophageal Reflux Disease</td>
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<tr>
<td>GT</td>
<td>Granulation tissue</td>
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<tr>
<td>HLA</td>
<td>Human Leukocyte Antigen</td>
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<td>IA</td>
<td>Interarytenoid</td>
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<tr>
<td>ICU</td>
<td>Intensive Care Unit</td>
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<tr>
<td>ISS</td>
<td>Idiopathic Subglottic Stenosis</td>
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<tr>
<td>IV</td>
<td>Intravenous</td>
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<tr>
<td>KTP</td>
<td>Potassium Titanyl Phosphate</td>
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<td>LMA</td>
<td>Laryngeal Mask Airway</td>
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<tr>
<td>MEF</td>
<td>Maximum Expiratory Flow</td>
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<tr>
<td>MIF</td>
<td>Maximum inspiratory Flow</td>
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<tr>
<td>MLT</td>
<td>Microlaryngoscopy and Tracheoscopy</td>
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<td>MMC</td>
<td>Mitomycin-C</td>
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<tr>
<td>MRC</td>
<td>Medical Research Council</td>
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<tr>
<td>NSA</td>
<td>National Screening Unit</td>
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<tr>
<td>PAPC</td>
<td>Posterior Arytenoidectomy and Posterior Cordectomy</td>
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<td>PCT</td>
<td>Primary Care Trust</td>
</tr>
<tr>
<td>PEEP</td>
<td>Positive End Expiratory Pressure</td>
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<td>PEF</td>
<td>Peak Expiratory Flow</td>
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<tr>
<td>PEFR</td>
<td>Peak Expiratory Flow Rate</td>
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<tr>
<td>PET</td>
<td>Positron Emission Tomography</td>
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<tr>
<td>PIF</td>
<td>Peak Inspiratory Flow</td>
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<td>PR3</td>
<td>Proteinase 3</td>
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<tr>
<td>RD</td>
<td>Respiratory Diverticulum</td>
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<tr>
<td>RF</td>
<td>Rheumatoid Factor</td>
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<tr>
<td>RTA</td>
<td>Road Traffic Accident</td>
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<td>S</td>
<td>Swallowing</td>
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<tr>
<td>SAH</td>
<td>Subarachnoid Haemorrhage</td>
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<tr>
<td>SD</td>
<td>Standard Deviation</td>
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<tr>
<td>Abbreviation</td>
<td>Definition</td>
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<tr>
<td>SEM</td>
<td>Standard Error of Mean</td>
</tr>
<tr>
<td>SG</td>
<td>Subglottis</td>
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<tr>
<td>SH</td>
<td>Stenosis Height</td>
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<tr>
<td>TNFA</td>
<td>Tumour Necrosis Factor Alpha</td>
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<tr>
<td>Trach.</td>
<td>Tracheostomy in Situ</td>
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<tr>
<td>TV</td>
<td>Tidal Volume</td>
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<tr>
<td>V</td>
<td>Voice</td>
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<tr>
<td>VHI-10</td>
<td>Voice Handicap Index-10</td>
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<tr>
<td>WG</td>
<td>Wegener's Granulomatosis</td>
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I wish to dedicate this work to my wife Neelam and to my two children, Shona and Arvin.
Chapter 1

1.1 Background & Aims of Thesis

The larynx, trachea and bronchi form the conduit between the external environment and the lungs through which respiratory gases are transported and pulmonary secretions are expectorated. The principle function of the larynx is to protect the airway from aspiration during swallowing, but the larynx is also involved with phonation and Valsalva. The narrowest sites of the adult airway are the larynx and trachea (illustration 1.1).

Illustration 1.1 The narrowest site in the adult airway is the glottis followed by the trachea

Upper airway stenosis can have a significant impact on the quality of life and sometimes on life itself (illustration 1.4). Abnormal narrowing of the laryngotracheal complex causes breathlessness, especially during physical activity. Retention of pulmonary secretions may lead to lung infection or collapse. Laryngeal stenosis can
interfere with phonation and a dysfunctional larynx can affect swallowing safety. Due to medical advances, more patients are surviving periods of ventilation on intensive care units (1, 2). The incidence of laryngotracheal injury is probably increasing but remains unknown.

To appreciate the impact of airway stenosis one must have a basic understanding of the rules governing fluid dynamics (3):

*The Venturi effect states that the velocity of a fluid flowing through a pipe increases as the cross sectional area decreases. The velocity must increase to satisfy the law governing conservation of mass and to satisfy the law governing conservation of energy the static pressure in this fluid must decrease.* [The Venturi effect is named after the Italian Physicist, Giovanni Venturi (1746–1822)].

![Illustration 1.2 Experiment to demonstrate the ‘Venturi Effect’.](image)

*The Bernoulli's principle states that for an inviscid fluid (no viscosity), an increase in the speed of the fluid occurs simultaneously with a decrease in the pressure, or a*
decrease in the fluid’s potential energy. [Named after the Dutch-Swiss mathematician, Daniel Bernoulli (1700-1782)].

**Poiseuille’s law**

\[ R = \frac{8n l}{\pi r^4} \]

- R = resistance
- n = viscosity
- l = length
- r = radius

**In laminar airflow, airway resistance is dictated by the diameter of the airway and by the density of the inspired gas (Poiseuille’s law).** Because of the fourth power in the denominator, resistance increases rapidly as diameter decreases. However, an area of airway stenosis also produces turbulence, which adds to resistance, but cannot easily be calculated.

During inspiration, the intrathoracic airways expand along with the expanding lungs.

However, the extrathoracic trachea will have a reduced lumen during inspiration because the intraluminal pressure is lower than atmospheric. The reverse happens during expiration. A variable obstruction of the airway also changes size with breathing.

Hence an extrathoracic variable tracheal stenosis will limit inspiration whereas an intrathoracic variable lesion will limit expiration. A fixed obstruction, whether intrathoracic or extrathoracic, will limit peak airflow on inspiration and expiration in equal proportions and produce a characteristic flow volume loop (illustration 1.3). The exact physiological causes of dyspnoea are not known, however, the extra work of breathing, altered afferent input from the respiratory tract and the tendency towards carbon dioxide retention must play a part.
Illustration 1.3 Patterns of flow volume loops - these graphically depict the rate of airflow on the Y-axis and the total volume expired (above) inspired (below) on the X-axis. The patient is asked to take the deepest breathe, apply the mouth to the device, and breathe out as hard as possible and for as long as possible. This is followed by a maximum and rapid inspiration. (COPD= chronic obstructive pulmonary disease)

Paediatric laryngotracheal stenosis is a well-researched area of medicine and treatments include airway augmentation with rib grafts as well as tracheal and cricotracheal resections. At the start of this investigation in January 2004, adult laryngotracheal stenosis was poorly researched and the surgical options included tracheostomy, tracheal resection or cricotracheal resection (4). In the United Kingdom the majority of adult airway stenoses were being managed by paediatric airway surgeons. Most were using primary rib grafts for augmentation, even though there is no published series on the successful application of this technique in adult patients. There was no appreciation of the fact that there is a high incidence of ischaemic necrosis of primary rib graft in adult patients (5). Furthermore, the quality and quantity of rib cartilage that can be harvested diminishes with age (5). Paediatric airway stenosis nearly always involves the subglottis (6). Early, during the process of data collection for this thesis, it became clear
that the lesional anatomy, anatomical sites and pathologies behind adult laryngotracheal stenosis differed greatly from the paediatric group.

Illustration 1.4 Different sites of adult airway stenosis (central pictures are normal, right are stenosed). A=glottis, B=subglottis, C=trachea and D=bronchi.

There was very little quality research to use as a guide to the types of cases that could be expected. Most of the adult literature and ‘evidence’ referred to subglottic and tracheal stenosis where the “gold standard” was cricotracheal or tracheal resection and success rates were quoted in various papers ranging from 70-90% (7). However, these articles do not make clear the selection or exclusion criteria for surgery. As well as open surgical procedures, some surgeons had considered endoscopic surgery for adult airway stenosis (8), however, the procedures were technically challenging and not widely adopted. At the start of this research, it was accepted wisdom that surgery should only be undertaken on the airway once an airway stenosis had “matured” and the inflammatory changes had subsided (9).

Systemic inflammatory disorders, such as Wegener’s granulomatosis and sarcoidosis, sometimes lead to laryngotracheal airway compromise. Medical science has made it
possible to treat these, once potentially fatal, conditions. This has produced a group of patients who have had to live with the restrictions of their damaged airways, often progressing to airway stents or tracheostomies.

Illustration 1.5 Myer-Cotton grading system for paediatric subglottic stenosis

The most widely used grading system to describe the degree of airway stenosis is the Myer-Cotton grading system (10) which refers to the surface area of the stenosis (illustration 1.5) as opposed to the size of the patient’s airway. This grading system was developed to help with decision making in paediatric airway surgery with respect to conservative or surgical treatments. In paediatrics, a decanulation was deemed a successful outcome and in the adult population, the outcomes were often graded as “excellent”, “good”, “satisfactory”, “failure” or “death” with little mention of swallowing or voice outcomes.

In January 2004, a database was constructed using FileMaker Pro® (FileMaker Inc, Santa Clara, USA) installed on a small portable notebook computer. This has been used to collect prospective data on all new referrals of adult benign laryngotracheal stenosis made to the Airway Reconstruction Team based at the Royal National Throat, Nose &
Ear Hospital and Charing Cross Hospital, both in London. The author of this thesis has been the operating surgeon on all the patients and has been responsible for entering all the surgical and out-patient information on the database. All the anaesthetic data has been entered by the anaesthetist at the time of surgery in the operating room. The database recorded the medical history, demographics related to the patient and details of each operation and out-patient visit. Each surgical entry has been illustrated with photographs taken during the procedure. In each case the definitive diagnosis, with respect to the aetiology of the airway stenosis, was made based on all the assessments discussed in this thesis. This is probably the largest prospective database on this condition.

Since the start of this project in January 2004 and the commencement of writing the thesis in January 2010, just over 400 adult patients had been entered on the database. Of the relative aetiological factors presented in table 1.1, more than half the cases of adult laryngotracheal stenosis were due to a period of ventilation on an intensive care unit. The incidence of stenosis in patients who were ventilated with endotracheal tubes or converted earlier to tracheostomies was very similar, only the site of the injury differed. Early tracheostomy did, however, reduce the incidence of damage to the vocal folds and their mobility. Unlike paediatric laryngotracheal stenosis, which almost always affects the subglottis (the narrowest part of the paediatric airway), in the adult population, one third of the patients had stenosis of the cervical trachea. Nearly half of the adult patients had airway compromise due to other disease processes such as Wegener’s granulomatosis, sarcoidosis and idiopathic subglottic stenosis.
Table 1.1
Four Hundred Consecutive Adult Referrals with Laryngotraheal Stenosis

- **48%** Acquired laryngotracheal stenosis
  - 34.75% subglottic stenosis
  - 13.25% tracheal stenosis

- **14.75%** Bilateral vocal cord mobility impairment
  - 8.75% nerve injury
  - 4.75% scar/fixation
  - 1.25% rheumatoid arthritis

- **11.25%** Wegener’s granulomatosis

- **9.75%** Idiopathic subglottic stenosis

- **5.5%** Supraglottic stenosis (2.5% sarcoid, 3.0% other)

- **3.25%** Previous papillomatosis treatment

- **3.25%** Glottic web

- **2.0%** Tracheomalacia (1.25% relapsing polychondritis)

- **1.0%** Amyloidosis

- **0.75%** Vascular lesion

- **0.5%** Subglottic stenosis congenital

This thesis has set out to look at the aetiology, incidence, screening and alternative procedures for the management of adult benign laryngotracheal stenosis. Due to the diverse causes of adult airway stenosis, it has not been possible to apply this research to all 400 cases. Instead I have concentrated on previously difficult to treat groups and specific conditions drawn from this pool. A critical review of the literature and respective research is discussed in the appropriate chapters. As a part of this project it is hoped that the treatment pathways, algorithms and outcome measures proposed could be adopted by other groups working in this field.
Chapter 2

2.1 Embryology

The first sign of the respiratory system is seen as an epithelial thickening and outpouching along the ventral aspect of the primitive foregut known as the respiratory diverticulum (RD). This appears at the end of the fourth week of gestation. The RD is separated from the hepatic diverticulum by the septum transversum (illustration 2.1), a structure that eventually develops into the central tendon of the diaphragm. Inside the RD is the laryngotracheal groove which extends lengthwise in the floor of the gut just caudal to the pharyngeal pouches (11).

Illustration 2.1 The larynx and respiratory system arise from an out-pouching of the primitive foregut called the Respiratory Diverticulum (RD)(11)

As the upper foregut region and RD migrate superiorly, the RD gives rise to bilateral projections called bronchopulmonary buds which are drawn caudally. These projections or buds soon divide into the right and left bronchial buds and grow into the pericardio-peritoneal cavities. These primitive lung buds then subdivide into secondary
and tertiary bronchi. Throughout foetal development, the surrounding pulmogenic mesoderm continues to develop into the lung parenchyma. The larynx develops in the proximal end of the laryngotracheal groove between the fifth and sixth gestational weeks as three swellings which appear at the laryngeal aditus. The anterior swelling becomes the future epiglottis and the lateral masses give rise to the future arytenoids. The two lateral swellings migrate cranially and medially to oppose each other (illustration 2.2). Together with the epiglottic swelling, they surround a T-shaped laryngeal aditus (12). The laryngeal lumen becomes occluded at the eighth week of gestation due to epithelial proliferation.

Illustration 2.2 The embryological development of the epiglottis and arytenoids(11)

If normal recanulation does not occur during the tenth gestation week, a laryngeal web develops. The formation of the vocal and vestibular folds is related to the condensation of mesenchyme and the out-pouching of the laryngeal ventricle. The two vocal folds separate during the third gestational month and failure of this process results in
congenital atresia of the larynx. The thyroid cartilage develops from the fourth and fifth branchial arches as two lateral plates that fuse in the midline (illustration 2.3). The cricoid cartilage develops from the fifth arch (13). The rostral advancement of the tracheo-oesophageal septum results in the fusion of the dorsal cricoid lamina. Failure of advancement results in either a fistula or a cleft. The arytenoids are initially fused to the cricoid cartilage, but they eventually separate, forming the cricoarytenoid joints. The intrinsic muscles of the larynx develop from the mesoderm of the fourth and fifth arches.

Illustration 2.3 Branchial arch origins of the Larynx (13)
2.II Anatomy

The larynx is positioned between the tongue base and the trachea and separates the airway from the digestive tract. It lies at the level of the second or third cervical vertebrae in the infant and descends to the adult position during the first few years of life to lie at the level of the fifth and sixth cervical vertebrae. The male and female larynx differs little in size up until puberty. The adult larynx undergoes significant growth and the female larynx to a lesser degree under the influence of the hormones responsible for secondary sexual characteristics. The adult male larynx averages 44 mm in length and the female larynx 36 mm (14). The antero-posterior length in the adult male averages 41 mm, and 26 mm in the female. Contrary to traditional teaching, the diameter of the trachea relates to height regardless of sex (illustration 2.4), both in children and adults (15).

Illustration 2.4 Graph to show relationship between height and tracheal diameter
(adapted from Griscom (15))
The larynx is composed of several interconnected cartilages that are moved by muscles. The three unpaired laryngeal cartilages are the epiglottis, the thyroid and the cricoid cartilages and the three paired laryngeal cartilages are the arytenoid, the corniculate and the cuneiform cartilages (illustration 2.5). The larynx has four synovial joints. The paired cricothyroid joints are between the lateral aspect of the cricoid cartilage and the inferior horn of the thyroid cartilage and permit rotation of the thyroid cartilage on a horizontal axis. This has the effect of shortening the cricothyroid gap. The cricoarytenoid joints are present between the superior border of the lamina of the cricoid cartilages and the base of the arytenoid cartilages allowing for gliding and rotational movements of the arytenoid cartilages.

Illustration 2.5 Cartilages of the human Larynx (14)
The arterial supply to the larynx is from the superior and inferior laryngeal arteries which are branches of the superior and inferior thyroid arteries respectively (14). The superior laryngeal artery accompanies the internal branch of the superior laryngeal nerve on each side and the inferior laryngeal artery enters the larynx with the recurrent laryngeal nerve. Within the larynx, the two arteries join to form a vascular arcade from which a number of end arteries are given off to supply the endolarynx (16). The venous drainage of the larynx follows its arterial supply.

The lymphatic drainage of the larynx above the level of the vocal folds is to the superior and middle deep cervical lymph nodes which lie along the carotid sheath. The supraglottic larynx has bilateral drainage and this has an impact on the spread of supraglottic malignancy. The infero-glottic larynx drains to the paratracheal and the lower deep cervical lymph nodes. Currently, the anatomical upper limit of the glottis is defined as the apex of the laryngeal ventricle. The lower limit is defined as 1 cm below the most medial part of the vocal fold. These limits reflect the changes in lymphatic drainage and have implications in the management of laryngeal malignancy (17).

The vagus nerve carries sensory fibres from the larynx above the vocal folds. The laryngeal mucosa is supplied by the internal branch of the superior laryngeal nerve and below the vocal folds the sensory supply is from the recurrent laryngeal nerve. Motor supply to all the intrinsic laryngeal muscles, except for the cricothyroid, is through the recurrent laryngeal nerve, which is a branch of the vagus nerve. Motor supply to the cricothyroid muscle is by the external laryngeal branch of the superior laryngeal nerve, itself a branch of the vagus nerve. There is, however, some crossover between the superior and internal laryngeal nerves in respect to proprioceptive supply to the intrinsic muscles of the larynx.
The larynx as a whole can be elevated and depressed by the action of the suprathyroid and infrathyroid strap muscles. Laryngeal elevation is an important mechanism for protecting the airway during swallowing and also has the effect of changing the length of the vocal tract as occurs during singing.

The intrinsic muscles can also be divided into muscles that open and close the laryngeal inlet and muscles that regulate the vocal folds. The posterior cricoarytenoid muscles are the principle abductors of the vocal folds. The thyroarytenoid, vocalis and cricothyroid muscles, and the transverse and oblique arytenoid muscles, contribute towards adduction of the vocal folds. The posterior cricoarytenoid muscle extends laterally from the posterior aspect of the cricoid cartilages to the muscular process of the arytenoid cartilage and rotates it laterally (illustration 2.6). It is the principle respiratory laryngeal muscle and its bilateral paralysis can lead to acute airway compromise.

Illustration 2.6 Posterior cricoarytenoid muscle action (14)
The lateral cricoarytenoid muscles are the principle adductors of the larynx. The lateral cricoarytenoid muscles extend from the arch of the cricoid cartilage to the muscular process of the arytenoid cartilage rotating it medially. This has the effect of bringing the vocal folds together for vibration and for airway protection during swallowing. The oblique and transverse arytenoids muscles unite the arytenoid cartilages and maintain approximation of the posterior portion of the vocal folds during phonation.

After closure of the glottis, the vocal cords can be tightened and lengthened by the cricothyroid muscles to change the pitch and tone of the voice. The cricothyroid muscle has the effect of bringing the thyroid and cricoid cartilages together anteriorly, thus increasing the anterior posterior dimension of the larynx and tightening the vocal cords. The thyro-arytenoid muscles can finely regulate the tension and pliability of the vocal folds during phonation (illustration 2.6).

The anterior relations of larynx are the suprathyroid and infrathyroid muscles and the thyroid gland. Its most important lateral relations are the superior laryngeal nerves superiorly and the recurrent laryngeal nerves inferiorly. Its posterior relations are the cricopharyngeus muscle, the upper oesophageal sphincter and the vertebral bodies. Postero-laterally the larynx is related to the carotid sheath which contains the common carotid artery, the internal jugular vein and the vagus nerve (14).

The trachea is a tube that spans between the lower border of the cricoid cartilage of the larynx, at the level of the sixth cervical vertebra, to the carina at the level of the sternal angle. At the carina, the trachea divides to give rise to the right and left main bronchi. In the adult, the trachea varies between 10-13 cm in length and in the adult is composed of approximately 20 C-shaped cartilaginous rings that are connected by fibrous bands and covered by respiratory mucosa. Posteriorly, the tracheal wall is composed of a flat
fibro-muscular structure which spans between the arms of the C and contains the unpaired trachealis muscle (18). The trachealis constricts the trachea during a cough allowing the high velocity passage of air during a cough.

**Illustration 2.7 Segmental blood supply to the trachea (19)**

The trachea has a segmental blood supply (Illustration 2.7). The cervical trachea receives its blood supply primarily from the inferior thyroid arteries. The superior thyroid arteries do not directly supply the trachea, but can anastomose with the inferior thyroid arteries and supply blood to the trachea via the thyroid gland (18). The lower cervical and thoracic trachea is supplied by direct branches of the brachiocephalic and the left subclavian artery, as well as the supreme intercostal arteries and the right internal thoracic artery. The lower thoracic trachea and the carina are predominantly supplied by bronchial arteries that are direct branches of the aorta (20). The diagrams are reproduced from ‘Surgery of the Trachea and Bronchi’ by Grillo (19). These arteries enter the tracheo-oesophageal groove laterally and divide into tracheal and oesophageal branches. Tracheal branches, having contributed to the lateral longitudinal anastomosis, pierce the tracheal wall as transverse intercartilaginous arteries and divide
into anterior and posterior branches that supply the anterior and posterior parts of the trachea respectively. These blood vessels terminate in a rich circumferential mucosal vascular plexus. Venous drainage of the trachea appears to follow its arterial supply (20). The oesophageal branches also make a contribution to the arterial supply of the posterior trachea. The lymphatic drainage of the trachea is to the pre-tracheal, paratracheal and subcarinal lymph nodes (18). The trachea appears to have a segmental lymphatic drainage with each segment of the trachea draining into the pre- and paratracheal lymph nodes closest to it.

Sensory and motor innervation of the trachea has been extensively studied in animal models but not in humans. Retrograde neurone staining techniques have shown that the afferent nerve supply to the trachea is provided by the vagus nerve. Sympathetic neurones supplying the trachea are found throughout the sympathetic chain from C1 to T8, but have a higher concentration, at the severus, cervical and stellate ganglia (21). The vagus nerve also provides motor innervation to the trachea. The cervical trachea receives its motor supply both from superior and recurrent laryngeal nerves and the thoracic trachea is predominantly supplied by the recurrent laryngeal nerves with a smaller contribution from the superior and para-recurrent laryngeal nerves (22).
Illustration 2.8 Anatomy and relations of the human trachea (A1 view from right, A2 view from left) (20)

The trachea is an unpaired midline structure that is surrounded by loose, essentially avascular peri-areolar tissue throughout its course, except the point of its attachment to the thyroid isthmus (18). Illustration 2.8 demonstrates the relations of the trachea (20). Posteriorly, the trachea is intimately related to the oesophagus throughout its course, except for its right posterior margin which lies directly against the vertebral bodies (18). Anteriorly the thyroid isthmus overlies the cervical trachea and is connected to it by means of the ligament of Berry. The thyroid lobes lie over the antero-lateral and lateral portions of the cervical trachea. Laterally, the trachea is related to the recurrent laryngeal nerves which are branches of the vagus. The left nerve originates underneath the aortic arch and lies in the tracheo-oesophageal groove throughout its entire course, often posterior to the branches of the inferior thyroid artery. The left vagus nerve itself lies antero-lateral to the trachea throughout its thoracic descent. The right recurrent
laryngeal nerve loops around the subclavian artery and frequently lies between the branches of the inferior thyroid artery. The brachiocephalic artery crosses the mid trachea obliquely to reach the right side of the neck where it gives rise to the right common carotid and the subclavian arteries which lie antero-lateral to the right cervical trachea. The lower thoracic trachea and the carina are related to the aortic arch on the left and the superior vena cava and azygos vein on the right. The pulmonary artery crosses in front and just inferior to the carina.
2.III History of Airway Surgery

2.III.a Tracheostomy and Airway Intubation

The earliest description of a surgical tracheostomy is found in the Rig Veda, the ancient Hindu book of medicine, that appeared as oral tradition at around 2000 BC (23). Five centuries later, in Egypt, following the work of Imhotep, a technique resembling tracheostomy was first documented in written form to treat respiratory obstruction (Edwin Smith’s Papyrus). Hippocrates in Greece at around 460-380 BC described the intubation of the trachea of humans to support ventilation. Alexander the Great (356-323 BC) reportedly used his sword to cut open the trachea of a soldier suffering from an aspirated bone. The first recorded successful tracheostomy was for treatment of a pharyngeal abscess by Antonio Musa Brasavola of Ferrara in 1546 (24). Marco Aurelio Severino used tracheostomy during an epidemic of diphtheria in Napoli in 1610. Lorenz Heister in 1718 was the first to use the term “tracheostomy”. Many descriptions are reported thereafter. The first modern description of a tracheostomy was by Chevalier Jackson in 1909 (25). Andreas Vesalius, a Flemish physician working in Padua, in 1543 reported the first tracheal intubation in an animal. In early 1871, Trendelenberg from Germany performed the first endotracheal anaesthesia in man. General anaesthesia itself had been performed previously in 1846 in Boston using ether. The first elective surgical procedure performed using oro-tracheal intubation was by an Edinburgh surgeon, William MacEwen, in 1878 to remove an oral tumour.
2.III.b Laryngoscopy

Before the 1800’s, physicians could only surmise how the larynx functioned from examination of autopsy specimens. Diseases of the airway were usually infectious or inflammatory in origin. The infections included syphilis, diphtheria and tuberculosis. Medical historians conventionally date the beginning of laryngoscopy as 1855, when Spanish voice teacher, Manuel Garcia, first visualised his own larynx using a dental mirror fixed at 45 degrees to a handle and a second hand-held mirror to reflect sunlight. This work was presented at the Royal Society of Medicine (26). However, a more detailed review of the literature reveals that the French Accoucheur Leveret, in 1743, devised a bent mirror for examining the larynx and even a snare for removing laryngeal polyps (26). In 1807, Bozzini, a German physician, published an account of his speculum called the “light conductor”. His device was for examining internal cavities, including the larynx. Benjamin Guy Babington was another predecessor of Garcia’s. In 1829, he exhibited to the Hunterian Society of London an instrument which was a combination of an epiglottic retractor and laryngeal mirror. This he used to examine the larynx (26, 27).

Johann Czermak, Professor of Physiology at the University of Pest, first tried Garcia’s mirror in examining patients. In 1858, Czermak presented his work to the Viennese medical community. Indirect laryngoscopy blossomed in the last decades of the 19th Century. Surgical instruments were developed which allowed the laryngologist to cut, cauterise and remove laryngeal tissue with indirect visualisation. In Vienna, the German surgeon, Billroth, performed the first laryngectomy in 1873 (28).

The first physician to directly visualise the larynx, in 1864, was the Berlin laryngologist, Tobold (29). His patient was a female singer with papillomatosis of her
larynx who was able to suppress her gag reflex such that a tongue depressor could be used to glimpse the larynx without instrumentation. It was Gustave Killian who first performed suspension laryngoscopy in 1909. He used a tubular spatula, an early laryngoscope, to visualise the larynx initially in cadavers, but later in patients. Chevalier Jackson was probably the first to describe the “sniffing the morning air” position (illustration 2.9) for microlaryngoscopy in his book dated 1915 (30).

Illustration 2.9 Demonstrating the ‘sniffing the morning air’ position originally described by Chevalier Jackson in his book of 1915 (30).

2.III.c Bronchoscopy

Gustave Killian in Freiburg University in 1897 removed a bone splinter from the right main bronchus of a farmer using an oesophagoscope, forceps and a head mirror as a light source (31). In 1904, Chevalier Jackson in Philadelphia produced a bronchoscope with a light bulb at its distal end and a suction device. Professor Harold Hopkins held is Chair in Physics at Reading University but his earlier work in optics was done at Imperial College. In addition to his theoretical work, his many inventions are in daily use throughout the world. These include zoom lenses, coherent fibre-optics and more
recently the rod-lens endoscopes which 'opened the door' to modern key-hole surgery (32). Rod lens endoscopes consist of a series of glass and air lenses that transfer the image from the tip of the device to the eye and became commercially available in 1966 (illustration 2.10). These were adopted for use with bronchoscopes.

Illustration 2.10 Design of the modern rod-lens endoscope developed by Prof Harold Hopkins (32)


2.III.d Surgery for Laryngotracheal Stenosis

The Rig Veda noted that the trachea could re-unite “when the cervical cartilages are cut across, provided they are not entirely severed”. This description dates from about 2000 BC. The earliest description of surgery for laryngo-tracheal stenosis was by L.Von Schroetter in Vienna in 1871. He described two techniques. The first involved the use of metal “olives” after placement of a tracheostomy. The second procedure was dilatation of the airway with hard rubber bougies delivered through the mouth (33, 34). In 1885, O’Dwyer in New York (35) described similar techniques of dilatation that
became used widely in the USA. Gluck and Zeller in 1881 demonstrated healing after end-to-end tracheal anastomosis in dogs and believed that the technique could be applied in man (36). Primary anastomosis of the trachea after limited resection for post-traumatic stenosis was performed by Kuster in 1886 in man (37). Nowakowski in 1909 (38) described complex methods of repair of cervical tracheal defects and through cadaver studies placed the limit of tracheal resection at 3-4 cm. This was following cadaveric studies. It was many years later before Conley successfully resected the second and third tracheal rings for scar in 1953 with primary end-to-end anastomosis (39). In 1968, Grillo reported the length of trachea that could be resected for post-intubation stenosis at 4.5 cm (approximately 7.2 rings). He discovered that the length that could be resected in older patients was progressively shorter because of the reduced elasticity between the cartilaginous rings. He further demonstrated that it would be possible, with additional manoeuvres involving release of pulmonary ligaments and suprahyoid laryngeal release, to resect a further 2 cm (40).

Open approaches for the treatment of subglottic stenosis can be traced as far back as the late 1800s and early 1900s. Killian in Germany described an operation referred to as “laryngo-tracheostomy” (34). A vertical skin incision and a median vertical fissure of the larynx and trachea were created. A fistula was maintained and progressively larger soft rubber tubes were inserted through the tracheostomy site. There is also a description in the German literature in 1896 (41) describing the use of rib cartilage graft in a two stage procedure to close an open tracheal wound. These original papers were essentially case reports but modifications of these techniques are still used in modern airway surgery (42).

In 1927, M F Arbuckle in St Louis, described his experience with three children who had been treated unsuccessfully with repeated intubations after a diphtheria throat
The larynx and subglottis were exposed after a median vertical incision through the skin and the airway. Arbuckle excised all visible scar tissue and placed a skin graft over the denuded area within the lumen of the airway. The graft was held in place with a rubber balloon attached inferiorly to a string which was brought out through the tracheotomy. He also described a similar technique with a balloon which was held by a stay suture from the outside, transfixing the larynx, graft and balloon. In each case the balloon was removed after 8 days.

Schmiegelow (43) from Copenhagen described, in 1927, a surgical technique which he said he had been using since 1910. Via a laryngo-tracheal fissure, he entirely removed any structures or scar tissue encroaching on the lumen such that it appeared normal in size. He then placed an India rubber drain slightly wider than the lumen, fixed into position using silver wire through the soft tissues and skin of the neck. This “stent” was left in place for several weeks or months.

Before the 1930s the majority of stenoses of the airway resulted from infections and inflammatory processes. Often this was exacerbated by iatrogenic injuries from surgery. In 1921 Chevalier Jackson (25) from Philadelphia cautioned against the placement of a “high tracheotomy” which he described as on or near the cricoid cartilage. Le Jeune and Owens (44) from New Orleans noted in 1935 that 90% of their cases of laryngo-tracheal stenosis were caused by disease or trauma. They advocated complete dissection of all scar, granulation, cartilage and osseous tissues via laryngofissure and application of a skin graft over a stent, their argument being that primary tissue healing where there is skin approximation produces less scar tissue than healing by secondary intention. Jackson in his article of 1936 (33) stated that all cases of congenital or acquired stenosis of the larynx were curable. He also stated that the wearing of a canula (tracheotomy) would dominate the entire life of a person and create
an inferiority complex. Jackson favoured the placement of elastic rubber core moulds changed weekly and slowly increasing in size. These rubber stents were placed above the tracheotomy. Jackson admonished the cutting of the cricoid cartilage even in laryngeal atresia as “it is the only complete ring in the airway”. Some of the principles described by Jackson are part of modern laryngology teaching. The work of Le Jeune and Owens has formed the basis of some techniques employed in this thesis (section 2.III.e).

In 1938, Edward Looper from Baltimore described the use of the hyoid bone as an autologous material for grafting in airway reconstruction. He described it as being advantageous over the use of rib or ear cartilage (7). This is the first reference to cartilaginous graft tissue for airway reconstruction. As well as performing the first tracheal resection in 1953, John Conley of New York (39) summarised several techniques for treatment of subglottic stenosis. He performed a laryngofissure, removed all scar tissue and placed a split skin graft over a Vaseline gauze over a foam rubber sponge. He also mentioned that autologous cartilage could be used to assist in reconstructing the tubular form of the trachea. He did not discuss specific cases but the ideas are in use in paediatric airway reconstruction today (45).

In 1971, Grahne of Helsinki (46) continued to completely remove scar tissue, but described a hole placed through an Aboulker stent to accommodate a metal tracheostomy tube. This stent was left in place for 4 months. By the 1970s, the principal cause of airway stenosis was no longer infectious diseases, high tracheostomies or surgical dilatations. The principal cause now was a period of prolonged ventilation using an endotracheal tube. In 1972, Fearon and Cotton in Toronto (47) published an experimental procedure where thyroid cartilage was used to augment an anteriorly split thyroid cartilage in a monkey. They also demonstrated that
there was no inhibition of laryngeal growth following this. In 1974, Evans and Todd in London (48) reported the use of rib cartilage in laryngo-tracheoplasty, but favoured a castellated laryngofissure to expand the airway over a piece of rolled silastic sheet used as a stent for 6 weeks. Cotton in Cincinnati in 1978 (42) described in detail laryngo-tracheal reconstruction (LTR) with an anterior costal cartilage graft. Later, in 1984, Cotton (49) published a series of 100 cases of LTR in children over a decade. He emphasised that the stenosis should be mature before undertaking open surgery. In 1985, Fearon and McMillin in Toronto (50) described cricoid resection and thyro-tracheal anastomosis in primates. They demonstrated that there was no interference with normal laryngeal growth following this. Ranne in Kansas City is credited with the first cricoid resection in patients (51), published in 1991. This procedure, originally described by Pearson (52), was adopted by Monnier in Switzerland, who subsequently published his series in 1993 (53). Robin Cotton’s group in Cincinnati, when considering an open procedure for subglottic stenosis, primarily perform anterior and posterior augmentations. In only 15% of cases, usually those that have failed augmentation surgery, do they consider cricotracheal resection.

One other technique, originally described by Herberhold (54), was the use of preserved tracheal allografts. These held the promise of being able to treat long-segment tracheal stenosis in children and adults without the need for immunosuppression. These grafts consisted of chemically treated cadaveric tracheas to remove donor cells and antigenicity. The simplicity of the technique was the ability to tailor the size and shape of the tissue to suit the patient’s requirements (illustration 2.11). However, like other teams (55, 56) our unit discovered that, following an intense inflammatory response lasting several weeks, these grafted tracheas were replaced in time by host scar tissue. When the technique worked, it appeared to do so if the scar tissue retained the size and
shape of the original graft. Herberhold’s publications did not give detailed follow-up data to allow full appreciation of the long-term results.

Illustration 2.11. A preserved tracheal homograft is cut to the desired size and shape (left) and sutured into the airway as an anterior augment (right).

Resection of the damaged airway had become the ‘gold standard’ for treating laryngotracheal stenosis in adults at the start of this research. Grillo (7) had the largest experience of this technique in adult patients and most other publications were case series. He achieved ‘successful’ outcomes in the majority of his patients, however, the possibility of bias based on patient selection cannot be ruled out. These results are all the more difficult to interpret as there were no standardised and validated outcome measures in widespread use. As Abraham Maslow (57), a psychologist, wrote in 1966 “it is tempting, if the only tool you have is a hammer, to treat everything as if it were a nail.”

2.III.e Tracheobronchial Stenting

Charles Thomas Stent was a British dentist in the late 19th Century. He developed dental impression material that was used as a template to support skin grafts for repair of oral trauma. Initially the term “stent” was used to describe artificial structures for preserving the viability and function of tissue. Today, the term is used to describe devices for maintaining the patency of tubular structures, including the tracheo-
bronchial tree. Early experience of stents was gained through their use in the biliary tree, oesophagus, urinary tract and blood vessels. There has likewise been a proliferation of devices for airway stenting. There are currently a variety of silicone and expandable metal stents. The metal stents can be uncovered, covered or partially covered (hybrid). Wire stents tend to be covered with polyurethane, although Teflon sheeting is used in some designs. The next generation of stents will be reabsorbable or bioengineered in other ways, negating the need for subsequent removal.

In benign and malignant disease, stents have been used to palliate the effects of large airway obstruction caused by extrinsic compression, endoluminal disease or loss of cartilaginous support. Indications in benign disease include long length stenoses, failed previous repair, patient co-morbidities that restrict reconstructive surgery or patient preference. Stents are also used temporarily following airway surgery.

The first airway stent was a metal alloy stent described by William Hankins of St Louis, USA, in 1952 (58). However there were problems related to repeated obstruction and migration of this stent, this led to the development of the silicone T-tube, first used by Montgomery in the 1960’s (59). The T limb prevented migration of the endolumenal tube. In 1982 Westaby described his modification of this silicone stent, which included a bifurcation at the lower end, allowing stenting of the trachea and both bronchi (60). In the 1990’s, Dumon produced the first dedicated endobronchial silicone stent (61). Current metal stents tend to be made from steel or nitinol (a titanium and nickel alloy with a memory) wire mesh. The Gianturco metal stent is an uncovered stainless steel mesh stent and was first described in 1986 (62).

Although patients with metal stents enjoy immediate palliation of symptomatic tracheal stenosis, metal stents are associated with a high incidence of obstruction with
granulation (63). They are also susceptible to metal fatigue and fracture over time. Based on personal experience and a review of the literature (64), I feel that uncovered or hybrid metal stents should only be used in a select group of patients with a short life expectancy. If not removed within the first few weeks of deployment, they become a permanent fixture in the airway (illustration 2.12).

Illustration 2.12 A partially uncovered (hybrid) wire stent inserted in the airway to deal with a benign post-intubation stenosis has caused worse damage to the airway and had to be removed via laryngotraceal-fissure and sharp dissection.

During the period of this research a 36-year-old female patient was referred to The Airway Reconstruction Unit. She had had an uncovered metal stent inserted in the left main bronchus to deal with compression from a thoracic lymphoma 8 years earlier. She received chemoradiotherapy and made a complete recovery from this malignancy. However, years later she was being treated for repeated airway compromise due to granulation and wire fragments obstructing the left main bronchus. She later presented to a local emergency department with a small haemoptysis and died some hours later from a massive haemorrhage. The post mortem examination revealed migration of the wire stent into the pulmonary artery.

Silicone stents also have complication rates, ranging from 21.5% (65) to 42% (66). There is a high incidence of bacterial colonisation of all stents, which can lead to granular tissue formation (67, 68), the most common organisms being staphylococcus...
 aureus and pseudomonas aeruginosa in most series. The difficulty in culturing the
airway and stents by conventional flexible or rigid bronchoscopy is that the passage of
these devices introduces contamination from oral and pharyngeal secretions. Our study
was unique in that we used suspension laryngoscopy and an apnoeic technique for
‘clean’ removal of the stent before starting supraglottic jet ventilation(67) in a paralysed
patient.

The Airway Reconstruction Team have over 15 years experience of using
tracheobronchial stents of all designs. It is widely accepted that wire stents have a
higher incidence of granulation formation, especially at their ends. Some authors report
that silicone stents have a higher incidence of mucus plugging than wire stents (63).
However, this experience largely relates to the use of stents in the bronchi. In the upper
trachea, biofouling and mucus plugging is much greater in wire stents than in silicone
stents. This may be due to the relative lower humidity in this area. The incidence of
stent migration is widely reported as being higher in the subglottis than in the remainder
of the tracheo-bronchial tree. The reason for this appears to be due to the fact that the
subglottis is a fixed structure which is narrower than the trachea, especially with the
expansion allowed by trachealis. Hence there is a natural tendency for stents to be
pushed down. Stents placed high into the subglottis also run the risk of damaging the
vocal folds and causing granulation in this area. There is very little data on migration
rates of different tracheo-bronchial stents. Table 2.1 lists the largest recent published
series for airway stent, for both malignant and benign lesions. The author and his
predecessor, Professor David Howard, have for over 15 years been using the vertical
limb of a silicone T-tube as a stent. Different diameters of T-tubes are available and can
be cut to a suitable length and are placed in the airway under general anaesthesia and
suspension laryngoscopy. The stent is held in place with a suture through the tissues of the neck which is buried under the skin(69).

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Pathology</th>
<th>Stent type</th>
<th>Number of Stents in Series</th>
<th>Stent Migration Rate (%)</th>
</tr>
</thead>
<tbody>
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<td>1996</td>
<td>Mixed</td>
<td>Silicone</td>
<td>926</td>
<td>9.5</td>
</tr>
<tr>
<td>Wood et al (66)</td>
<td>2003</td>
<td>Mixed</td>
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<td>Hybrid</td>
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<td>Gottlieb et al (77)</td>
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<td>Benign</td>
<td>Metal wire</td>
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<td>Dooms et al (78)</td>
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<td>Silicone</td>
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<td>Charokopos et al (80)</td>
<td>2011</td>
<td>Benign</td>
<td>Metal wire</td>
<td>11</td>
<td>18.2</td>
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<tr>
<td>Chung et al (81)</td>
<td>2011</td>
<td>Mixed</td>
<td>Metal wire</td>
<td>149</td>
<td>32</td>
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</table>

Table 2.1 Illustrates the quoted migration rates for different types of airway stents for benign, malignant or mixed benign/malignant case series

A departmental audit has shown that migration of this type of stent, following failure of the suture, occurred in 2:200 cases (1%) without detriment to the patient. This review included patients in whom the stent was left in for more than a year. This is the lowest migration rate of any endoluminal stenting device. The added advantage of using this stenting technique is that it is not reliant for its fixation on firm adherence to the
tracheal wall. As a result, ciliary action continues to take place between the stent and the tracheal wall. This limits the degree of mucus plugging.

**Insertion of tracheo-bronchial stents**

Silicone stents usually have to be placed under general anaesthesia, using a ventilating rigid bronchoscope. The team uses a technique of suspension laryngoscopy with supraglottic jet ventilation and placement of a silicone stent with rigid stent forceps. Visualisation is assisted by a $0^\circ$, 30 cm Hopkin’s optical endoscope, which is 4 mm in diameter or a flexible bronchoscope. Wire stents come preloaded in delivery devices and can be passed parallel to a flexible bronchoscope in a spontaneously breathing, sedated patient, or using fluoroscopic screening techniques. Wire stents can also be inserted under general anaesthesia. Stent removal is easiest using a general anaesthetic technique. This allows the use of rigid biopsy or grasping forceps to firmly grip the stent even if embedded in granulation. Uncovered wire stents that have been in place more than three months will usually require an open surgical approach for removal (63).

**Post-operative care of a tracheo-bronchial stents**

All patients with stents are prescribed daily saline nebulisers. Carbocysteine can be added in those patients where there is evidence of mucus plugging. There is no research evidence to support the use of any of these measures.
Different types of Airway Stents

Illustration 2.13 Two types of laryngeal stents. These have to be closed superiorly to prevent aspiration. Eliachar (Hood Laboratories) stent and over-sewn silastic T-tube (white)

Illustration 2.14 Various tracheal stents. Cut length of silastic T-tube (left), Boston Scientific partially covered wire stent (middle of left picture), Dumon silastic stent (right of left picture), Alveolus Aero expanding wire stent (82) covered with polyurethane (right)
Illustration 2.15  Showing superficial skin graft, with epidermal surface in contact with paraffin-gauze sheet (left), draped over a silastic stent and sutured in place (middle). The finished composite stent is used for laryngotracheal reconstruction. This covered stent is associated with a reduced foreign body response and keratinocytes have fibro-inhibitory properties (83).

2.III.f  Lasers

Otolaryngology was the first surgical discipline to successfully apply the CO\textsubscript{2} laser. Jako (84) collaborated to develop the endoscopic attachment to a CO\textsubscript{2} laser and performed the first in vivo experiment on the canine larynx in 1969. Bredemeir in 1971 attached the manipulating arm of the CO\textsubscript{2} laser to the operating microscope providing binocular vision and depth of field. Strong and Jako (85) began applying the CO\textsubscript{2} laser to laryngeal microsurgery. The laser delivery system was further developed by Ossoff and Karlan (86) allowing delivery of the CO\textsubscript{2} laser under direct visualisation through the bronchoscope (illustration 2.16).
The laser allows precise ablative or cutting manoeuvres in the airway with reduced bleeding as compared to cold steel. Laser exposure time can be minimised by adjusting time of exposure, pulsing and super pulsing, and also adjusting the power delivery. Using the smallest spot size also minimises adjacent tissue damage. The CO$_2$ laser has a shallow depth of penetration with minimal adjacent thermal effect. The carbon dioxide laser operates at an invisible wave length (10.6 micrometres) and consequently requires an aiming beam which consists of a superimposed helium-neon laser. In the adult airway, the laser is set between 6-10 watts continuous delivery with the finest spot size to enable radial cuts in airway lesions. Treatment for papillomatosis requires a significantly lower power setting and super pulsing (1-5 watts). The spot size can also be reduced to use the laser in a superficial ablative mode. Developments in the use of the CO$_2$ include computerised scanning devices which attach to the micromanipulator and allow lasering to a defined depth and specific pattern as dictated by the software of the device. The disadvantage of the carbon dioxide laser is that it has not been possible to use it in a fibre delivery format until recently. Omniguide (Cambridge, Massachusetts, USA) have developed a fibre delivery system for the CO$_2$ laser. It
essentially consists of a tube with a shiny inner surface which allows the carbon dioxide laser beam to travel down its lumen. When the laser makes contact with the wall of this tube and reflected, heat is dissipated into this wall. As a result, this fibre is contained within a larger tube through which helium gas is delivered as a cooling agent. Currently no aiming beam is available with this laser. Lumenis Surgical (USA) have recently launched a CO₂ laser fibre, which also reflects the laser inside a reflective tube, but has an aiming beam. The cooling for this laser is with air pumped down the same channel as the laser light. Unlike the Omniguide system, which can precipitate air emboli if used below the carina, the Lumenis system is said to be safer (company communication).

The KTP laser emits a wavelength of 532 micrometres and this is preferentially absorbed by haemoglobin and other red pigments. This makes the KTP laser very useful in the treatment of vascular lesions. A fibreoptic delivery system enables its use in the distal airway, including the bronchi. When compared with the CO₂ laser, its tissue penetration is significantly deeper (4 mm versus 0.9 mm). There is therefore a risk of excessive scar formation due to greater tissue injury. The use of the KTP laser should be limited in airway surgery except in rare cases of bronchial surgery and occasionally for tracheobronchial papillomatosis.

The microdebrider was first used in respiratory papillomatosis in 1999 (87). The advantage of the microdebrider in tracheobronchial papillomatosis is in its ability to engage papilloma only and avoid damage to the healthy underlying epithelium. In addition, it avoids the potential risk of virus particles in the laser plume to theatre staff. It is therefore the preferred tool for tracheal papillomatosis.
2.III.g Mitomycin-C

Mitomycin-C (MMC), a potent antibiotic derived from the Streptomyces caespitosus bacteria, can modify wound healing at the molecular level and has been used to interfere with post surgical scar formation. Available since the 1960’s as a systemic chemotherapeutic agent in the treatment of solid tumours, Mitomycin-C was first applied topically for the treatment of superficial bladder tumours. Later, ophthalmologists pioneered its use in preventing scar tissue after surgery. It was first reported in the ENT literature for the treatment of tracheal scarring after tracheal reconstruction in a small case series (88). The mechanism of the drug’s anti-cellular action has not been definitively characterised. It is known to be a pro-drug that is activated into toxic forms that produce oxygen free radicals creating DNA strand breaks. Mitomycin-C also induces apoptosis in fibroblast cells (89). A number of randomised prospective animal studies have shown impressive results in prevention of post-operative glottic and subglottic stenosis following surgery to the airway (90-93). Its use in airway surgery has become fairly routine, despite no randomised controlled trials proving its efficacy. It is used in various concentrations and durations of application because optimum guidelines have not been firmly established. Its use in the airway in the USA is for 0.4 mg/ml, although some units have used higher concentrations (0.6 mg/ml). Philippe Monnier (Lausanne, Switzerland) has used Mitomycin at a concentration of 2 mg/ml applied topically for 2 minutes. This concentration and application time has been adopted by Great Ormond Street Hospital in London. For this research we have used Mitomycin at 1 mg/ml applied topically for 2 minutes. At one time, it was used routinely in the Airway Reconstruction Unit, but no discernible difference in symptom free intervals was apparent when comparing endoscopic surgery before Mitomycin and after Mitomycin. There is also concern
expressed regarding the long-term consequences of having used Mitomycin for benign disease.
Chapter 3

3.1 Surgery and Anaesthesia for Patients with Airway Compromise

Endoscopic airway assessment is performed by respiratory physicians, thoracic surgeons and otolaryngologists. Pulmonologists and thoracic surgeons are trained to use both flexible and rigid bronchoscopes. **Flexible bronchoscopy** is usually performed in the spontaneous breathing and sedated patient who has had topical anaesthetic applied to the upper aero-digestive tract. This technique allows assessment of the dynamic airway, the trachea and bronchi with the ability to perform the full spectrum of interventions. However, with a flexible bronchoscope placed through a narrow stenosis, the patient’s airway becomes obstructed. Similarly, attempted dilatation of an airway stenosis leads to temporary airway obstruction. The **rigid ventilating bronchoscope** (illustration 3.1) requires the patient to be paralysed and ventilated by a face mask or endotracheal tube until the bronchoscope is inserted. For assessment of the airway beyond an area of stenosis, the bronchoscope has to be forced through the stenosis. This has the effect of dilating the stenosis, but also causes stripping of the mucosa in a longitudinal fashion.

Illustration 3.1 Rigid ventilating bronchoscope (left) and flexible bronchoscope (right)
Neither flexible bronchoscopy nor rigid bronchoscopy allows prolonged access or endoscopic surgery on the larynx or subglottis.

**Suspension laryngoscopy** is performed routinely by otolaryngologists for access to the supraglottic and glottic larynx. Laryngologists are also comfortable operating on the subglottis via the microscope or rigid endoscopes. The advantages of the microscope are binocular vision, depth of field, superior axial illumination and it allows two hands free for instrumentation. Also, the laser can be used with a “line-of-sight” technique through a micromanipulator attached to the microscope. Many otolaryngologists still use the ventilating bronchoscope for tracheal or bronchial assessment and surgery. Suspension laryngoscopy allows the use of both optical rigid endoscopes and flexible bronchoscopes to access the airway. The advantages are that the patient is paralysed and the full spectrum of rigid instrumentation, dilators, lasers and stents can be inserted and used with relative ease. As the patient is ventilated using a supraglottic jetting technique, lasers can also be used without the risk of airway fires (illustration 3.2).

![Illustration 3.2 Suspension laryngoscopy (left) and Mistral (Acutronic, Switzerland) automated high frequency jet ventilator (right)](image)

**Paediatric airway surgery** performed by an otolaryngologist differs in that the child is usually breathing spontaneously and oxygen or a combination of oxygen and an
anaesthetic gas is delivered by a naso-tracheal tube withdrawn into the hypopharynx. Endoscopes and instrumentation can then be passed through the glottis to access the trachea and bronchi. This type of prolonged spontaneous breathing technique is not possible in an adult patient. Adults tend to lighten from anaesthesia much quicker with the associated risk of laryngospasm. Also, access to the larynx in an adult is much easier in a paralysed patient.

I prefer a technique of suspension laryngoscopy and supraglottic jet ventilation via a cannula attached to the laryngoscope (illustration 3.2). Illustration 3.3 demonstrates the differing views of the glottis in the same patient having supraglottic jet ventilation, subglottic jet ventilation and a microlaryngoscopy endotracheal ventilating tube.

Illustration 3.3 Demonstrates the improving access to the posterior glottis and subglottis when ventilating with a microlaryngoscopy endotracheal tube (left), subglottic jetting catheter (middle) and supraglottic jetting (right)

The jetting is delivered at high frequency (up to 100 jets per minute) using an automated device by Mistral (Acutronic, Switzerland). This device has built-in safety that sets an alarm if either the delivery of the jet or the return of gas is obstructed in the airway. There has been no incidence of a pneumothorax using this device is adult patients in our department over the last 10 years. This amounts to nearly ten thousand procedures. Pneumothorax has been described when using jet ventilation delivered by a ‘manual jet’ Sanders type device (94). This is probably related to the fact that the
delivery of the anaesthetic agents is less well controlled and there is no safety cut-out mechanism.

3.II Anaesthetic Technique

It is the practice in the Airway Reconstruction unit that all patients with airway stenosis have anaesthesia induced with an intravenous bolus of Propofol 3 mg/kg, Fentanyl 1-1.5 µg/kg and Atracurium 0.5 mg/kg for muscle relaxation. The vocal cords are sprayed with Lidocaine at 4 ml of 4% solution through an atomiser device. Intermittent positive pressure ventilation is established using a classical laryngeal mask airway (LMA) (Intavent, Orthofix, UK).

Illustration 3.4 Laryngeal Mask Airway in place

Once ventilation is established, the patient is transferred from the anaesthetic room to the operating theatre. The patient is transferred to the operating table and the laryngeal mask airway (illustration 3.4) is only removed when the surgeon is ready to perform suspension laryngoscopy and supraglottic jet ventilation can take place. Total intravenous anaesthesia is maintained using an infusion of Propofol and Alfentanil. At the end of the operation, the laryngoscope is removed and the LMA is re-inserted to support intermittent positive pressure ventilation. At this stage, neuromuscular block is antagonised with Neostigmine 2.5 mg and Glycopyrrolate 0.5 mg. The exception to the
use of an LMA is in a patient who already has a tracheostomy in place. The tracheostomy can be removed and the stoma covered with a wet swab to allow unencumbered access to the airway while performing supraglottic jet ventilation.

3.III Is it Safe to Paralyse a Patient with a Stenosed Airway?

3.III.a Introduction

The technique of paralysing and taking over the ventilation of a patient who has a severely compromised airway is contrary to anaesthetic teaching and understanding. Traditional teaching is for a patient with an airway compromise to be slowly “breathed down” with an anaesthetic agent and oxygen combination (an example is oxygen and Sevoflurane). The argument for this practice is that if the patient’s airway obstructs at any point during the induction, he or she will no longer breathe in anaesthetic gases and wake up. There is no research in the literature to support this practice, yet it is passed down from one generation of anaesthetists to another. A clear understanding of ventilatory changes associated with induction of anaesthesia and a safe approach to management that is based on sound physiological principles is essential in ensuring patient safety.

To address this, a collaborative study was undertaken with the anaesthetic team. This compared spontaneous and positive pressure ventilation in patients with laryngotracheal stenosis to determine the optimum method of ventilation in this patient group.

3.III.b Materials

Prospective study

Surgical anaesthetic records of 30 adult patients with laryngotracheal stenosis with or without a tracheostomy undergoing endoscopic airway surgery in our unit over a nine
month period in 2006 were prospectively studied. Information about patient
demography and lesion characteristics at the time of surgery was recorded. Formal
ethical approval for this observational study was sought but not deemed necessary by
the local ethics team. The reason for this was the fact that all the measurements reported
in this present study formed part of our standard clinical practice and no additional tests
were performed.

Patients

There were 19 male and 11 female patients, and the mean age was 47 (19 SD) years
(range 17-82 years) of ASA grade III or IV. The commonest aetiologies were post-
tubation tracheal stenosis which occurred in 23 (77%) patients and idiopathic
subglottic stenosis in 23%. Airway lesions were on average located 31 mm below the
vocal folds (SD 10) with a range of 5-50 mm. Twelve lesions (40%) caused luminal
obstruction of about 0-50% (Myer-Cotton grade I) while 9 lesions represented 51-70%
airway narrowing (Myer-Cotton grade II). A further 9 lesions led to an airway
obstruction between 71-79% (Myer-Cotton grade III).

3.III.c Methods

All patients underwent spirometry and flow volume loop examinations in the
anaesthetic room before general anaesthesia. None of the patients received pre-
medication. Measurements were performed according to the American
Thoracic/European Respiratory Society guidelines (95) using a MicroLoop portable
spirometer. Anaesthesia was induced as described above and at the end of the surgical
procedure, the laryngeal mask was replaced to support ventilation until the patient was
able to manage spontaneous breathing and control of reflexes. The anaesthesia details
are as described in section 3.II.
Flow volume loop measurements were obtained at the beginning of each procedure, after muscle paralysis, before establishment of supraglottic positive pressure ventilation and before any surgical manipulation had occurred. In all cases, the driving pressure was 20 cm H₂O, the ventilation frequency was 10 per minute and the inspiratory to expiratory (I-E) ratio was 1:1. These ventilatory settings are chosen to minimise auto-PEEP (positive end expiratory pressure). After steady-state conditions were reached, anaesthetised flow volume loops and inspiratory and expiratory tidal volumes (TVs) were recorded using a Datex Ohmeda AS₃ anaesthetic monitor.

Awake spirometry and flow volume loop variables were calculated using Spida 5.0 software. To assess the degree of airway obstruction within individual patients between awake and anaesthetised conditions, the ratio of peak expiratory (PEF) and peak inspiratory (PIF) rates was calculated (96).

3.III.d Results

The mean PEF/PIF ratio measured from awake flow volume loops of 2.4 (standard deviation 1.3) decreasing to 1.0 (0.1) during anaesthesia (p = <0.001, students T test) (illustration 3.5). The mean inspiratory and expiratory tidal volumes were 647 millilitres (193) with a range of 267-1,153, and 560 (158) range 219-930 respectively. In all cases, oxygen saturation remained above 95% throughout induction of anaesthesia. There was a significant correlation between awake PEF and anaesthetised expiratory tidal volume, but not between awake peak inspiratory flow rate (PIF) and anaesthetised inspiratory tidal volume. (Spirometry findings are in Table3.1).
Illustration 3.5 Awake flow-volume loops (A) obtained from a patient with extrathoracic airway stenosis showing significant diminution of the inspiratory component. Anaesthetised flow volume loops (B) from the same patient showing near symmetrical inspiratory and expiratory components. Awake peak expiratory flow (PEF) to peak inspiratory flow (PIF) measurements (C). During spontaneous ventilation, most extrathoracic intralumenal airway lesions selectively impair inspiratory airflow as a result of negative intratracheal pressure generated during inspiration. This elevates the PEF/PIF ratio. Anaesthetised PEF/PIF ratios obtained from the same patients (D), showing a highly significant reduction in the physiological degree of airway obstruction with positive pressure ventilation through a laryngeal mask airway.
Table 3.1 Spirometry findings

<table>
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<td><strong>FEV₁ (L)</strong></td>
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<tr>
<td>Grade I stenosis</td>
<td>3.28±.98 [1.81-2.55]</td>
<td>2.19±.30 [1.81-2.55]</td>
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<tr>
<td>Grade II stenosis</td>
<td>2.46±.14 [2.29-2.55]</td>
<td>1.82±.55 [1.13-2.63]</td>
</tr>
<tr>
<td>Grade III stenosis</td>
<td>2.03±.78 [1.67-2.59]</td>
<td>1.61±.81 [.95-2.79]</td>
</tr>
<tr>
<td><strong>FVC (L)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade I stenosis</td>
<td>4.50±.74 [3.50-5.43]</td>
<td>2.82±.17 [2.64-3.05]</td>
</tr>
<tr>
<td>Grade II stenosis</td>
<td>3.52±.57 [2.94-4.07]</td>
<td>2.88±.69 [1.69-3.54]</td>
</tr>
<tr>
<td>Grade III stenosis</td>
<td>3.21±1.01 [1.95-4.67]</td>
<td>2.36±1.07 [1.58-3.93]</td>
</tr>
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<td><strong>MEF₅₀ (L/s)</strong></td>
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</tr>
<tr>
<td>Grade I stenosis</td>
<td>3.48±1.45 [1.58-5.92]</td>
<td>2.46±1.02 [1.19-3.97]</td>
</tr>
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<td>Grade II stenosis</td>
<td>2.26±.33 [2.02-2.63]</td>
<td>1.73±.77 [1.07-3.05]</td>
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<td>1.94±1.06 [.16-2.88]</td>
<td>1.49±.96 [.62-2.87]</td>
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<td><strong>PEF (L/s)</strong></td>
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<tr>
<td>Grade III stenosis</td>
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<tr>
<td><strong>MIF₅₀ (L/s)</strong></td>
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<tr>
<td><strong>PIF (L/s)</strong></td>
<td>2.0 ± 1.2 [.7 – 5.7]</td>
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</tbody>
</table>

All variables were expressed ±SD and [range].

*Myer-Cotton stenosis grading system:* Grade I: 0-50% lumen stenosis; Grade II: 51-70% lumen stenosis; Grade III: 71-99% lumen stenosis; Grade IV: no lumen; FEV₁: Forced Expiratory Volume in one second; FVC: Forced Vital Capacity; MEF₅₀: Maximal Expiratory Flow at mid vital capacity. Variables found to be independently associated with FEV₁, FVC and MEF₅₀ on backward multiple regression were Myer-Cotton grade of the stenosis and patient age which was dichotomized at 45; PEF: Peak Expiratory Flow. The only variable found on backward multiple regression to be independently associated with PEF was Myer-Cotton grade of the stenosis. MIF₅₀: Maximal Inspiratory Flow at mid vital capacity; PIF: Peak Inspiratory Flow. No variables were found to be independently associated with MIF₅₀ and PIF.
3.III.e Discussion

This study found that in patients undergoing general anaesthesia for extra-thoracic intra-luminal laryngotracheal stenosis, intravenous induction of anaesthesia, muscle paralysis and positive pressure ventilation through an LMA is an effective method of ventilating patients during anaesthesia, regardless of the severity of the stenosis. The degree of upper airway obstruction observed and quantified using flow volume loops was significantly less than when anaesthetised flow volume loops were recorded under conditions of muscle relaxation and positive pressure ventilation in comparison with awake spontaneous ventilation. There was also a significant correlation between anaesthetised expiratory tidal volume and awake peak expiratory flow, but not between anaesthetised inspiratory tidal volume and awake peak inspiratory flow.

These observations can be explained by the physiological principles that govern air flow through the upper airway during inspiration and expiration and the impact of an extra-thoracic intra-luminal airway stenosis on ventilatory dynamics. During spontaneous inspiration, there is a negative extra-thoracic intra-tracheal pressure that causes indrawing of the mobile tracheal segments, further narrowing the lumen and limiting inspiratory air flow. In contrast, during expiration, there is a positive intra-tracheal pressure which improves airway dimensions and air flow (97). Thus, under conditions of spontaneous ventilation, laryngotracheal stenosis relatively impairs inspiratory air flow as detected on flow volume loop examination (98). With positive pressure ventilation, however, there is a positive intra-tracheal pressure during both phases of ventilation delivered during inspiration by the anaesthetic machine and during expiration by the elastic recoil of the lungs (97). With positive pressure ventilation therefore, the mechanics of both inspiration and expiration are favourable in respect of their impact on the stenosis.
These findings have implications for managing patients with laryngotracheal stenosis undergoing general anaesthesia. The optimal method for inducing anaesthesia in these patients is controversial. The traditional view is that spontaneous respiration is maintained and anaesthesia introduced with a volatile inhalation anaesthetic given by a face mask (99). This is based on the assumption that this is safer than IV induction and muscle paralysis because if apnoea occurs, the patient will stop inhaling the anaesthetic and will awaken to regain airway control and spontaneous ventilation. Our results demonstrate the this approach is unsafe in patients with intraluminal laryngotracheal stenosis and that muscle paralysis and supraglottic positive pressure ventilation using an LMA is more effective.

The use of an LMA is already recognised as being integral to managing the difficult airway. The Difficult Airway Society guidelines indicate that an LMA should be used as a rescue device after unanticipated failure to intubate the trachea and after failure of mask ventilation (100). Thus, the use of the laryngeal mask airway immediately after induction of anaesthesia in patients with laryngotracheal stenosis who can be considered to be anticipated impossible intubations is both logical and consistent with published guidelines. We have found that lesion consistency (soft fibro-inflammatory lesions or mature fibrotic lesions) does not appear to have a bearing on the improvement in ventilation after transition from spontaneous to positive pressure ventilation. However, large pedunculated and mobile supraglottic lesions can obstruct the laryngeal inlet. Assessment of size, mobility and site of lesions is therefore essential before this method is used. In our practice, this involves visualisation of the supraglottis and the laryngotracheal complex with flexible nasendoscopy before induction of anaesthesia in all patients. This assessment generally is performed in the out-patient department and findings appropriately documented.
In the presence of an extra-thoracic airway stenosis, spontaneous ventilation is associated with significant ventilatory impairment, even in awake, upright patients as a consequence of the effect of the stenosis on ventilatory dynamics. Spontaneous ventilation during induction of anaesthesia makes use of these same “disadvantaged” ventilatory dynamics. An increased collapsibility of the upper airways (101), added work of respiration (102) and reduced functional residual capacity add to this disadvantaged physiology. Therefore, spontaneous ventilation during induction of anaesthesia is less reliable and more dangerous (103).

In contrast, the use of muscle relaxants followed by positive pressure ventilation through an LMA lessens the detrimental impact of the stenosis on the ventilatory dynamics, achieving adequate ventilation to maintain safe levels of oxygenation. We have used this method extensively in this group of patients and have not encountered major problems related to induction of general anaesthesia.

In conclusion, this study demonstrates that in the presence of an upper airway obstruction as a result of an intra-luminal, extra-thoracic, laryngotracheal stenosis, placement of a laryngeal mask with muscle paralysis and positive pressure ventilation is associated with improved ventilatory dynamics compared with spontaneous ventilation. It is proposed that in patients with known laryngotracheal stenosis undergoing shared airway reconstructive surgery or in patients who present as an emergency and in who extra-thoracic laryngotracheal stenosis is expectedly diagnosed, an LMA with positive pressure ventilation offers the most physiological method of achieving and maintaining a safe airway during induction of anaesthesia.
Chapter 4

4.1 Aetiology of Adult Post-intubation Laryngotracheal Stenosis

In 1950, anaesthesiologist, Peter Safar, established the concept of “advanced support of life”, keeping patients sedated and ventilated in an intensive care environment. During the polio epidemic in Copenhagen in 1952 (where paralysed patients had to be ventilated for prolonged period), Bjorn Ibsen set up the first Intensive Care Unit (ICU) (23). This led to an ever widening use of mechanical ventilation to treat respiratory failure. The iatrogenic lesions that resulted provided a whole new field of endeavour for surgeons. In the 1960s, scores of papers appeared in Europe and North America, describing surgical resection of post intubation strictures. Prevention of post intubation injury quickly became a priority once the origin of these lesions was evident. Initially high pressure cuffs were used and risked ischaemic injury to the mucosa and necrosis of the cartilage of the trachea. Carroll and colleagues in 1969 recommended a cuff with a large volume and low pressure which only resulted in small increases in tracheal wall pressure with over-inflation (104). Although the incidence of post intensive care unit airway stenosis is unknown and can only be approximated at between 1- 4%(105-108), a significant early injury is evident in 47% of patients (109). This is despite the use of these high volume, low pressure cuffs on endotracheal and tracheostomy tubes. This is the only paper in the literature where the trachea has been examined at the time of endotracheal tube removal. Unfortunately it does not make clear the definition of ‘significant injury’.

The anatomical and pathological differences between stomal and cuff stenoses and other post intubation injuries were described at this time by Pearson, Grillo and Harley. They also stressed the importance of allowing florid inflammation to subside prior to surgical
correction (110-113). They demonstrated that surgical resection and anastomosis produced better results than repeated dilatation, steroid injection or cryotherapy. The results of treating post intubation stenosis with resection by the same colleagues achieved an 87.5% “cure” in 200 patients in 1992. The definition of ‘cure’ appears to include patients with a suboptimal airway. Couraud and colleagues reported a 96% success rate in 217 patients in 1994, and Grillo and colleagues cited a 94% success in 503 patients in 1995 (4, 114, 115). They also described the correction of post intubation stenosis involving the subglottic area as being more difficult than lesions of the trachea.

The aetiology of post intubation stenosis injuries was initially unclear. At first it was thought to be due to irritation from the materials from which tubes and cuffs were made(116). Later it became clear that pressure necrosis from tubes and cuffs leading to circumferential injury and contracture was the principal explanation(117).

The risk factors for laryngotracheal stenosis following a period of ventilation on the intensive care unit include: sizing of endotracheal tubes, excessive lateral cuff pressure due to poor cuff pressure monitoring, hypotension, local infection, duration of intubation, use of steroids and other causes of reduced patient immunity, patient movement and agitation, tracheostomies and bilateral injuries of posterior vocal cords. The majority of patients ventilated on ICUs do not appear to develop airway stenosis. Although there are many aetiological factors, patients who tend to scar excessively following injury, may self select for airway stenosis although there is no clinical study to support this.

With respect to endotracheal tubes, modern tubes are of a high volume, low pressure design to reduce the risk of airway injury. To prevent ischaemic damage, the cuff should not exceed a pressure greater than the capillary perfusion pressure of the mucosa. The mean capillary blood pressure is about 20 mmHg. This is 27.2 cm H₂O pressure
The recommendation is that the cuff inflation pressure, of a ventilation tube, should not exceed 30 cm. Seegobin (119) studied four types of large volume, low pressure cuff types. Following periods of endotracheal intubation, photographs were taken of the circumferential trachea at the site of cuff contact. Photographs were taken for varied cuff pressures after a period of 15 minutes. The conclusion of the study was that lateral wall pressures above 30 cm of water compromise mucosal capillary blood flow leading to pressure necrosis of the adjacent mucosa and eventually the cartilage.

The other risk factors for laryngotracheal injury in a ventilated patient on the ICU (illustration 4.1) probably include gastric reflux, infection, coexisting health problems (such as diabetes mellitus and arteriopathy) and altered immunity as part of the stress response. There is, however, no research to support these as potential risk factors.

![Illustration 4.1 Typical appearance of tracheal injury at extubation on the ICU](image)

Post tracheostomy stenosis had been described as early as 1886 when Colles found four strictures in 57 patients treated for diphtheria (120). In my series of 400 adult patients with benign laryngotracheal stenosis the incidence of airway stenosis from endotracheal tubes was approximately the same as the incidence from tracheostomies. Damage to vocal fold anatomy and impairment of vocal cord mobility is more common with
endotracheal tubes (121, 122). Surgical management of bilateral vocal fold immobility is always a compromise between voice and airway. There is very little evidence supporting early tracheostomy on ICUs (123). The TracMan study was a multicentre UK study designed to look at the timing, morbidity and mortality associated with tracheostomies on intensive care units. Although the trial phase of this multicentre study took place in 2004, the main phase of the study failed to progress. Although this thesis cannot comment on the morbidity and mortality associated with early versus late tracheostomy, following review of the 400 patients in the database, some conclusions can be reached. There is a real risk of damage to the normal function of the glottis and vocal folds that exists with endotracheal intubation that does not occur in patients with a tracheostomy. As the surgical results of restoration of impaired glottic function remain suboptimal, early tracheostomy would minimise the risk of glottis stenosis and bilateral vocal fold mobility impairment.

4.II Theories of Wound healing

The classical model of epithelial wound healing is divided into three sequential yet overlapping phases (124). Using injury to the skin as an example; a set of complex biochemical events take place to repair the damage. Within minutes post-injury, platelets aggregate at the injury site to form a fibrin clot. This clot acts to control active bleeding through haemostasis. The first phase of wound healing is the inflammatory phase, in which, bacteria and debris are phagocytosed and removed. Factors are released that cause the migration and division of cells involved in the proliferative phase. The proliferative phase is the second phase of wound healing and is characterised by angiogenesis, collagen deposition, granulation tissue formation,
epithelialisation and wound contracture. Fibroblasts grow and form a new provisional extra-cellular matrix by excreting collagen and fibronectin. Re-epithelialisation of the epidermis occurs in which epithelial cells proliferate and grow across the wound bed, providing cover for the new tissue. At the same time, the wound is made smaller by the action of myofibroblasts which establish a grip on the wound edges and contract themselves using a mechanism similar to that in smooth muscles (illustration 4.2).

Illustration 4.2 To show healing of a skin wound by secondary intention. The myofibroblasts contract to approximate the epithelium and resorption of fibrosis takes place.

Once the cells’ roles are close to complete, redundant cells undergo apoptosis (125).

The third phase of wound healing is the maturation and remodelling phase. Collagen is remodelled and realigned along tension lines and cells that are no longer needed are removed by apoptosis. The remodelling phase can last from 3 weeks to 2 years.

It is clear that keratinocytes have a significant effect on fibroblast wound healing activities and the lack of an epidermis results in fibrosis of the underlying or adjacent tissues (83). Epidermal cells regulate the activity of dermal fibroblasts. In particular, epidermal keratinocytes decrease collagen production and increase the replication rate of these cells. Therefore, early wound closure will decrease wound fibrosis (126).

Approximately 130,000 patients each year, in the United Kingdom, are ventilated on intensive care units (127) and very few have subsequent laryngotracheal stenosis. The
factors at play in the patients who do develop laryngotracheal stenosis are discussed later in this chapter. There is very little research to date on the variability of wound healing in this group of patients. It is already recognised that some patients are prone to hypertrophic scar formation and others have a more aggressive healing biology that results in the formation of keloid scars. It is therefore likely that some of the patients who go on to develop laryngotracheal stenosis, do in fact have a more aggressive healing biology. This needs to be investigated in a future research project. I decided at the outset, in order to minimise scar tissue formation and wound contracture, with open reconstructive procedures requiring stenting, the stent would be covered by a superficial skin graft (dermis outmost) as a biological dressing. This was to use the ability of epidermal keratinocytes to down regulate fibrosis and scarring (83). In a circumferential injury in the airway (illustration 4.3), covering the wound with keratinocytes in one sense replicates early wound closure. One adverse side effect of this approach is that there is a degree of keratosis within the airway where keratinocytes have colonised the wound. This decreases over time and in only one case it has been necessary to laser ablate these colonies of keratinocytes.
Illustration 4.3 The process of repair of a circumferential injury, in an organ with a lumen, is the same as for healing by secondary intention. However, the process of healing by contracture continues because there are no epithelial ends to come together.

Illustration 4.4 If the circumferential airway injury is separated by new tissue (grey) then it is not possible for healing and contracture to produce a significant stenosis. This may explain the successful outcomes in cases of adult airway repair with primary rib cartilage or tracheal homografts. (If the augment tissue survives, even for a few weeks, it will separate any attempts at healing by circumferential contracture.)
4.III What is the Incidence of Post-intubation Laryngotracheal Stenosis in Adult Patients in the UK

The incidence of adult post-intubation laryngotracheal stenosis in the UK is unknown. For the purpose of this research, an estimate of its incidence was made by calculating the incidence within one individual primary care trust (PCT). A PCT is a body which commissions and purchases secondary and subspecialist services on behalf of a defined population of patients.

A review was carried out of the number of referrals over a 3-year period (2004-2006) from those PCTs in the Greater London area which are in the geographical vicinity of the two hospitals offering a subspecialist airway reconstruction service. The average of the number of cases referred per year was divided by the overall population of adult patients within the referring PCTs to obtain the rate. Over this period, these units received 13.3 patients per year from a catchment area of 2.72 million, which gave an incidence of 4.9 cases per million per year.

Assuming that the national variation in incidences is comparable with local variation within Greater London, the extrapolated number of new cases likely to arise in England per year is 197, with a binomial 95% confidence interval of 170-226. This methodology only provides a rough estimate and in particular there can be no certainty that every patient referred for airway reconstruction from this catchment area is referred to these units. This can lead to underestimation. It is not likely, however, that this calculation omits a large number of thoracic surgical cases as the overall number of tracheal operations performed for adult post-intubation laryngotracheal stenosis by thoracic surgeons is relatively small (Professor Peter Goldstraw personal communication). It must be accepted that there are significant methodological
limitations in the absence of longitudinal population level epidemiological research in this area.

The average number of admissions to all intensive care units in the UK is 130,000 per annum (127). It is not precisely known how many patients receive mechanical ventilation and for how long, but 34.2% of UK patients stay in intensive care units for more than 2 days and this group has a survival rate of 70.2% (128). An international study of 15,757 patients estimated that 32.9% of intensive care patients receive mechanical ventilation for more than 12 hours with a survival rate of 69.3% (129). We can therefore assume that only 33% of UK intensive care unit patients receive mechanical ventilation and that their survival rate is 70%, which gives an estimate of 30,030 annual survivors of mechanical ventilation and therefore represents an estimate of the at risk population of the UK.

The incidence of late post-intubation laryngotracheal stenosis can be estimated from a prospective study of 654 consecutive intensive care patients undergoing mechanical ventilation receiving post extubation bronchoscopy and long-term follow-up. This identified 12 cases of severe glottic, subglottic or tracheal stenosis 6-12 months following extubation among the 389 survivors. This translates to an incidence of post-intubation laryngotracheal stenosis of 3.1%. If a lesser degree of subglottic or tracheal stenosis is to be considered, the incidence of late post intubation laryngotracheal stenosis rises to 4.6% (109). The same paper identifies significant tracheal and airway injury at the time of extubation at 47%. This gives an estimate of the incidence of severe late post-intubation laryngotracheal stenosis of 926 new cases per year. Based on the number of referrals to the airway reconstruction team, I have estimated that the annual population incidence to be 197 (130). This reveals a discrepancy in that as many as 4 out of 5 patients with post-ICU laryngotracheal stenosis may not receive treatment.
There must therefore be a considerable pool of patients who are suffering a respiratory handicap which is potentially treatable. If these findings are confirmed, they lend support to the establishment of routine post ICU follow-up clinics where post-intubation laryngotracheal stenosis and other ICU complications can be identified early and treated. The difficulty, however, remains that a number of these patients may live some distance from the intensive care unit where they were treated and may not return for follow-up. Routine post-ICU screening could be performed by primary health care practitioners at 3 to 6 months using standard spirometry and a modification of the Empey Index (131) as discussed in section 6.1. The cost effectiveness of such a screening programme would have to be weighed against improvements in quality of life. This would need to be preceded by a dedicated study looking at the airway following discharge from the ICU.

**4.IV Out-patient Evaluation**

The majority of patients referred to the Airway Reconstruction unit already have a diagnosis of airway stenosis as they have been seen by a respiratory physician and appropriately investigated. Some ‘breathless’ patients, with inflammatory diseases such as sarcoidosis and Wegener’s granulomatosis, are referred for examination of the airway to screen for laryngotracheal airway compromise. A much smaller number of patients are referred because they have failed extubation or decannulation on the ICU and laryngotracheal airway compromise is suspected. An accurate clinical history is therefore important. It is also important to determine the duration of symptoms and whether there were preceding health problems contributing to dyspnoea. Details related to the period of time on the intensive care unit and whether the patient was intubated or
weaned with a tracheostomy should be determined. A history of vasculitis or connective tissue disorders is also relevant. The patient should be questioned as to whether there is a cough, about the degree of limitation to daily activities, voice changes and swallowing problems. Clinical examination should determine whether there is stridor or voice changes. The degree of recession of the chest, if present, is also important to document. Flexible endoscopic examination of the upper aerodigestive tract will allow assessment of vocal cord function, evidence of reflux, demonstrate pooling of secretions and may also determine the site and degree of airway stenosis. A detailed assessment of vocal cord function and swallowing is vital if laryngotracheal surgery is to be considered (table 4.1).

The body mass index also has a bearing on a patient’s oxygen demand and the likely success of surgery (section 4.VIII.c). Significant pre-existing lower respiratory tract pathology may also be a contraindication to decannulation.

Baseline respiratory function tests, which include flow volume loops, are arranged in all patients and computer tomographic (CT) imaging of the airway if not already performed. The problem with assessing airway stenosis on a CT scan relates to the fact that imaging is a form of sampling. Unless fine cuts are made through the airway at 1-2 mm, the apex of the stenosis may be missed and the degree of stenosis underestimated. Similarly, if there are secretions overlying the apex of the stenosis, then it may be overestimated. CT scans help to confirm airway compromise and act as a guideline to its severity. Definitive assessment of the airway injury is made at laryngotracheoscopy under anaesthesia.
Table 4.1 Outpatient assessment of patients with chronic airway compromise

**History**
- Aetiology
- Disability
- Voice/swallowing problems

**Examination**
- Stridor and voice
- Chest recession on breathing
- Body morphology (body mass index)
- Fibreoptic nasal endoscopy
  - Vocal cord mobility
  - Evidence of GORD
  - Pooling of hypopharyngeal secretions
  - View of subglottic stenosis (not always possible)
- Fibreoptic endoscopic view of airway via tracheotomy

**Investigations**
- High definition computed tomography (CT) with reconstruction
- Respiratory function test
  - Spirometry
  - Flow volume loops
  - Testing exercise limits
- Videofluoroscopy/fibreoptic endoscopic evaluation of swallowing (FEES)
- Investigations for GORD
- Blood tests for inflammation, vasculitis and sarcoidosis

**4.V Airway Assessment Under Anaesthesia**

The procedure is performed in the operating room. General anaesthesia is introduced intravenously and muscle relaxants are administered in all cases (96). A total intravenous anaesthesia technique is maintained throughout the procedure and the airway is initially secured with a laryngeal mask airway (LMA). (The anaesthetic technique is described in detail in section 3.II). The LMA is replaced with high-
frequency (up to 100 cycles/min) supraglottic jet ventilation delivered through a suspension laryngoscope. I prefer the Dedo-Pilling (Pilling, USA) laryngoscope for endoscopic airway surgery with the laryngostat supported on a modified Mayo Table which is attached to the operating table. The airway and lesion are visualised using a combination of microscope and 4mm, 0 degree, 30cm Karl-Storz rigid endoscope.

Illustration 4.5 Showing the set-up in an airway theatre. The patient’s face is covered with wet swabs while the laser is being used

4.VI Objective Airway Sizing

4.VI.a Introduction

Objective sizing of laryngotracheal stenosis can be performed using computed tomography (CT), especially high resolution imaging with multi-planar reconstruction (illustration 2.3). This provides the best anatomical information (132). CT scans cannot, however, differentiate between the true lumen and overlying secretions which introduces inaccuracies in the presence of blood, mucous or crusting (133).
Furthermore, a CT scan works on the principle of cross-sectional sampling of anatomy and since the calibre of the airway is not orientated perpendicular to the plane of the scan, the combination of slice thickness and image reconstruction can introduce further inaccuracies (118). High definition CT scans which largely overcome these problems are expensive and introduce a high dose of radiation, making them unsuitable for monitoring patients through what can be a multi-stage treatment process (illustration 4.6 right).

Pulmonary function testing (134) does provide an indication of the severity of airway stenosis, but does not provide accurate anatomical information. Other methods proposed for airway sizing have included acoustic reflection techniques (135). Endoscopy is the main tool for assessing and treating laryngotracheal stenosis. It allows direct visualisation of luminal pathology, observation of laryngotracheal dynamics and institution of endolumenal therapy (133, 136, 137). Robin Cotton of Cincinnati Hospital, Ohio, originally devised a grading system of airway stenosis in paediatrics based on leaks around different sized endotracheal tubes at ventilating pressures of just beyond 30 cm of water. The system was revised into the Myer-Cotton grading system. This classifies subglottic stenosis into 4 grades (Illustration 4.6 left).
Illustration 4.6 The Myer-Cotton Grading System (left) for paediatric laryngotracheal stenosis (10). CT scan with image reconstruction to show subglottic stenosis (right).

The grades relate to the surface area of the stenosis and provide a guide to the type of management necessary for the patient. Symptomatic paediatric laryngotracheal stenosis grade II and III is most appropriately managed with a laryngotracheal reconstruction using cartilaginous augmentation either anteriorly, or anteriorly and posteriorly placed in the subglottis. Cricotracheal resection is reserved for a grade III or grade IV stenosis which does not involve the vocal folds or used as a salvage procedure after failed laryngotracheal reconstruction. The Myer-Cotton grading system is useful tool for stratifying airway stenosis so that guidance on surgical management can be formulated.

In terms of symptoms, resistance to air flow is inversely proportional to the fourth power of the radius of the airway at the stenosis. As a result, there can be an exponential increase in air flow resistance (symptoms) within one Myer-Cotton grade (illustration 4.7).
As the Myer-Cotton grading system does not measure absolute cross-sectional diameter of the airway, there can be errors in its assessment, for example when there is an hour glass deformity of the trachea associated with a stenosis. Quantitive assessment of airway cross-section is, however, compounded by the fact that endoscopic images lack calibration and suffer from a non-linear optical distortion which is a function of the lens to object and centre to periphery distances (133, 136-138); variables not easily measurable in vivo. Moreover, a hand held endoscope invariably has a small, but difficult to determine, tilt in relation to the airway. I therefore felt that a method had to be devised for precise determination of airway dimensions.

Illustration 4.7 To show the relationship between airway radius and Myer-Cotton grades of stenosis (Resistance \( \propto \frac{1}{\text{radius}^4} \))
4.VI.b Analysis of Airway Assessment

Experimental validation - Impact of tilt

It is impossible in a clinic setting to guarantee perfect alignment between the endoscopes and the instruments introduced intra-luminally and the long axis of the airway, nor is it easy to measure such angles of tilt (illustration 4.8). The first objective was therefore to assess the impact of tilt on image characteristics to determine whether accurate measurements could be made independently of it. Images of a 9 mm diameter circle with a 4 mm 0° Karl Storz endoscope (Karl Storz, Tuttlingen, Germany). The endoscope was mounted on a micromanipulator with the tip suspended 15 mm above the circle and images were taken with tilt between 0° and 45° (illustration 4.8).

Illustration 4.8 Experiment set-up to evaluate the effect of endoscopic tilt on image characteristics. With the endoscope perpendicular to the object being measured, the endoscopic image of a circle is circular (y = x; panel A). If, however, the endoscope is tilted (α), the endoscopic representation of a circle tends to be an ellipse, with the relationship between the short and long diameters of the apparent ellipse (x’ and y’; panel B) a function of cos(α)(133)

Three measurements of the surface area of the endoscopic image of the circle were obtained with planimetry software (Carnoy, Laboratory of Plant, Flanders) using the
apparent horizontal and vertical diameters of the image for calibration. The ratio of averages of the two sets of measurements was expressed as a function of endoscopic tilt. All measurements were then averaged to give a biaxial calibrated calculation of the surface area. Measurement accuracy was assessed by comparing the calculated surface area with the actual value \((\pi r^2; r = 4.5)\) and expressed as a function of tilt.

**Experimental validation - Impact of lens distortion**

Four circles with diameters of 6, 9, 12 and 15 mm were drawn. A 22 mm diameter circle was concentrically drawn around them. A number of 4 mm diameter circles were then drawn so as to occupy the space between the centre and periphery of the 22 mm circle. A 3 cm long tube of 22 mm internal diameter was then placed over the outside circle to simulate a lumen (illustration 4.8).

A 4 mm 0° Karl Storz endoscope was held by hand within the lumen to take images. Images were obtained at different ‘lens to object’ distances with the examiner attempting to minimise image tilt and maintaining the endoscope at the centre of the lumen (illustration 4.9). The 4 mm diameter circles were used for biaxial image calibration and from their ‘known’ dimensions, the surface area of the central circles were calculated by an examiner blinded to the dimensions. Measurement accuracy was calculated as the percentage of the measured surface area to the actual values \((\pi r^2:\) where \(r = 3, 4.5, 6 \& 7.5\) mm) expressed as a function of the percentages of the field of view.
Illustration 4.9 shows the experimental set-up used to obtain endoscopic images for experimental validation. The endoscope was held above the image within the lumen of a 30mm long bronze tube with an internal diameter of 22mm (top panel). As the endoscope is withdrawn, smaller portions of the endoscopic image and more of the luminal wall will be visualised (middle panel). This was used to determine the field of view (%FOV: b/a) occupied by the measured image (bottom panel). This was used as an indicator of the distance between the endoscope lens and the object being measured.

4.VI.c Materials and Methods

The cross-sectional areas of the stenosis was evaluated in ten patients undergoing microlaryngoscopy and endoluminal laser therapy and dilatation for upper airway stenosis. A circular endoscopic probe in the shape of a ring of 4mm internal and 4.36mm external diameter was designed in such a way that the ring was at right angles to the long axis of the handle. The probe was introduced into the lumen of the airway alongside the endoscope (illustration 4.10).
Illustration 4.10 The probe (left) is used to determine the length and location of an upper airway stenosis. The probe is advanced to the lower level of the stenosis and the position is marked on the probe handle (c). The probe is then withdrawn to the proximal level of the stenosis (b), and then to the level of the vocal folds (a). The length bc marked on the probe handle denotes the length of the stenosis and ab the distance from the vocal folds. Endoscopic view of the probe in position at level of stenosis (right).

The probe was advanced under endoscopic vision to a level just beyond the level of the stenosis. Gentle traction was used to confirm that the probe was resting at the distal level of the stenosis. The position of the handle of the probe in relation to the edge of the laryngoscope was marked with a sterile marking pen. The probe was then withdrawn to the proximal level of the stenosis, and its position confirmed under endoscopic vision, and then to the level of the glottis. Each position was marked with the marking pen. From these marks the location of the stenosis in relation to the vocal folds and the length of the stenosed segment were calculated. The cross-sectional area of the stenosis was measured at its narrowest point and photographs taken with the probe in position. Two independent observers calculated the cross-sectional area of the stenosed airway, Pearson’s coefficient of correlation was used to assess inter-observer concordance.
4.VI.d Results

Assessing the impact of endoscope tilt

Illustration 4.11 shows the impact of endoscope tilt on image properties. As the endoscope is progressively tilted the apparent dimensions of the captured image change as a function of the cosine of the tilt angle. As this angle is unknown in the clinical setting, the image was calibrated using both horizontal and vertical diameters of the circle. Using biaxial calibration the effect of tilt on measurement accuracy was eliminated. All subsequent measurements were taken with biaxial image calibration.

Illustration 4.11 Bottom panel – impact of uncorrected endoscopic tilt on apparent image dimensions. Top panel – Biaxial calibration eliminates the impact of endoscopic tilt on measurement accuracy

Assessing the impact of endoscopic distortions

Previous work has shown that the visuo-spatial distortion, which is inherent to the optics of the wide-angle lenses used to obtain endoscopic images, is a function of the
distance between the lens and object being measured, and the distance from the centre to the periphery of the endoscopic image. Objects at the periphery of the endoscopic view appear smaller than central objects (radial distortion), and the degree of this central-to-peripheral distortion changes as a function of the distance between the endoscope lens and the object being measured (distance distortion). In other words, a small object located at the centre of the endoscopic field, viewed with the endoscope some distance away from it will suffer less distortion than a large object occupying most of the field of view, with the endoscope placed close to it (133, 136, 137, 139).

Illustration 4.12 Effect of lens-to-object distance, expressed as %FOV, and the accuracy of obtaining surface area measurements. For a small object placed at the centre of the field of view (6mm circle), the impact is negligible because the diameter of the object is comparable to that of the calibrating probe. However, for a larger object (12mm circle), occupying both the centre and periphery of the endoscopic image, the impact is considerable and increases as the endoscope moves closer to the object.

Illustration 4.12 (bottom panel) shows that the surface area of a small, centrally positioned object, calibrated with a single centrally placed circular calibrator, could be precisely determined independent of radial or distance distortions. By contrast, the
dimensions of larger objects, spanning into the periphery of the endoscopic image, could not be accurately determined if a single calibrator was used (top panel). A centrally placed calibrator increasingly underestimated true dimensions as visuospatial distortion increased with increasing lens-to-object proximity. The reverse was true if a peripherally placed calibrator was used.

Illustration 4.13 shows measurements obtained from a 12mm diameter circle with the endoscope lens in close proximity. Three calibrating circles, placed at the centre, mid-periphery and periphery of the image were used to biaxially calibrate the image. Using the central calibration alone, the true surface area was underestimated. While using the peripheral calibrator, the true surface area was overestimated. However, combining the three calibrations (i.e. “sampling” the endoscopic field of view at different radial points), the average of the three calibrations was a highly accurate measurement.
Illustration 4.13 Overall measurement accuracy, combining the principles of biaxial and radial span calibrations. Accurate surface area measurements could be obtained regardless of the size of the object being measured (6, 9, 12, 15mm circles), and the distance between the endoscope and the object. Inset An illustration of the principle of covering the ‘radial span’ of the object being measured.

Obtaining an overall measurement

Taking the above observations into account, we obtained measurements from circles of different diameters, with the endoscope placed at different distances from them using the following rules: 1. Trying to place the endoscope at the centre of the lumen and attempting to minimize tilt. 2. Obtaining biaxial calibrations 3. Calibrating the image at
more than one radial point in such a way that the calibrators traversed the radial extent of the area being measured (illustration 4.13 inset). Illustration 4.13 also shows overall measurement accuracy for circles of different sizes using this method, indicating that cross-sectional area could be calculated from endoscopic images with >95% accuracy, independently of the size of the object, lens-to-object distance, and without the need to make assumptions about the degree of optical lens distortion.

Clinical Application

Ten adult patients with an average age of 48 years (range 24-63) were anaesthetised with total intravenous anaesthesia. Supraglottic jet ventilation allowed unencumbered surgical access to the airway. Table 4.2 shows the background and quantitative measurements of length, location and cross-sectional area of stenosed airways in 10 patients.

Two independent observers calculated airway cross-sectional from intra-operative images. Pearson’s co-efficient of correlation was 0.98 with a slope and interceptor 0.93 +/- 0.05 and 7.67 +/- 3.02 mm respectively indicating a high degree of inter-observer concordance (illustration 4.14).
Table 4.2 Background and Measurements of Stenosed Airways in 10 patients

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Aetiology</th>
<th>GD</th>
<th>SL</th>
<th>Pre-CS</th>
<th>Post-CS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>mm</td>
<td>mm</td>
<td>mm²</td>
<td>mm²</td>
</tr>
<tr>
<td>24</td>
<td>M</td>
<td>post-intubation</td>
<td>42</td>
<td>10</td>
<td>9.4 ± 3.3⁺</td>
<td>141.2 ± 4.1</td>
</tr>
<tr>
<td>51</td>
<td>F</td>
<td>Amyloidosis</td>
<td>30</td>
<td>10</td>
<td>71.9 ± 2.9</td>
<td>75.1 ± 3.1</td>
</tr>
<tr>
<td>41</td>
<td>F</td>
<td>Post-intubation</td>
<td>39</td>
<td>10</td>
<td>32.3 ± 1.1</td>
<td>122.0 ± 2.0</td>
</tr>
<tr>
<td>60</td>
<td>M</td>
<td>Post-intubation</td>
<td>35</td>
<td>6</td>
<td>47.2 ± 0.5</td>
<td>124.7 ± 4.4</td>
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<tr>
<td>43</td>
<td>F</td>
<td>Idiopathic</td>
<td>23</td>
<td>17</td>
<td>14.2 ± 3.4⁺</td>
<td>164.7 ± 4.1</td>
</tr>
<tr>
<td>41</td>
<td>F</td>
<td>Papillomatosis</td>
<td>21</td>
<td>9</td>
<td>14.0 ± 3.4⁺</td>
<td>164.7 ± 1.8</td>
</tr>
<tr>
<td>58</td>
<td>M</td>
<td>Wegener’s</td>
<td>33</td>
<td>5</td>
<td>41.2 ± 5.9</td>
<td>131.7 ± 10.4</td>
</tr>
<tr>
<td>46</td>
<td>F</td>
<td>Post-intubation</td>
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<td>7</td>
<td>142.1 ± 2.1</td>
<td>146.6 ± 3.4</td>
</tr>
<tr>
<td>63</td>
<td>F</td>
<td>Post-intubation</td>
<td>38</td>
<td>10</td>
<td>63.9 ± 2.7</td>
<td>185.3 ± 1.9</td>
</tr>
<tr>
<td>54</td>
<td>M</td>
<td>Post-intubation</td>
<td>44</td>
<td>9</td>
<td>46.3 ± 1.3</td>
<td>156.1 ± 2.0</td>
</tr>
</tbody>
</table>

All measurements are ± standard deviation

1. Glottic Distance (Distance from vocal folds to the proximal level of the stenosis; ‘ab’ on illustration 4.10).

2. Stenosis Length (bc on illustration 4.10).

3. Pre-treatment cross-sectional area of the stenosis.

4. Post-treatment cross sectional area of the stenosis.

* These patients had a tracheostomy at the time of endoluminal surgery
Illustration 4.14 Correlation between clinical measurements of airway dimensions obtained by two independent observers. The measurements are displayed with vertical and horizontal error bars (1 SD). The Pearson coefficient of correlation was 0.98, with a slope of 0.93 +/- 0.05 and an intercept of 7.67 +/- 3.02 mm, indicating a high degree of interobserver concordance.

4.VI.e Discussion

By investigating each of the confounding variables under controlled laboratory conditions and developing a simple set of clinically applicable rules, we have been able to accurately calculate airway cross-section from endoscopic images. This was achieved without need to measure the angle of tilt, making assumptions about the optics of the endoscope or the lens to object distance.

The effect of tilt was eliminated by using a circular calibrator with biaxial calibration. To correct for visuo-spatial distortion, rather than pre-calibrating a designated endoscope, attempting to make measurements at a predetermined lens to object distance, or trying to calculate the degree of optical distortion with post-acquisition signal processing, we again made use of the calibrator probe and simple mathematics.
This was based on the assumption that with a probe at the level of the stenosis, it would be subject to the same degree of optical distortion as the stenosis itself. By using the probe to cover the radial span of the area being measured and averaging the measurements, we consistently obtained measurements with >95% accuracy within the diameter ranges of neonatal, paediatric and adult airways, independent of tilt and radial or distance distortions. The calibrator probe could be introduced through and beyond a stenosis without compromising the airway.

The technique is limited in that it requires suspension laryngoscopy and tracheoscopy using a rigid endoscope. Most physicians assess airways using flexible bronchoscopy. The majority of airway surgeons continue to grade stenosis based on the stratification of the Myer-Cotton grading system. Due to conventional teaching, most airway surgeons continue to perform assessments and surgeries using rigid ventilating bronchoscopes. This therefore limits the wider clinical use of our technique and presently confines it to experimental comparison of different surgical techniques where accurate measurements of airway dimensions are required as a comparison with physiological outcome measures.
4.VII Outcome of Early Endoscopic Treatment of Acute Inflammatory Airway Lesions in Post-intubation Airway Stenosis

4.VII.a Introduction

In clinical practice, the majority of patients with post-intubation upper airway stenosis have mature fibrotic airway scars with minimal evidence of ongoing airway inflammation. These patients typically have had an intubation episode in the relatively distant past and some of them have been treated for “adult onset asthma” for some time before the diagnosis is secured. Less commonly, patients are referred within a few weeks of extubation with airway symptoms during the active fibro-inflammatory phase of tracheal injury (illustration 4.15).

Illustration 4.15 Endoscopic (left) and histological (right) views of acute airway granulation

Illustration 4.16 Endoscopic (left) and histological (right) view of ‘mature’ airway scar
These two presentations occur at different times within the natural history of the same disease process. The early phase of the post-intubation airway stenosis is characterised by mucosal ulceration and pericondritis followed by the formation of exophytic granulation tissue. As healing progresses, granulation tissue is gradually replaced with mature fibrotic tissue and the wound contracts giving rise to the classical picture of mature airway scar (illustration 4.16). It is already known that inflammatory conditions in the airway do respond to intra-lesional steroids (108). In this study, a comparison is made of the results of treating patients with acute fibro-inflammatory airway lesions with intra-lesional steroids, laser reduction of granulation tissue and balloon dilatation, with those patients presenting with mature airway lesions who are initially treated with radial laser incisions, balloon dilatation and topical Mitomycin-C application. The aim of this study was to investigate whether early intervention can affect outcome contrary to traditional teaching which recommends waiting for maturation of inflammatory tissue before treatment (7).

4.VII.b Methods

Between 2003 and 2005 Thirty-one patients with a new diagnosis of post-intubation airway stenosis were treated. To ensure uniformity of surgical approach, this series did not include patients who were referred to our unit with previous surgical treatments. There were 18 males and 13 females and the average age of presentation was 47 ± 2.7 years (Mean ± SEM; range 23 to 72). A wide range of clinical conditions necessitated respiratory support on intensive care unit, with pneumonia being the commonest indication (illustration 4.17).
Eleven patients in this series had been referred with airway symptoms within an average of three months from an episode of intubation on an intensive care unit (mean 2.3 ± 0.3 months). These patients invariably had an inflamed airway with obstructive exophytic granulation tissue (illustration 4.15). The remaining twenty patients presented on average 47 months following intubation. In these patients airway symptoms were caused by a mature fibrotic scar with minimal airway inflammation (illustration 4.16). There were no significant differences between the two groups with respect to sex distribution, ventilation time or the use of tracheostomy in the ICU, tracheostomy at the start of laryngotracheal surgery, site of lesion, extent of airway injury, or the length of follow-up. Table 4.3 provides further comparative information about patient and treatment characteristics.
Table 4.3 Patient, lesion and treatment characteristics

<table>
<thead>
<tr>
<th></th>
<th>Fresh Stenosis</th>
<th>Mature Stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of patients</td>
<td>11</td>
<td>20</td>
</tr>
<tr>
<td>Age (years ±SEM)</td>
<td>46.6 ± 4.9</td>
<td>47.5 ± 8.9</td>
</tr>
<tr>
<td>Male Sex</td>
<td>64%</td>
<td>55%</td>
</tr>
<tr>
<td><strong>Lesion Characteristics at the start of treatment</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ITU Ventilation Time (days)</td>
<td>28.7 ± 8.7</td>
<td>28.5 ± 5.2</td>
</tr>
<tr>
<td>Tracheostomy on ITU</td>
<td>6 (55%)</td>
<td>16 (80%)</td>
</tr>
<tr>
<td>Extubation to first treatment time (months)</td>
<td>2.3 ± 0.3</td>
<td>47.4 ± 13.3 *</td>
</tr>
<tr>
<td>Distance from glottis (cm)</td>
<td>2.6 ± 0.5</td>
<td>3.3 ± 0.45</td>
</tr>
<tr>
<td>Myer &amp; Cotton Grade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>0</td>
<td>2 (10%)</td>
</tr>
<tr>
<td>II</td>
<td>1 (9%)</td>
<td>6 (30%)</td>
</tr>
<tr>
<td>III</td>
<td>10 (82%)</td>
<td>9 (45%)</td>
</tr>
<tr>
<td>IV</td>
<td>1 (9%)</td>
<td>3 (15%)</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prosthetic airway in situ at first treatment</td>
<td>4 (36%)</td>
<td>9 (45%)</td>
</tr>
<tr>
<td>Patients needing stents during treatment</td>
<td>5 (45%)</td>
<td>8 (40%)</td>
</tr>
<tr>
<td>Median Treatment Episodes</td>
<td>1 (1-2)</td>
<td>2 (1-6) ***</td>
</tr>
<tr>
<td>Endoscopic Therapy</td>
<td>13</td>
<td>36</td>
</tr>
<tr>
<td>External Surgery</td>
<td>0</td>
<td>6 (30%)</td>
</tr>
<tr>
<td>Tracheal Resection</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Trachea / Cricoid Cartilage Resection</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Sternohyoid Flap</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Tracheal Homograft</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Mean Follow-up (months)</td>
<td>13.8 ± 1.2</td>
<td>15.4 ± 1.8</td>
</tr>
</tbody>
</table>

* p < 0.0001 (Unpaired Student’s t-test)

** Chi-square tests for independence and trend were not significant (p>0.1)

*** p < 0.03 (Mann-Whitney-U test)
Anaesthesia and the surgical approach are described in section 3.II. Mature lesions were treated with radial incision with a carbon dioxide laser, taking particular care to preserve intact mucosal bridges between incisions to avoid circumferential restenosis. The airway was then dilated with a CRE™ Pulmonary Balloon Dilator (Boston Scientific, Natick, MA, USA), followed by a three-minute topical application of mitomycin C at a concentration of 1mg/ml.

Fresh granular lesions on the other hand were treated with intralesional steroid injection, followed by laser reduction of the granulation tissue and balloon dilatation. 40-80mg of methylprednisolone acetate (Depo-Medrone®; Pharmacia; Walton-on-the-Hill, UK) was injected using a 27 gauge BD Valu-Set™ butterfly needle (BD Infusion Therapy, Helsingborg, Sweden) with the wings cut, and the needle grasped using microlaryngeal forceps (Xomed Ltd, Watford, UK). The needle was bent to slight angles to allow the tracheal wall to be injected, and was advanced into the airway under endoscopic vision. The granular lesions were injected circumferentially at the base (Illustration 4.18).

Illustration 4.18 Shows a 27 gauge butterfly needle (left) adapted for intralesional steroid injection (right)
The granulation tissue was then reduced with a carbon dioxide laser, preserving intact mucosal bridges whenever possible. Care was exercised to avoid over-aggressive photoresection of the lesion. The trachea was then dilated using a CRE™ Pulmonary Balloon dilator. A soft silastic stent was placed in all patients who had a stenosis greater than 70% and longer than 5mm for a period of four weeks to aid healing. Details of the material used and the method of stent placement and removal used have previously been described (69).

**Data Analysis**

Demographic information and details regarding the precipitating ventilation episode, the indication and length of ventilation, the time taken from extubation to the initiation of the first treatment were obtained. Characteristics of the lesion at the start of the treatment, and the nature and timing of each treatment episode were recorded. Intervention-free interval was the time between one treatment episode and the next surgical treatment performed to restore airway patency as previously defined (140). Data was presented either as means with standard errors or as percentages when appropriate. Parametric normally-distributed data was compared using unpaired student’s t-test, and binomial data were compared using the chi-square test. Intervention-free intervals were calculated, and illustrated using the method of Kaplan and Meier, and compared with log-rank statistics. A stepwise Cox proportional hazards ratio model was constructed to identify potential independent predictors of intervention-free interval. Data was analyzed and displayed using SPSS release 12.0 for Windows (SPSS Inc., Chicago, IL, USA).
4.VII.c Results

Patients in the “mature stenosis” group required a median of 2 surgical interventions (range 1-6). Patients with fresh stenoses on the other hand required fewer procedures (range 1-2) (p < 0.03; Mann-Whitney-U test). Six patients in the mature stenosis group required external laryngotracheal reconstruction. This included three tracheal resections, two airway augmentations using the pedicled sternohyoid flap (141), and one tracheal homograft (table 4.2). By comparison, none of the patients in the fresh stenosis group required an external approach airway reconstruction (p < 0.001; chi-square test).

The average intervention-free interval in the fresh stenosis group was 17 months and this was achieved with a single endoscopic operation in the majority of patients. Airway appearances at follow-up in this group did not demonstrate evidence of recurrent granulation tissue or stenotic scarring (illustration 4.19).

Illustration 4.19 Early granular subglottic stenosis treated (A) and appearance six months after treatment (B). Patient remained well until dischargee 19 months later.

By contrast, the average intervention-free time in patients with mature stenoses was 9 months, with 55% of patients in this group requiring more than one procedure. The
difference in the intervention-free interval between the two groups was statistically significant (p < 0.02; log-rank analysis) (illustration 5.20). To which group patients belonged was the only factor predictive of the intervention-free interval on Cox regression analysis. In particular, length of intubation, anatomy of the lesion at the start of treatment, and the need for prosthetic airway support at the start of treatment did not influence the intervention-free interval.

Illustration 5.20 Intervention-free interval as a function of the maturity of the airway lesion at the time of treatment (Kaplan-Meier analysis)

4.VII.d Discussion

The results of this study show that intra-lesional steroid injection, reduction of granulation tissue and balloon dilatation can be a viable and effective treatment for acute post-intubation airway stenosis. Patients receiving this treatment required significantly fewer surgical interventions, had significantly longer intervention free intervals and did not require external approach laryngo-tracheal reconstruction surgery compared with patients presenting later with mature airway lesions. It is also evident from this research that patients with early granular airway stenosis treated with intra-
lesional steroids appear to regain normal airway appearances (illustration 4.19) and remained free of recurrent scarring and stenosis which often blights endoscopic treatment for mature airway stenosis. This study shows that early treatment of acute airway lesions may prevent the development of long-term sequelae which are more difficult to treat. These findings have important implications for the post-intubation management of intensive care patients. Given that early intervention could improve the outcome of this condition, it lends to the argument for screening patients for upper airway obstruction after long-term intubation on intensive care units. Whilst half of patients (109) have a significant tracheal injury at the time of extubation, and 4% go on to have long-term airway compromise, fortunately the natural history of this condition is towards spontaneous resolution. However, there is very little research and the actual incidence of post-intubation airway compromise is probably underestimated. Screening for post-ICU patients is discussed in chapter 6 of this thesis.
4.VIII  Outcome of Endoscopic Treatment of Adult Post-intubation

Subglottic and Tracheal Airway Stenosis

4.VIII.a  Introduction

The primary objective of airway reconstruction is to restore and maintain a safe and patent airway capable of meeting the ventilatory demands of the patient while minimising the risk of further iatrogenic injury to the laryngotracheal complex and the structures that surround it. Tracheal and cricotracheal resection have become the standard of care for tracheal and subglottic stenosis respectively. The efficacy of these techniques in treating post-intubation airway stenosis have been well documented (4, 7, 111, 142, 143). By contrast, endoscopic laryngotraceoplasty has largely been viewed as ineffective and temporising, suitable at best for treating a subset of patients with thin and mild lesions (18). The treatment philosophy of primary open surgery rests almost exclusively on evidence published following retrospective analysis of data generated towards the end of the last century (142) and while its efficacy in selected cases is not disputed, it is a treatment approach that even in the very best of hands can lead to significant morbidity and prolonged hospitalisation, and carries major risks including peri-operative mortality (144). It was felt important as a part of this thesis to explore a minimally invasive approach which, if effective, would have clear advantages over first line employment of major open surgery.
4.VIII.b Methods

Between the end of 2003 and 2006, 62 patients with post-intubation tracheal stenosis were all treated initially with an endoscopic approach. Demographic information, indications for surgery and the duration of the intubation event, use of tracheostomy, lesional characteristics and follow-up durations were all prospectively recorded. Details of endoscopic and open surgeries, decannulation, insertion and removal of airway prostheses, and post-operative complications and surgical outcomes were recorded.

Illustration 4.21 Details of medical events precipitating intubation and ventilation. (SAH= subarachnoid haemorrhage, RTA= road traffic accident).

There were 34 males (55%) and the average age at presentation was 45±16 years. Most patients (53, 86%) had a tracheostomy during their intensive care stay, and 30 patients
(48%) were tracheostomy-dependent at the time of their first treatment. Illustration 4.21 and table 4.4 provide further information about patient and lesion characteristics.

**Table 4.4 Patient and lesion characteristics.**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>62</td>
</tr>
<tr>
<td>Age (± SD) [range]</td>
<td>45.6 ± 16 [16 – 72]</td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>34 (55)</td>
</tr>
<tr>
<td>Length of intubation (days ± SD)</td>
<td>26 ± 28 [4 – 140]</td>
</tr>
<tr>
<td>Intubation-to-first-treatment latency (months ± SD)</td>
<td>29 ± 47 [1 – 230]</td>
</tr>
<tr>
<td>Tracheostomy during acute episode</td>
<td>53 (86)</td>
</tr>
<tr>
<td>Tracheostomy at first visit</td>
<td>30 (48)</td>
</tr>
</tbody>
</table>

Characteristics of the lesion at first endoscopy

- Glottis-to-lesion distance (mm ± SD) 36 ± 19 [5 – 100]
- Myer and Cotton Grade
  - I 0
  - II 11 (18)
  - III 40 (64)
  - IV 11 (18)
- Height of the lesion (mm ± SD) 18 ± 12 [5 – 55]

Details of anaesthesia are discussed in 3.II, however, there are subtle differences in the surgical technique and for this reason there is some repetition. Patients underwent diagnostic laryngotracheoscopy, followed by endoscopic lumen-restoring surgery. The airway was visualized with a combination of microscopic and endoscopic techniques, using an operating microscope and a 4mm 0º Karl-Storz airway endoscope (Karl Storz GmbH & Co KG, Tuttlingen, Germany). Carbon dioxide laser was delivered using a microscope-mounted Sharplan® Acuspot® micromanipulator (Lumenis UK Ltd, London, UK). Lesions beyond the microscope’s line of sight were treated with KTP
laser delivered via 0.4mm disposable fibreoptic filaments (Laserscope, San Jose, CA, USA). Fresh granular lesions were treated with 60-80mg of methylprednisolone acetate (Depo-Medrone®; Pharmacia; Walton-on-the-Hill, UK) circumferentially injected at the base of the lesions as previously reported. (145) Laser radial incisions were made into the lesion, taking care to preserve mucosal bridges between the cuts to prevent circumferential restenosis. Dilatation was undertaken using the CRE™ Pulmonary Balloon dilator (Boston Scientific, Natick, MA, USA), followed by topical mitomycin C application (Kyowa Hakko UK Ltd, Slough, UK; 1mg/ml for 3 minutes). Patients with Myer-Cotton grade 4 lesions and patients with grade 3 lesions >15mm in length also received a silicone stent cut from soft silastic Montgomery T-tubes (Boston Medical Products, Westborough, MA). Stent diameter was chosen based on an estimate of tracheal diameter, and the length was 1-2cm longer than stenosis length. Stents were introduced through the laryngoscope using laryngeal forceps and sutured with a 2-0 polypropylene (Prolene; Ethicon Inc, Somerville, NJ) as previously described. (69) Stents were removed during a subsequent laryngotracheoscopy. The suture was endoscopically cut using laryngeal microscissors and the stent was removed with forceps. The decision to redeploy a stent was based on the degree of residual inflammation and was made on a case-by-case basis. At the start of therapy patients were usually readmitted within eight weeks or sooner if symptomatic, for a further laryngotracheoscopy, during which further endoscopic laryngotracheoplasty, if indicated, was undertaken. The process was repeated until a normal airway was attained and maintained.

Patients whose lesions proved recalcitrant to endoscopic therapy, and this usually became evident by the third procedure, underwent open laryngotracheal surgery. The operative techniques used have previously been described (143, 146-148). As a rule,
patients undergoing endoscopic surgery, including those who were stented, were admitted to the surgical high-dependency unit overnight and were discharged home on the morning following surgery.

Data Analysis

Data were presented as means with standard deviations or binomial percentages where appropriate. Actuarial statistics was used to determine success rates for decannulation and attainment of a prosthesis-free (no stent/tracheotomy) airway, and Cox regression was used to determine independent predictors of failure to attain a prosthesis-free airway. Actuarial analysis was also used to determine predictors of success or failure of endoscopic therapy alone to achieve a cure. In patients who were successfully treated using purely endoscopic techniques, ordinal regression was used to investigate whether any pre or perioperative factors were associated with the need to perform multiple endoscopic procedures. Data were analyzed and illustrated using SPSS release 12.0 for Windows (SPSS Inc., Chicago, IL). P < 0.05 was considered significant.
4.VIII.c Results

Endoscopic assessment and surgery were the initial treatment for all patients. The mean number of endoscopic operations was $2.3 \pm 1.4$ [range 1 – 5].

**Table 4.5 Details of endoscopic surgery.**

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>62</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of endoscopic operations performed per patient (%)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>23 (37)</td>
</tr>
<tr>
<td>2</td>
<td>16 (26)</td>
</tr>
<tr>
<td>3</td>
<td>11 (18)</td>
</tr>
<tr>
<td>4</td>
<td>5 (8)</td>
</tr>
<tr>
<td>5</td>
<td>7 (11)</td>
</tr>
<tr>
<td>Number of intralumenal stents deployed per patient</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>28 (45)</td>
</tr>
<tr>
<td>1</td>
<td>15 (24)</td>
</tr>
<tr>
<td>2</td>
<td>8 (13)</td>
</tr>
<tr>
<td>3</td>
<td>6 (10)</td>
</tr>
<tr>
<td>4</td>
<td>4 (6)</td>
</tr>
<tr>
<td>5</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Overall stent deployment time (months ± SD) [range]</td>
<td>12.4 ± 12.5 [0.5 – 39]</td>
</tr>
<tr>
<td>Stent deployment time (excluding long-term stents)</td>
<td>6.7 ± 5.7 [0.5 – 26]</td>
</tr>
<tr>
<td>Use of topical mitomycin C during therapy</td>
<td>47 (76)</td>
</tr>
<tr>
<td>Use of intralesional steroids during therapy</td>
<td>18 (29)</td>
</tr>
</tbody>
</table>

Table 4.5 provides details of endoscopic surgeries performed. In patients where endoscopic therapy was successful in achieving a cure, Kruskal Wallis analysis
identified morbid obesity (BMI > 45), use of mitomycin-C (MMC) or use of steroids, and the Myer-Cotton grade of the lesion at the start of therapy as predictors of the number of endoscopic treatments required. Factors remaining significant following ordinal regression were use or steroids or MMC, and morbid obesity. Endoscopic surgery had an actuarial success rate of 72% in curing postintubation tracheal stenosis (illustration 4.22).

Illustration 4.22 Actuarial success rate of endoscopic surgery to treat postintubation tracheal stenosis ((log-rank analysis). (A) shows likelihood of endoscopic success as a function of the height of lesion. (B) Likelihood of success as a function of time from intubation to first treatment. (C) Overall success rate of endoscopic surgery.

Univariate log-rank analysis identified Myer-Cotton grade and height of the lesion, tracheotomy at the start of therapy, and whether the patient was referred to the airway unit within six months of intubation were identified as predictors of endoscopic success.
Factors remaining independently significant on Cox regression analysis were the vertical height of the lesion, and whether the patient was referred within six months of intubation (illustrations 4.22 and 4.23). Ninety six percent of patients with lesions shorter than 3cm were successfully managed endoscopically, but the success rate fell to 20% in patients with lesions longer than 30mm who underwent a full trial of endoscopic surgery with curative intent (illustration 4.23).

![Illustration 4.23 Likelihood of success of endoscopic management of a lesion as a function of its height. The numerators above the bars refer to the number of cases that were successfully managed with endoscopic surgery, and the denominators are the overall number of patients within that group.](image)

Fourteen patients (23%) underwent open airway surgery. The average time from start of therapy to open surgery was 16±11 months [range 1–39]. There were 11 augmentation procedures, consisting of hyoid-on-sternohyoid pedicled flaps (n=4) (147), Eliachar sternohyoid flap (n=4) (146), tracheal homografts (n = 3) (148), and three tracheal resections (143). One tracheal homograft was extruded into the airway and removed endoscopically, necessitating a total of five endoscopic procedures, ultimately resulting in a patent airway and an MRC Dyspnea grade of II (149). Two augmentation procedures failed due to recurrence of stenosis at the lower border of the
augment, necessitating reinsertion of internal stents. These two patients were referred to us after failure of tracheal resection in one case, and failure of endoscopic procedures, cartilage augmentation, and tracheal resection in another. Neither patient was a candidate for further resection. The remaining 11 procedures were successful in achieving and maintaining normal airways. The average number of endoscopic procedures following open surgery was 1.2 ± 1 (range 0 – 3), including a postoperative laryngotracheoscopy in all patients.

In 98% of patients, re-intervention occurred within six months of the previous therapy (illustration 4.24). Patients who did not require re-intervention retained scores of 1 to 3 on the Medical Research Council Dyspnoea Scale.

Illustration 4.24 Cumulative distribution of the likelihood of the need for surgical reintervention.

One patient with a tracheotomy died from an unrelated cause before treatment could be completed. All other patients were decannulated within an average of 2±3.6 months. A Cox regression model was constructed to determine predictors of delayed decannulation. Variables entered were patient age sex and body mass index, height, Myer-Cotton grade of the lesion, use of internal stents and use of open surgery. None
of these variables were found to be associated on univariate or multivariable analysis with time to decannulation. Another outcome assessed was freedom from any airway prosthesis (stent/tracheotomy). Stents were deployed in 34 patients (55%) for an average of 12.4±12.5 months [range 1–39] (table 4.4). Overall, 83% of patients achieved a prosthesis-free airway (illustration 4.25).

![Illustration 4.25 Actuarial decannulation rate ((black line) and attainment of a prosthesis-free airway (grey line)](image)

Illustration 4.25 Actuarial decannulation rate ((black line) and attainment of a prosthesis-free airway (grey line)

Statistically significant univariate predictors of attaining a prosthesis-free airway were the Myer-Cotton grade of the lesion, presence of a tracheotomy at the start of therapy and the patient’s body mass index (BMI). The only independent predictor of failure to attain a prosthesis-free airway on multivariable analysis was BMI>45. In these patients, although the lesion itself could be treated, the airway remained dynamically compromised due to anterior bulging of the trachealis (illustration 4.26). These patients were maintained on long-term intralumenal airway stents and were encouraged to lose weight.
Illustration 4.26 The top two figures show endoscopic airway appearances of two patients with morbid obesity and excessive anterior bulging of posterior tracheal membrane leading to dynamic airway compromise. The bottom figure shows a patient who continues to suffer with dynamic airway collapse.

There was one death due to mucus plugging of a stent in a heavy smoker two weeks following an otherwise uneventful procedure. There were three deaths from unrelated causes. There were two neck infections following augmentation surgery which settled with antibiotics and one case of stitch infection associated with stent placement. There were two cases of stent migration which necessitated emergent airway intervention with no permanent sequelae. Seventy stents were placed during the study period, with the six complications described above, this gives a complication rate of 8.5%. There were no major complications in patients who underwent endoscopic therapy without stent deployment.
4.VIII.d Discussion

The findings show that minimally invasive surgery is effective in treating post-intubation tracheal stenosis. The present series consists of an unselected group of consecutive patients who were initially treated endoscopically with almost three quarters (72%) of patients being successfully managed without open surgery. For those patients who required open surgery, initial endoscopic laryngotracheoplasty restored luminal patency, allowing a proportion of patients to be decanulated during the first visit. When initial decanulation was deemed to be unsafe, stent placement above the tracheostomy restored voice, which some patients had been deprived of for many years. Moreover, initial endoscopic lumen restoration followed by mobilisation of the inflammatory process with stent and mitomycin-C made it possible for most patients requiring open surgery to be managed with airway augmentation rather than resection. Tracheal resection was preserved for patients who had long segment complete or near complete collapse of cartilaginous tracheal support. These results stand in contrast with much of the published literature on the treatment of post-intubation tracheal stenosis which favours tracheal resection and anastomosis as a first line therapy (7, 142, 143). The effectiveness of the endoscopic approach demonstrated in this study may be due to advances in minimally invasive surgery and anaesthesia, but may also be due to changes in post-intubation tracheal stenosis as a disease entity. In this study, the majority of cases of airway compromise were caused by encroachment into the airway lumen by circumferential granular or mature scar tissue, with reasonable cartilaginous support, rather than localised structural failure and withering of the trachea. In cases where the cartilaginous tracheal rings had disintegrated and resorbed, open surgical procedures had to be considered.
Predictors of success of endoscopic surgery were early referral to the Airway Reconstruction Unit and the vertical height of the lesion. I hypothesise that patients with short intubation to treatment latencies were more likely to have granular lesions which respond well to intra-lesional steroids, laser and dilatation.

The association between vertical lesional height and success of endoscopic surgery has previously been noted (7, 18). Illustration 4.23 shows that the majority of lesions <30 mm could be endoscopically managed, but the likelihood of a successful outcome with endoscopic techniques falls significantly for lesions longer than 30 mm. These findings have refined my treatment approach. Endoscopic airway assessment is performed in all patients under general anaesthesia and initially lumen restoring endoscopic surgery is attempted in all patients. Assessment and initial endoscopic treatment provides valuable information in respect of the degree of tracheal cartilaginous support and selecting those patients in whom airway augmentation or tracheal resection should be considered. The initial endoscopic approach also allows restoration of vocal function to a sizeable proportion of patients and a number of them are decannulated during the initial visit. The endoscopic approach also allows treatment of the intra-luminal inflammatory process. The best outcome for open surgery is achieved in patients with minimal or no ongoing inflammation (4). This study has also raised the Unit’s threshold for stenting patients. The only treatment related mortality in this series was related to acute stent obstruction in a patient who was poorly compliant with post-operative advice.
Algorithms & treatment philosophy

The difficulty in treating adult laryngotracheal stenosis is that there are not sufficient numbers of patients to run randomised trials comparing different techniques. Also, the injuries differ significantly in anatomical sites and in relation to the anatomy of the injury itself. This is the reason that different endoscopic techniques have been employed depending on the nature of injury evident at the time of examination on the operating table. The resulting algorithms represent the current philosophy of the department in the management of new patients presenting with Laryngotracheal stenosis (illustration 4.27).

Illustration 4.27 Algorithm for the management of adult post-intubation laryngotracheal stenosis
4.IX  Endoscopic Tracheoplasty for Treating Tracheostomy Related Airway Stenosis

4.IX.a  Introduction

A less common variant of post-ventilation tracheal stenosis is seen in a small number of tracheostomy patients. This is caused by over-resection or fracturing of anterior tracheal rings during tracheostomy. At decannulation, there is scarring and contracture at the stoma site which draws in the lateral ring remnants as a result of the wound contracture leading to a “Lambda-shaped” stenotic deformity and airway compromise. The lesion usually extends over 1-2 tracheal rings with normal proximal and distal trachea. The trachealis is not involved and there is usually a small anterior bridge not contributing to the stenosis (illustration 4.28).

Illustration 4.28  Formation of ‘lambdoid’ deformity (D) of trachea. On decannulation, excessive scar contracture at the stoma draws in remnant tracheal cartilage rings (B-D). These encroaching cartilage rings can be ablated with a CO₂ laser (E) to produce a near normal airway (F).

Tracheal resection and anastomosis has been recommended for this condition (7), but this is a major operation with associated morbidity and a small mortality rate. This prospective study set out to look at endoscopic resection of these collapsed tracheal
cartilages without injuring the normal trachealis and leaving an anterior strip at the apex of the lesion untouched (illustration 4.28E). This avoids causing a circumferential injury and exacerbating the stenosis.

**4.IX.b Patients and Methods**

Between April 2004 and 2006, 11 patients were treated with a new diagnosis of airway compromise due to post-tracheostomy lambdoid deformity. To ensure uniformity of approach, this series did not include patients who had received airway treatment prior to referral to our institution. As this was simply a modification of an endoscopic lasering technique used for over a decade on the unit, ethical consideration was not specifically sought.

General anaesthesia was intravenously induced as described in section 3.II, and suspension laryngoscopy with supraglottic jet ventilation and the use of a microscope is the standard approach to this surgery. The CO₂ laser was used using a ‘line-of-sight’ technique delivery through a micromanipulator device. In all cases, the lesions were treated with the carbon dioxide laser at 8-10 watts continuous setting. The proximal and distal trachea is used as a guide to the limits of resection and the collapsed cartilage is vapourised on each side (illustration 4.29).
The resection initially was conservative, but it was soon evident that it could be extended to the tracheal fascia if necessary. At the end of the surgery, a CRE™ Pulmonary Balloon dilator (Boston Scientific, Natick, MA, USA), 15-18 mm was used to expand the airway. An important consideration is to preserve the mucosa over the trachealis and at the apex of the lambda deformity to avoid a circumferential laser injury. In this series of 11 patients, topical mitomycin-C was applied on a neuro-surgical patty at a concentration of 1 mg/ml for 3 minutes. One patient in addition had a laryngofissure and anterior augmentation with hyoid bone on sternohyoid pedicled muscle as an anterior augmentation flap for a concomitant glottic stenosis.

Patient demographics and details of the event requiring tracheostomy placement were obtained. Lesion characteristics and the nature and timing of treatments were recorded. The degree of dyspnoea at last follow-up was evaluated using the Medical Research
Council (MRC) dyspnoea scale (150). Data was presented either as mean values with standard deviation or binomial percentages when appropriate. A timeline plot was used to illustrate the number and nature of the treatment episodes that each patient received. Data were analysed and displayed using SPSS12 for Windows (SPSS Inc, Chicago, Illinois, USA).

4.IX.c Results

There were 7 males and 4 females and the average age at presentation was 56 ± 14 years (Mean ± SD; range 20 to 70). None of the patients had a tracheostomy at the time of presentation. One patient had an MRC Dyspnoea grade of 3, and the others had grades of 4 or 5. Table 4.6 provides further information about patient and lesion characteristics.

<table>
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<tr>
<th>#</th>
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<th>Sex</th>
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<th>GL-L-D (mm)</th>
<th>Follow-up (months)</th>
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<td>10</td>
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M-C Grade: Myer and Cotton Grade.

SH: Stenosis Height; GL-L-D: Glottis to Lesion distance. The methodology for measuring SH and GL-L-D has previously been described.

RTA: Road Traffic Accident

COPD: Chronic Obstructive Pulmonary Disease

MRC Dyspnoea Grade
The median number of endoscopic treatments required to achieve a cure was 3 (range 1-5) and three patients required endolumenal stent placement as part of their treatment. The median number of endoscopic treatments per patient fell from 4 at the start of the series to 2 at the end, when more extensive initial cartilage resections were being undertaken (p = 0.08). Illustration 4.30 provides a detailed treatment timeline for all patients.

**Illustration 4.30** Treatment timelines for individual patients. *Laryngofissure procedure for concomitant glottis reconstruction*

The average follow-up was 17 ± 8 months (range 7-32) and no patient required re-intervention after six months of symptom-free follow-up. At the last follow-up, with the exception of one patient with pre-existing chronic obstructive pulmonary disease, all patients achieved and maintained MRC Dyspnoea Scale grades of I or II. All patients returned to their pre-injury level of physical activity. There were no cases of dysphagia, and, with the exception of one patient with concomitant glottic stenosis who had mild dysphonia, all patients had normal voices at the last follow-up.
4.IX.d Discussion

The results of this study show that endoscopic tracheoplasty can be an effective treatment and a viable alternative to tracheal resection for airway stenosis caused by post-tracheostomy stomal contracture. The lambdoid tracheal deformity is a specific and predominantly anatomical cause of post-intubation airway stenosis. This is a relatively uncommon cause of post-intubation tracheal stenosis occurring in 9.6% of the patients that we treated for post-intubation airway compromise. Traditionally, tracheal resection end-to-end anastomosis has been recommended as a first line treatment for this condition (7) and given that the combination of a short length of stenosis and favourable wound healing, these patients are likely to do well following this operation. However, tracheal resection remains a major procedure with associated morbidity and very occasionally mortality. It also requires a prolonged hospital stay.

The net effect of my technique is to achieve what is essentially an endoscopic tracheal resection but without open neck surgery and tracheal anastomosis. There was a learning curve associated with this technique as initial concerns were related to possible surgical emphysema or haemorrhage into the airway. At the outset, I decided to re-examine the airway at 4-6 weeks and remove any granulation tissue with microsurgical instruments or a minimal lasering technique. Depending on the appearance of the airway at the second visit, the patient was either placed under surveillance or rescheduled for endoscopy to ensure that any further granulation tissue was treated before it progressed and mature scar. Initially, patients were kept in hospital overnight for observation, but later, the majority of the patients were discharged home the same day.
4.X The Prefabricated Sternohyoid Myocartilaginous Flap

4.X.a Introduction

Section 4.VIII above shows that over 72% of adult patients with post-intubation laryngotracheal stenosis can be treated endoscopically and most of the remaining patients can be managed using standard open surgical resection or augmentation techniques. However, it became evident that a minority of patients who had long or multi-segment disease with concomitant tracheomalacia failed to respond to standard therapy. Grillo (7) has already demonstrated that 4 cm of trachea can usually be resected in an adult patient and with pulmonary ligament and suprahypoid laryngeal release techniques another 2 cm could be made available for an extended resection. Extended tracheal resection carries a higher morbidity and mortality rate (151). However, three patients had been referred to The Unit over the period of this study having failed resection and augmentation procedures. Tissue engineering for tracheal and bronchial reconstruction is a new development which is still not widely available and certainly was not on the horizon when these patients were being treated. Primary augmentation with rib graft in adult patients is difficult for two reasons. First, rib grafts do not reliably survive when used as a primary augment in adults (5) and second, unlike paediatric airway reconstruction, in adults the only cartilaginous part of the rib is the costo-sternal junction.
4.X.a Methods

Stage 1.

Details of anaesthesia and endoscopic surgical techniques have previously been described in section 3.II. During the first stage of the procedure, costal cartilage is harvested from the fifth, sixth and, if required, seventh rib on the right side of the thorax. A transverse neck incision is made and a subplatysmal dissection carried out superiorly to the level of the hyoid and inferiorly to the level of suprasternal notch. A number of these patients have had previous cervical surgery and the most intact sternohyoid muscle is exposed. The pieces of cartilage are sliced to a thickness of 2-3 mm and sutured end-to-end with a resorbable suture material as demonstrated in illustration 4.31.

Illustration 4.31 Costal cartilage is harvested, sliced 3mm thick and sewn end to end as shown (left). This construct is then sewn to the anterior surface of the left sternohyoid muscle (right).

The length of this cartilage construct is marginally longer than the length of the damaged airway and the end pieces of cartilage are tapered as demonstrated. This construct is then sutured on to the anterior surface of the sternohyoid muscle with absorbable sutures medially and laterally. The wound is closed above the construct and a wound drain is usually not necessary.
Stage 2

The second stage of the procedure is performed 10-12 weeks later. There is a preceding ultrasound scan to confirm that this cartilaginous construct has survived. The neck wound is re-opened and subcutaneous dissection extended from the hyoid to the suprasternal notch. The sternohyoid muscle with its cartilaginous construct is mobilised as a single composite flap.

Illustration 4.32 Composite myocartilaginous pedicled flap (left) is mobilised retaining the blood supply from the inferior thyroid artery (middle). The flap is rotated to act as an extended anterior augment to the airway, split anteriorly (right)

The muscle can be mobilised and even detached from the hyoid as its principle blood supply is through the inferior thyroid artery. This allows the composite myocartilaginous flap to be mobilised in a longitudinal fashion and used as an anterior laryngotracheal augment. As a part of the second stage, a laryngotracheofissure is performed and where there is a tracheostomy tube already present, it is lowered into a new position in a healthy part of the trachea. Where no previous tracheostomy was present, a new tracheostomy site is fashioned in a healthy part of the lower trachea. Any scar tissue encroaching into the lumen of the damaged airway is surgically removed. However, it is important not to breach the posterior tracheal wall. A length of silastic tubing extending just beyond the injured airway is fashioned from a
Montgomery silastic T-tube. This T-tube is covered with a superficial skin graft as described in the section on stents 2.III.e. This stent, with its biological dressing, is then secured in the airway with a 2.0 Ethilon suture as previously described (69). The sternohyoid myocartilaginous flap is then rotated on its pedicle and secured into the airway using a suitable resorbable monofilament suture (illustration 4.32). A temporary wound drain is placed and the surgical site is closed. The wound drain is usually removed 24-72 hours later and the tracheostomy is removed 3-5 days later. The stent and the skin graft is removed after a period of 3 weeks using suspension laryngoscopy and endoscopic techniques.

4.X.c Results

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<th>Table 4.7 Patient Details</th>
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Prospective information about the demographics, clinical, surgical and airway outcomes were obtained. In none of the cases had there been resorption of the construct. Table 4.7 illustrates patient details.
4.X.d Discussion

This procedure addresses some of the limitations associated with previous approaches to airway reconstruction. The ability to make a precise 3-dimensional cartilaginous construct allows for the creation of a flap with the right size, shape and contour tailored to address the reconstructive requirements of a particular lesion. This has proven incredibly useful in the area of paediatric reconstruction. A reliable technique had to be devised for those patients who had failed previous airway surgery, including tracheal resection. With this technique, a thin cartilaginous construct is formed which is allowed to derive a blood supply both from the sternohyoid muscle and the overlying platysma muscle over 3 months. During dissection, the fibres of the platysma are not removed from the anterior surface of the construct. It was also fortuitous that the pieces of cartilage did not fuse, but instead were united with fibrous union (illustration 4.33) allowing mobility of flexion of the neck. This virtually mirrored the biomechanical properties of the normal trachea and I hypothesise that this prevented tracheomalacia. The thin layer of platysma fibres present protect the exposed cartilage and form a surface for respiratory re-mucosalisation. The net result is a reconstruction that introduces fresh vascularised tissue into the airway, restores normal tracheal dimensions, mirrors the biomechanical properties of the trachea and achieves a luminal surface that although is initially lined by squamous epithelium, is soon replaced by respiratory epithelium which is capable of supporting mucociliary transport.

The major limitations of this procedure are that it is staged. It had to be performed in this manner to guarantee that there is a viable composite flap for reconstruction. The second limitation of this procedure is that it creates 3 surgical sites which include the neck, chest and thigh. It does, however, provide a solution to a difficult problem where previous techniques have failed. It is a method of reconstructing complex recalcitrant...
long segment tracheal stenoses. Until tissue engineering techniques for these types of injuries are proven and readily available, this new surgical technique provides a further option for managing difficult adult laryngotracheal stenosis.

Illustration 4.33 Histological appearance of a segment of the myocartilagenous flap, stained with Masson’s trichrome and visualized with ×25 magnification. A. The musculocartilagenous interface. Skeletal muscle (m) and cartilage (c) are joined together by a vascular fibrous stromal layer. The presence of vacuolated cartilaginous nuclei (black arrow) confirms cartilage viability. B. Two separate pieces of cartilage (c1 and c2) are joined together by a vascular fibrous joint (j). These histological appearances confirm that separate pieces of cartilage integrate to form a single rigid fibrocartilagenous construct, which is viable, and is closely adherent to the underlying sternohyoid muscle.
4.XI Bilateral Vocal Cord Mobility Impairment

Bilateral vocal fold palsy (BVFP) or bilateral vocal fold immobility (BVFI) are both terms commonly used to describe the lack of movement of both vocal folds. The terms do not, however, include cases where there is reduced mobility rather than immobility. The term bilateral vocal cord mobility impairment (BVCMI) is more accurate and preferred as it includes cases where there may be partial recovery or some degree of motion in at least one of the vocal folds. The analysis of the cases in the series is part of a future research project, but some of the preliminary findings are included in this thesis. It is quite clear that there are three mechanisms of injury:

1. Bilateral denervation (thyroid surgery or neck and chest malignancy)
2. Cricoarytenoid joint fixation (rheumatoid arthritis or trauma)
3. Inter-arytenoid scarring (post intubation)

The management of bilateral vocal fold mobility impairment remains controversial and unsatisfactory. It is my experience that the majority of current techniques lead to a compromise between voice, airway and swallowing. Bilateral recurrent laryngeal nerve injuries leave the vocal folds in the paramedian position and patients suffer with significant shortness of breath and demonstrate stridor. They often end up with a tracheostomy in the acute situation. Various techniques have been described to manage this problem and these include laser to the posterior vocal fold or arytenoid and suture lateralisation of the vocal folds. Various reinnervation techniques have been described, which include ansa cervicalis to recurrent laryngeal nerve, ansa to thyroarytenoid neuromuscular pedicle, and hypoglossal to recurrent laryngeal nerve as well as various muscle nerve pedicle procedures. Most of these techniques lead to synkinesis and work best with unilateral cord palsies in restoring voice (152). More promising techniques, as
yet unpublished and pioneered by Professor Jean-Paul Marie in France, involve a 
technique of mobilising one division of the phrenic nerve or accessory phrenic nerve 
and anastomosing it to the posterior cricoarytenoid muscle. This manages to produce 
abduction on inspiration in the more successful cases. Other groups have looked at 
reanimation of the paralysed human larynx with implantable electrical stimulation 
devices (153). These techniques are, however, in very early stage clinical trials. The 
patients in this series have to date been managed by a unilateral or a bilateral laser 
partial arytenoidectomy as shown in illustration 4.34.

Illustration 4.34 Showing right laser arytenoidectomy procedure for grade I 
BVCMI

The partial arytenoidectomy is performed very posteriorly into the body of the arytenoid 
cartilage, on the one side initially, and can be repeated in the opposite arytenoid if 
necessary. All patients need to be preassessed for baseline swallowing function. This 
technique has been successful in decannulating all patients with bilateral recurrent 
laryngeal nerve palsy and improving respiratory function in the others. However, the 
price paid by the patient is a breathy quality to the voice. This very posterior technique 
has the advantage that the whole vocal fold does not become lateralised as in techniques 
where the vocal process of the arytenoid is lasered or where a suture lateralisation is 
employed. Further research needs to be undertaken in this area to compare quality of
voice and improvement in respiratory function using different surgical techniques. Unfortunately, the numbers of these cases are very small and rather than being referred to specialist centres, are managed by surgeons in their individual hospitals.

The second type of injury leading to BVCMI is fixation of the cricoarytenoid joints. In this series, there were a number of cases where this was related to rheumatoid arthritis affecting the cricoarytenoid joints. Fixation of the cricoarytenoid joint does occur as a result of trauma leading to dislocation or subluxation of the cricoarytenoid joint. This generally occurs as a result of attempts at airway intubation, direct laryngoscopy or blunt laryngeal trauma. The incidence of these injuries is very small (122) and described at approximately 0.1% of tracheal intubations. Bilateral subluxation and fixation as a result of trauma is even more unusual (case reports only). The management of bilateral fixed cricoarytenoid joints is similar to that of recurrent laryngeal nerve palsy in that a laser arytenoidectomy can be performed unilaterally or bilaterally depending on the symptoms. It is even more important to assess swallowing difficulties in these patients as connective tissue disorders often lead to problems with the cervical spine and consequently impact on swallowing. Illustration 4.35 demonstrates a laser arytenoidectomy in a patient with fixation of the cricoarytenoid joints due to rheumatoid arthritis. Illustration 4.35 (centre) shows degeneration material exuding out of the cricoarytenoid joint during the laser procedure.

Illustration 4.35  Grade II BVCMI, Right laser arytenoidectomy performed, Degenerative material from cricoarytenoid joint (centre)
The third cause of fixation of the arytenoids relates to inter-arytenoid scarring. This is mostly a post-intubation finding. There were cases in this series where vocal process granulomas coalesce to form adhesions between the arytenoids, but sparing the inter-arytenoid mucosa (illustration 4.36).

Illustration 4.36  Left picture shows vocal granulation tissue formed as a result of endotracheal intubation coalescing. If undivided this will become mature scar tissue (right) and lead to ankylosis of cricoarytenoid joints.

In the case of illustration 4.36 (left), this adhesion can simply be divided and normal vocal fold function will return. If this granular injury is allowed to mature such as in illustration 4.36 (right) then there will be ankylosis of the cricoarytenoid joint and even division and balloon dilatation will not restore vocal fold function and the compromise between voice and airway remains as in the cases described above. In the cases of inter-arytenoid scarring, distinction must be made between early granular inflammatory (illustration 4.38) injury (grade III) and mature scar tissue between the arytenoids (grade IV). Grading of bilateral vocal fold mobility impairment is therefore as follows:
Illustration 4.37 Relative incidence of grades of Bilateral Vocal Cord Mobility Impairment (BVCMI) presenting to the Unit.

Management of grade 1 and grade 2 injuries has already been described. Grade 3 injuries present early and usually demonstrate a granular inflammatory injury between the arytenoids. This must be treated with steroid injection, gentle reduction of
granulation tissue, mitomycin-C topical application and balloon expansion of the posterior glottis at 2-3 weekly intervals to prevent mature scar formation between the arytenoids. Illustration 4.37 demonstrates grade 1-4 injuries and the percentage of each type of injury presenting to The Unit.

Illustration 4.38 To show the difference in the treatment of mature interarytenoid scar versus non-mature scar (granulation)

It is evident that grade 3 injuries are the type least frequently seen. Illustration 4.39 shows a thin web of inter-arytenoid scarring which could be treated by division with a sickle knife, balloon dilatation and then mitomycin-C application. This procedure, if repeated at 3-4 weekly intervals, may produce resolution of this injury.

Illustration 4.39 Thin interarytenoid scar
The majority of the mature inter-arytenoid scar cases are thicker and more fibrotic as demonstrated in illustration 4.40, which shows an attempt at a large laser arytenoidectomy, with subsequent reformation of the scar and narrowing of the posterior glottis (illustration 4.40 right).

Illustration 4.40  Thick interarytenoid scar (left), extended laser arytenoidectomy and scar division (centre), unfortunately the scar tissue quickly reforms (right)

The only technique that I have been able to use successfully in managing this type of dense posterior interarytenoid scar is to perform an anterior laryngofissure and posterior cricoid split, dividing this scar and separating it with a piece of costal cartilage (illustration 4.41) as a temporary spacing device. This provides separation of the posterior scar tissue so that recurrent interarytenoid scar and contracture does not recur.

Illustration 4.41  Posterior rib graft (as a ‘spacer’), is the only solution to separating thick interarytenoid scar. Case from illustration 4.40 above, following successful treatment (right).
In a large number of cases, this piece of cartilage is resorbed and cannot be considered as a reliable augment. Fortunately, the glottic aperture enlarges and patients can be decannulated. More research needs to be done in the area of bilateral vocal fold mobility impairment and this is a potential project for the future. Currently, all efforts must be made at prevention and it is therefore recommended that intensive care units consider early tracheostomy in patients who are potentially going to be ventilated for more than one week. Early intervention with steroids and mitomycin-C in grade 3 lesions also needs to be promoted. The future management of grade 1 lesions probably lies in laryngeal pacing or novel reinnervation techniques. The management of grade 2 and 4 lesions will, for the time being, be an unsatisfactory compromise between voice and airway.

Illustration 4.42 Algorithm for management of bilateral vocal fold mobility impairment (BVFMI). MLT=microlaryngoscopy and tracheoscopy, CAJ=cricoarytenoid joint, PAPC=posterior arytenoidectomy and posterior cordectomy and GT=granulation tissue
Chapter 5

Management of Inflammatory Conditions

5.1 Wegener’s Granulomatosis

Wegener’s granulomatosis (WG) is a multi-system inflammatory disease with an underlying vasculitis involving small and medium sized vessels. There is associated granuloma formation and necrosis (illustration 5.1), and the condition classically involves the upper and lower respiratory tracts and the kidneys.

Illustration 5.1 HE stain pathology slides of Wegener's Granulomatosis. Left, slide (x25) of respiratory mucosa showing granulomas. Right, slide (x200) showing vessels in respiratory epithelium with acute inflammatory infiltrate (vasculitis).

Wegener’s granulomatosis is believed to have been first described in 1931 by Klinger (154) who reported a patient with destructive sinusitis, nephritis and disseminated vasculitis. In 1936, Wegener clearly defined the disease as a distinct clinical and pathological entity (155). A Scottish otolaryngologist, Peter McBride (156) may in fact have been the first to describe the condition in 1897 in the British Medical Journal in a paper entitled “photographs of a case of rapid destruction of the nose and face”.

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More than 80% of patients with Wegener’s granulomatosis experience rhinological morbidity and 20-40% experience otological morbidity at some point during their lives (157). Seventeen to 23% of patients with Wegener’s granulomatosis develop a subglottic stenosis (158). This subglottic inflammation and narrowing does not uniformly respond to systemic immunosuppressives and may persist despite adequate disease control in other organ systems (158). Sometimes, localised subglottic stenosis may occasionally be the only presentation of WG. This type of focal disease may make it difficult to justify the use of systemic corticosteroids and cytotoxic drugs.

The diagnosis of Wegener’s granulomatosis is often made on clinical presentation when a patient has had the appropriate symptoms for a prolonged period of time. As well as the otolaryngological manifestations already mentioned, patients usually also have involvement of the lungs and kidneys and there may be an element of renal failure.

The Chapel Hill Consensus Conference on defining vasculitides (159), agreed the diagnosis of WG was supported by the following:

- Appropriate clinical history
- Granulomatous inflammation involving the respiratory tract
- Small-medium vessel necrotising vasculitis
- Positive cytoplasmic-pattern antineutrophil cytoplasmic antibodies (cANCA) to proteinase 3 (PR3)
- Necrotising glomerulonephritis.

The condition should therefore be managed in a multi-disciplinary setting which includes renal, respiratory and rheumatological physicians, as well as an
otolaryngologist. The presence of a positive cANCA may aid in the diagnosis, but positivity is not conclusive and negative ANCA results are not sufficient to reject the diagnosis. A definitive diagnosis of Wegener’s granulomatosis can be made by a biopsy of suspicious lesions (demonstrating granulomatous inflammation) in conjunction with positive serological analysis. However, it must be recognised that up to 20% of patients with untreated active Wegener’s granulomatosis lack cANCA (160) or may show positivity later on in the disease history.

Intra-lesional corticosteroid injections have previously been employed to treat subglottic stenosis in Wegener’s granulomatosis (161). However, the results have been inconsistent. Also there has been no study looking at the treatment of Wegener’s granulomatosis involving the remainder of the tracheo-bronchial tree. The treatment options described, apart from medical therapy, include tracheostomy (162) and stenting (163). The use of tracheostomies and long-term stents can lead to airway complications which are difficult to treat (4, 164).

The purpose of this prospective study was to determine the effectiveness of intra-lesional steroids with carbon dioxide laser radial cuts and dilatation as a treatment of airway compromise due to active tracheo-bronchial WG thus preventing infective complications during the active phase of the disease while minimising the risk of long-term iatrogenic morbidity.
5.II  Endoscopic Treatment of Airway Wegener’s Granulomatosis

5.II.a  Methods

Over the period of the study eighteen patients with airway compromise due to active WG were treated at our institution. All patients had active granulomatous lesions obstructing the central airways and no patient had a mature fibrotic airway scar. There were equal numbers of males and females. The average age at diagnosis was 40±16 years (±SD; range 13–74 years). Four patients presented with primarily tracheobronchial WG, while the remaining patients with systemic disease had an average time from diagnosis to airway treatment of 6.3±5.3 (range 1–23) years. The subglottis and the cervical trachea were affected in all patients, while five patients had concomitant bronchial lesions. The average lesion height was 7.8±2.7 (range 4–5mm), and tracheal lesions were on average located 22.7±9.5mm below the glottis. There were one, ten and seven Myer-Cotton grades I, II and III tracheal lesions respectively (10). Bronchial lesions were restricted to a main bronchus in three patients and affected the ostia of one or more of the lobar bronchi in two patients. An example of the characteristic computed tomography changes and associated endoscopic findings in a patient who presented with grade V shortness of breath (as determined by the Medical Research Council Dyspnoea Scale) (149) and pneumonia are shown in illustration 5.2
Prospective data was collected between 2004 and 2006 on all new patients referred with a diagnosis of Wegener’s granulomatosis affecting their airways and who had not previously undergone treatment before referral to The Airway Reconstruction Unit.

All the procedures were performed under general anaesthesia with a total intravenous anaesthesia technique (section 3.II). The airway was initially secured using a supraglottic laryngeal mask which was substituted in the operating theatre with a dedo pilling suspension laryngoscope through which high frequency supraglottic jet ventilation was delivered. The airway was visualised with a combination of microscopic and endoscopic techniques.

For subglottic/tracheal procedures the airway was visualized with a combination of microscopic and endoscopic techniques, using a standard operating microscope and a
4mm 0° Karl-Storz airway endoscope (Karl Storz GmbH & Co KG, Tuttlingen, Germany). Lesions were treated with 60-80mg of methylprednisolone acetate (Depo-Medrone®; Pharmacia; Walton-on-the-Hill, UK) circumferentially injected at the base of the lesions. This was delivered via a 27 gauge BD Valu-Set™ butterfly needle (BD Infusion Therapy, Helsingborg, Sweden) as previously described. (145). A carbon dioxide laser was then used to make radial incisions into the lesion, preserving intact bridges between the cuts to prevent circumferential re-stenosis. Laser surgery was used both to reduce the lesions and to improve the efficacy of the subsequent balloon dilatation. The subglottis/trachea was then dilated using a CRE™ Pulmonary Balloon dilator (Boston Scientific, Natick, MA, USA). In seven patients, topical mitomycin C (MMC) (Kyowa Hakko UK Ltd, Slough, Berks, UK) at a concentration of 1mg/ml was applied for 3 minutes at this point. Mitomycin C was used in selected patients with high-grade or recurrent lesions.

For patients undergoing treatment for bronchial lesions the operative sequence was almost identical, consisting of intralesional steroid injection, radial laser incision and balloon dilatation. The differences lay in the choice of equipment, and the fact that no patient received topical mitomycin C. The carinal/bronchial region was visualized either with a 4mm 0° Karl-Storz airway endoscope, or a flexible channelled bronchoscope introduced through the laryngoscope (illustration 5.6A). Intralesional steroids were delivered using transbronchial eXcelon™ needles (Boston Scientific, Natick, MA, USA) introduced via the channel of the bronchoscope (illustration 5.6B). KTP laser was delivered to the lesion via 0.4mm disposable fibreoptic filaments (Laserscope, San Jose, CA, USA) (Illustration 5.6C). Dilatation was performed using a bronchial CRE™ Pulmonary Balloon dilator (Boston Scientific, Natick, MA, USA) (illustration 5.6D and 5.6E). Since all patients with bronchial lesions had retention of

145
secretions, suction catheters were introduced alongside the bronchoscope and guided into the main and lobar bronchi to remove retained and often infected secretions. Examples of the results of treatment for both tracheal and bronchial lesions are shown in Illustration 5.3

Patients were observed for a few hours following the procedure on a surgical high-dependency unit and were subsequently managed in a multidisciplinary team facility.

Illustration 5.3 Intra-operative results of treating a tracheal lesion (A). Intra-operative results of treating a bronchial lesion (B). The white streaks are displaced methylprednisolone.

Illustration 5.4 Timeline plot detailing treatments received by individual patients
Illustration 5.5 Kaplan-Meier plot of intervention-free period following endoscopic treatment of active Wegener’s granulomatosis

Illustration 5.6 Diagram to outline the steps for treating bronchial WG. Suspension laryngoscopy and flexible bronchoscopy (A). Lesional steroid injection (B). KTP laser used to make radiate cuts into lesion (C). Pulmonary balloon insertion (D) and dilatation (E).
Data Analysis

Demographic information, characteristics of the lesions at the start of the treatment, and the nature and timing of each treatment episode were recorded. Intervention-free interval was defined as the time between one treatment episode and the next surgical treatment performed to restore airway patency as previously defined. (145). Data are presented either as means with standard deviations or as percentages when appropriate. Intervention-free intervals were calculated and illustrated using the method of Kaplan and Meier, and compared with log-rank statistics. A stepwise Cox proportional hazards ratio model was constructed to identify potential independent predictors of the intervention-free interval. Ordinal regression was used to identify predictors of the number of treatments required to achieve a sustained symptom-free period. Data were analyzed and displayed using SPSS release 12.0 for Windows (SPSS Inc., Chicago, IL, USA).

5.II.b Results

Eighteen patients underwent a total of 31 procedures, a median number of one procedure per patient (range 1–4). No patient required a tracheostomy or a tracheobronchial stent and no open surgical procedures were undertaken. There were no cases of significant postoperative haemorrhage or infection. Ordinal regression was undertaken to identify independent factors associated with the number of treatments each patient received. Variables entered into the model were patient age and sex, vertical height and Myer-Cotton grade of the lesion, distance from glottis, presence of concomitant bronchial lesions and whether or not mitomycin-C had been used at any time during treatment. No independent predictors of the number of treatment episodes per patient were identified. The treatment timelines for all patients in the series are
shown in illustration 5.4. The overall mean intervention-free interval following endoscopic treatment was 26.1±2.8 months (±SEM) (illustration 5.5). There was no significant difference in the durability of endotracheal and endobronchial treatments (p >0.8; log-rank analysis). Univariate log-rank analysis and multivariable Cox regression failed to identify any factors predictive of the post-procedural intervention-free period. Variables entered were lesional height and Myer-Cotton grade of the lesion, age and sex of the patients, and use of MMC. Topical mitomycin-C was used in seven patients with high-grade or recurrent lesions. It did not significantly increase the intervention-free interval and was associated with one patient developing stridor within one month of treatment due to airway crusting (illustration 5.7) which was managed endoscopically with no permanent sequelae.

Illustration 5.7 Shows subglottic crusting and airway compromise in one of the patients with topical mitomycin-C application.

5.II.c Discussion

The results of this study show that active obstructive tracheobronchial WG can be satisfactorily managed with endoscopic surgery, intralesional steroid therapy and balloon dilatation. Our findings are in accordance with the experience of Hoffman and Eliachar (161) and Langford and colleagues (158) who studied subglottic stenosis due
to WG. The present work extends the application of this treatment approach to bronchial lesions and differs from the above studies in excluding revision cases with mature fibrotic scars, focusing instead on patients with airway compromise due to active tracheobronchial WG without prior treatment.

There exists a divergence of opinion regarding the optimal treatment of active obstructive tracheobronchial WG. The traditional view, which continues to be advocated, (165) has held that, with the exception of life-threatening lesions, which need to be bypassed with a tracheostomy or opened with a stent, (163) active obstructive WG should not be approached surgically. Surgery should instead be directed towards decannulation and reconstruction of mature airway scars, once active inflammation has been brought under control. This treatment strategy is difficult to accept, given that tracheobronchial WG poses a serious, but essentially localized problem which has an underlying inflammatory cause. Given the advances in shared airway surgery and anaesthesia, the acute obstructive component of this problem can be treated with minimally-invasive surgery and dilatation. Furthermore, evidence is accumulating to suggest that the underlying inflammation can be adequately treated with high-dose intralesional steroid therapy. (145, 158, 161) It was possible, using this approach, to reduce the requirement for placing a tracheostomy from 40-50% (162, 163) to zero.

Current medical management of WG is based on classifying patients into severe generalised, early systemic, or limited disease. The first is defined as disease which poses an acute threat to life or function of a vital organ, and the latter as disease manifestations that do not pose such threats (160). Treatment of severe generalised disease necessitates induction immunosuppression with steroids and cyclophosphamide, (166) whilst early systemic disease may be managed with steroids and methotrexate
Limited disease may not require systemic immunosuppression at all. Patients with obstructive tracheobronchial WG may be classified as having severe disease, since airway obstruction impedes ventilation and mucociliary clearance, causing ventilatory insufficiency and pulmonary infection respectively which can be acutely life-threatening. The findings of the present study together with those of Hoffman and Langford (158, 161) suggest that local treatment of airway obstruction can effectively convert the disease from a severe form to a more limited one. Tracheobronchial WG often runs a course independent of other manifestations of WG (158), and effective local treatment of airway lesions can lead to early tapering of systemic immunosuppression in selected patients. This multidisciplinary treatment strategy, which is consistent with earlier recommendations, (158, 161) was deployed in all the patients in the present study and enabled a reduction in steroid dosage and use of steroid-sparing agents. Moreover, in those patients whose disease activity at distant sites necessitates continuing immunosuppression, treatment of tracheobronchial lesions leads not only to symptomatic benefit, but by improving mucociliary clearance, reduces the likelihood of pulmonary infections developing in immunocompromised individuals.

None of the patients in the present series required a tracheostomy or a stent, a finding that is in keeping with previous observations (158). Performing a tracheostomy, with its attendant severe impact on quality of life, or a stent procedure on any patient with tracheobronchial WG now seems unnecessary. Especially given that even patients with severe airway obstruction can be safely anaesthetized and treated with specialised shared-airway techniques. It must, however, be acknowledged that both of these procedures will continue to be performed on patients who acutely present with life-threatening airway compromise locally, who may not be safe for transfer to the nearest
airway unit. In these cases we recommend referral to an airway unit once the obstruction has been safely bypassed, so that lesions can be treated and the patient decannulated. For those patients who do require a stent, we urge that whenever possible, a removable stent like the Aero™ tracheobronchial stent (Alveolus Inc, Charlotte, NC, USA) be deployed, and removed at the earliest opportunity. If this is not locally available and a permanent stent is deployed as a life-saving procedure, the patient should be rapidly referred to an airway unit so that the stent can be removed before it is encased in granulation and scar tissue. There is no justification for placing and retaining a permanent stent for a benign disease with a favourable long-term prognosis(168) given the significant long-term complications that are associated with the placement of permanent stents for benign conditions. (169, 170).

In conclusion, the findings of this study show that active obstructive tracheobronchial Wegener’s Granulomatosis can be satisfactorily managed with minimally-invasive surgery undertaken using specialist shared-airway techniques, obviating the need for airway bypass surgery or stenting. This, in selected patients, can in turn reduce the need for and the duration of, high-dose systemic corticosteroids and cytotoxic therapy. Given the high incidence of tracheobronchial involvement in WG, we suggest that all patients with unexplained pulmonary symptoms should be screened for central airway stenosis with flow-volume loops as part of their diagnostic work-up and a physician-led coordinated multidisciplinary approach to the management of tracheobronchial WG should be adopted. Surgery for this condition should be conservative and aimed at relieving mechanical obstruction and delivering intralesional steroids. Wegener’s lesions are benign and transitory, and our research shows that placing permanent stents,
or performing complete circumferential endoluminal resections to achieve ‘normal’ intraoperative airway appearances are strongly contraindicated in this condition.

This study looked at the use of the KTP laser as a radiate cutting tool after steroid injection and before balloon dilatation in bronchial stenosis. The KTP laser does run the risk of collateral injury to the airway leading to further scarring and in safety terms, there is also risk to adjacent cardiopulmonary structures. There is also a significant learning curve in using fibre lasers through a bronchoscope. The next area of research will look at the use of a cutting balloon device (171) for bronchial stenoses. This allows cutting and dilatation to be performed in one simple manoeuvre without the potential risks of a laser.
5.III  Idiopathic Laryngotracheal Stenosis

Idiopathic subglottic stenosis (ISS) is a rare, slowly progressive, fibro-inflammatory process of unknown cause which leads to narrowing of the airway in the subglottic region and usually involves the first and second tracheal rings. This form of airway stenosis should strictly be called laryngotracheal stenosis as it involves the proximal trachea and extends up to the glottis (illustration 5.8).

Illustration 5.8 Shows typical appearance of idiopathic subglottic stenosis

It occurs predominantly in women post puberty, but has been reported in males (172-176). During the period of this research, the team have treated 50 patients with this condition. Only one of these is male. All the patients are Caucasian and of European origin. The diagnosis is one of exclusion and our criteria for making this diagnosis are included in the table 5.1 below. In each case, the anti-neutrophil cytoplasmic antibody (ANCA) and angiotensin converting enzyme (ACE) tests have to be repeated at intervals as neither test is 100% sensitive. Tissue for histology is also sent at each surgical procedure (illustration 5.9).
Illustration 5.9 HE staining (x25) of tissue biopsy of idiopathic subglottic stenosis. Respiratory epithelium (left) with stroma consisting of acute and chronic inflammation (polymorphs, histiocytes and plasma cells) and fibrosis.

Table 5.1 Diagnostic criteria for idiopathic subglottic stenosis.

<table>
<thead>
<tr>
<th>Clinical Features</th>
<th>Serum Biochemistry</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Female patient</strong> (Males very rare)</td>
<td><strong>Negative titres for:</strong></td>
</tr>
<tr>
<td><strong>No history of laryngotracheal injury</strong></td>
<td>o Angiotensin Converting Enzyme (ACE)</td>
</tr>
<tr>
<td>o No endotracheal intubation or tracheotomy / no occurrence of exertional dyspnæa within two years of intubation/tracheotomy.</td>
<td>o Antinuclear Antibody (ANA). Rheumatoid Factor (RF)</td>
</tr>
<tr>
<td>o No thyroid/anterior neck surgery.</td>
<td>o Anti-Neutrophil Cytoplasmic Antibody (ANCA)</td>
</tr>
<tr>
<td>o No neck irradiation.</td>
<td></td>
</tr>
<tr>
<td>o No caustic or thermal injuries.</td>
<td></td>
</tr>
<tr>
<td>o No significant anterior neck trauma (blunt or penetrating).</td>
<td></td>
</tr>
<tr>
<td><strong>No history of auto-immunity</strong></td>
<td></td>
</tr>
<tr>
<td>o Negative history for vasculitis, formally ascertained through a vasculitis-specific systemic enquiry and semi-quantified using the Birmingham Vasculitis Activity Scale (BVAS).</td>
<td></td>
</tr>
<tr>
<td>o No history to suggest sarcoidosis or amyloidosis.</td>
<td></td>
</tr>
</tbody>
</table>

**Gross lesion morphology**

- The stenosis must include the subglottis

**Histopathology**

- Exclusion of other pathological entities (e.g. tumours, vasculitides, amyloidosis...)
- Fibrosis restricted to lamina propria with normal perichondrium / cartilage
- Mixture of granulation and fibrosis with a prominence of keloidal fibrosis

* This is established with a deep endoscopic biopsy at the time of first treatment.
Unfortunately, seven of the women in my series were treated for asthma for many years and were finally intubated for supposed asthma which had proven refractory to medical treatment. At the point of extubation, they were then diagnosed with post-intubation airway stenosis. An assumptive diagnosis of idiopathic subglottic stenosis was made in these patients based on the history, anatomy of the lesion and the fact that tests for other causes of airway stenosis had proven negative. In addition these patients were ventilated for very short periods, making the diagnosis of post-intubation laryngotracheal stenosis unlikely. Each of the 50 patients in this series has had histological tissue sent for analysis (illustration 5.9) and the majority of patients have had this tissue tested for oestrogen and progesterone markers. All have proven negative. Although Shapsay (174) proposes a link with oestrogen, his group did not isolate oestrogen receptors in the tissue that they analysed. Most series (172-176) describe an initial assessment of the airway stenosis under anaesthesia with management using some form of dilatation.

Illustration 5.10 Complete stenosis of the glottis extending to the tracheostomy in a patient treated aggressively for idiopathic subglottic stenosis

Other groups have undertaken endoscopic procedures using local mucosal flaps (8) whilst others have explored the use of Mitomycin-C (174) and steroid injections. None of these have proven therapeutic benefits. Care must, however, be taken because patients with idiopathic subglottic stenosis have a highly reactive airway and injudicious
attempts at endoscopic laser photo resection of the stenosis, pushing rigid bronchoscopes through, or stenting will almost invariably produce aggressive scar formation which can wholly close up the airway (illustration 5.10). Similarly, long-term tracheostomy is not a solution as the airway above the tracheostomy will scar and close down and cause aphonia. The reason for the hyper-reactivity of the airway in these patients is unknown. The disease does not affect or infiltrate the adjacent cartilaginous framework of the airway (177). Embryologically, there does not appear to be any developmental significance to this anatomical site, although it is an area of intense immune activity. Table 5.2 illustrates all the published case series with greater than 15 patients compared with our figures.

Table 5.2 Review of the reported clinical series in the literature with greater than 15 patients with idiopathic subglottic stenosis (ISS)

<table>
<thead>
<tr>
<th>Authors</th>
<th>No. of patients</th>
<th>No. of patients treated</th>
<th>Period (years)</th>
<th>Endoscopically treated patients</th>
<th>No. of open-neck procedures</th>
<th>No. of failed open-neck procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dedo and Catten</td>
<td>52</td>
<td>50</td>
<td>30</td>
<td>50</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Grillo et al</td>
<td>65</td>
<td>65</td>
<td>31</td>
<td>2</td>
<td>65</td>
<td>6</td>
</tr>
<tr>
<td>Giudice et al</td>
<td>30</td>
<td>30</td>
<td>17</td>
<td>30</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Valdez and Shapshay</td>
<td>16</td>
<td>14</td>
<td>12</td>
<td>14</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Benjamin et al</td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>12</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Sandhu et al (unpublished)</td>
<td>50</td>
<td>50</td>
<td>7</td>
<td>41</td>
<td>9</td>
<td>0</td>
</tr>
</tbody>
</table>

The approach varies from crico-tracheal resection to repeated endoscopic procedures. Grillo (173) published a series of 73 patients which he had treated with crico-tracheal resection. Only 65 of these patients turned out to have likely idiopathic subglottic stenosis. He had 6 failures in this series of crico-tracheal resection. Herb Dedo
published a series of 52 patients (175), 7 of whom were treated with crico-tracheal resection and all failed. No other group has had a series as large as Grillo, nor have they been able to duplicate his success rate with crico-tracheal resection. My approach to open surgery differs from the orthodoxy of crico-tracheal resection and anastomosis. The reason being that idiopathic subglottic stenosis is primarily a mucosal disease which overlies healthy perichondrium and cartilage (177). In addition, no one has been able to duplicate the excellent cure rates reported by Grillo’s group using crico-tracheal resection. There is concern that crico-tracheal resection in a condition that predominantly affects females is likely to leave these patients with ‘male-type’ voices after the surgery (178). Moreover, crico-tracheal resection conceptually treats this condition as a benign neoplasm and in our series, the disease often extends up to the glottis (illustration 5.11) and it is difficult to conceive how a resection could be performed within millimetres of the vocal folds without leaving damage in this area.

Illustration 5.11 Typical appearance of idiopathic subglottic stenosis extending up to vocal folds
5.IV Treatment of Idiopathic Laryngotracheal Stenosis

5.IV.a Methods

From the start of data collection in the beginning of 2004 to starting data analysis in the beginning of 2010, 50 patients had been diagnosed with idiopathic subglottic stenosis based on the criteria described above. Only one was male. All the patients were post puberty and the age range was from 26-82 years with a mean age of 52 years. The length of lesion at presentation ranged from 0.75 cm to 5 cm with an average length of 2.75 cm. The lesion in all cases included the subglottis and first one or two tracheal rings with extension up to the glottis (illustration 5.11). One case at presentation had complete stenosis extending from the glottis down to the tracheostomy, in total a length of 5 cm. This patient will be discussed in detail later.

The incidence of laryngo-pharyngeal reflux in adult males and females is very similar and this is therefore unlikely to be the principle aetiological factor. Even so, all patients were started on anti-reflux therapy at first diagnosis. This comprised Omeprazole 20 mg each morning before breakfast and Ranitidine 150 mg in the evening. Gaviscon (Reckitt Benckiser, UK) was also prescribed to be taken after the evening meal. Gastro-oesophageal reflux management advice leaflets are offered routinely to all patients. The patients are advised to continue with this therapy long-term. Naturally, the majority of patients presented with dyspnoea and a smaller percentage had an associated cough. Most of the referred patients arrived with computer tomographic imaging of their airway. However, where this had not been performed, it has not been our practice to arrange this. This is because of the potential errors in estimating the size of the lesion that we have discussed previously. The next step is generally to perform examination under anaesthesia at which time lesional anatomy is further assessed and endoscopic
airway surgery is performed. An anatomical assessment consists of determining the cranio-caudal height of the lesion, its distance from the glottis and minimum airway cross-section. These are determined using quantitative endoscopic techniques as previously described. However, it is now my practice to stratify the cross-section using the Myer-Cotton grading system as the techniques of absolute measurement that I have deployed previously do not allow easy comparison with other groups’ work. All the patients in this series have been offered either repeated endoscopic procedures which are repeated on average every 7 months (range 4-12 months). Only two patients have required no further treatment after the first endoscopic procedure. All the patients have been offered an open reconstruction to provide a permanent solution to the airway problem. However, to date only 10 have elected to go down this path.

Surgical Technique

Airway surgery and assessment is always performed using a technique of suspension laryngoscopy as described in the chapter on surgical techniques (3.1). This gives an unencumbered no touch access to the laryngo-tracheal complex and allows for 2-handed minimally traumatic rigid instrumentation (illustration 5.12), microscope visualisation and line of site CO$_2$ laser surgery.

Illustration 5.12 View of subglottic stenosis using suspension laryngoscopy and the microscope
All patients receive intravenous induction of anaesthesia and supraglottic jet ventilation. A total intravenous technique is used for anaesthesia maintenance. Most other groups (172-176) use a technique which includes the use of rigid ventilating bronchoscopes. I find that this is unnecessary and as well as causing unnecessary trauma to tissues adjacent to the lesion, it also provides a less favourable view. Our method of anaesthesia induction and maintenance is described in section 3.II.

Illustration 5.13 Two cases of idiopathic subglottic before treatment (left) and after steroid injection, laser and balloon dilatation (right)

Once the anatomy of the lesion has been assessed, it is our practice to inject Depamedrone (40 mg/ml) using a 27 gauge butterfly needle with the wings trimmed as shown in the illustration (illustration 4.18). The butterfly is held in microsurgical laryngology forceps as shown and 3 ml of Methyl Prednisolone Acetate is injected. The use of this steroid is unproven and its use is based purely on the fact that there is an inflammatory component to the lesion on histological analysis and the technique has been continued following personal communication with Professor Eliachar from the Cleveland Clinic, who had considerable experience with this disease. Three or 4 radial incisions are made into the lesion using the Carbon Dioxide laser set at 8-10 watts (illustration 5.13). This laser is deployed through a micro-manipulator attached to the operating microscope. (It does not seem appropriate to use a KTP laser to treat
idiopathic subglottic stenosis because it causes deeper tissue penetration and more aggressive collateral tissue injury when compared with a CO₂ laser.) Following these radial cuts, the lesion is dilated using a pulmonary balloon dilatation system (Boston Scientific, Boston, USA) and the lesion is dilated to 15-16 mm. A deep tissue biopsy is taken at this stage using microcup forceps and haemostasis is achieved using topical adrenaline applied with a neurosurgical pattie soaked in 1:1,000 adrenaline.

My approach when performing open laryngotracheal surgery in these patients is to perform a laryngofissure with a posterior cricoid split. Some, not all, of the lesion is excised off the perichondrium on the lateral walls. Following the posterior cricoid split, a piece of costal cartilage is placed between the posterior cricoid split to separate the scar tissue and act as a temporary spacer. This piece of cartilage is not expected to survive in adult patients. Before closure of the laryngofissure, a closed silastic stent is fashioned as shown in the illustration (illustration 5.16) and then covered with a superficial skin graft with the dermis placed outwards. This skin graft is held in place with a single monofilament suture of 4/0 ethilon. The laryngeal anterior commissure is closed also with a 2/0 ethilon suture. The subglottic airway is not completely closed, but is instead augmented anteriorly with an inferiorly pedicled sternohyoid muscle flap sutured in place with 3/0 vicryl. A temporary tracheostomy needs to be fashioned below the reconstruction before the stent is stitched in place and the tracheostomy is left in place for 2 weeks. At 2 weeks, the stent is removed endoscopically as well as the skin graft and the tracheostomy. In all our patients, the area where the stenosis was excised is colonised with keratinocytes. This is seen as an anterior and posterior longitudinal strip at the site of the rib graft and the anterior laryngotracheal split where the muscle was placed. Keratinocytes also colonise some of the lateral walls where the stenosis was excised. Eight of the 9 patients who have had this surgical approach have
had one further inspection under anaesthesia 4-6 weeks after decannulation, but none have required subsequent endoscopic procedures. The 10th patient in the series was operated on in 2004 and the case is described below.

A 36-year-old white Caucasian female had been referred from a teaching hospital in Scotland having had 12 endoscopic airway laser procedures to deal with an idiopathic subglottic stenosis. She developed complete stenosis of her airway from the glottis down to the tracheostomy and had had no voice for 5 years. She had requested surgery to restore her voice as she had not spoken to any of her children in 5 years. The local surgical team’s recommendation was for a laryngectomy and surgical voice. Having declined this option, she sought a referral to the Airway Reconstruction unit. The appearance of the larynx at the time of first examination is shown in illustration 5.14. CT imaging revealed complete stenosis from the glottis to the tracheostomy (approximately 5cm)

Illustration 5.14 View of glottis in patient with complete stenosis of the airway from the vocal cords to the tracheostomy

Up until this time, I had performed no open surgical procedures on idiopathic subglottic stenosis. As the patient was prepared to try any measures that might work rather than lose her larynx, a new technique was devised. The airway was opened from
the level of the glottis to the tracheostomy using the CO₂ laser delivered through a micromanipulator attached to the microscope.

Illustration 5.15 Showing lasering (left) to open out airway, stenting (middle) and after removal of stent

Following balloon dilatation, a size 12 soft silastic stent was stitched in place for one month (illustration 5.15). The patient retained a tracheostomy and required nasogastric feeding only for the first few days. Once the stent was removed, the voice gradually deteriorated and endoscopic examination demonstrated gradual closure of the airway above the tracheostomy. An open laryngotracheal procedure was advised, to which the patient agreed. A laryngotracheal fissure, as described above, was performed with a posterior cricoid split and posterior augmentation with a piece of costal cartilage and anterior augment with a pedicled sternohyoid flap. The endoluminal stent in this case was a superficial skin covered Eliachar stent (illustration 5.16) which was left in place for 2 weeks. The stent was removed endoscopically and an adequate airway had been achieved. The tracheostomy, however, was left in place for a further 10 weeks to be sure that there was going to be no re-stenosis of the airway. The patient has had a 6-year follow-up with no further endoscopic procedures.
Illustration 5.16 Costal cartilage fashioned to fit in a posterior cricoid split (left), Eliashar stent (middle) in place in the larynx covered with superficial skin graft. Larynx four years after reconstruction (right)

Illustration 5.16(right) shows the appearance of her glottis at the last assessment. She eats and drinks normally and although her voice is very rough in quality, it is usable and she retains a Scottish accent. She does not describe dyspnoea and manages the normal activities of daily living.

5.IV.b Results

The study of idiopathic subglottic stenosis is incomplete as further patients need to be recruited. However, the results of the open surgical approach are exceptional and it was felt that an early mention should be made in this thesis. At first diagnosis, before endoscopic tracheoplasty, some patients report an MRC dyspnoea score of IV or V. Some have even been ventilated because of type 2 respiratory failure before the diagnosis was made. Following endoscopic surgery patients report normal airway swallowing and voice until recurrence. (typical flow volume loops 5.17).
All the open reconstructions report normal airway, voice and swallowing aside from two cases. The patient with complete laryngotracheal stenosis (described on previous page) has a very rough quality to her voice but it is functional. The other suboptimal result is in a relatively young patient (30-year-old female) has ended up with a weaker, breathier voice but excellent airway. She is the last patient in the series to have been treated and has had 15 months follow-up. The problem appears to be excessive separation of the posterior glottis leading to a persistent phonatory gap. The voice has gradually improved with speech and language therapy guidance, but the problem appears to be incomplete resorption of the posterior rib graft augment.

5.IV.c Discussion

Idiopathic subglottic stenosis is a rare condition of unknown aetiology of which there have only been a few hundred cases described in the world literature. The vast majority of the patients are female. My series is currently the third largest but has not as yet been published. All the patients in my series are of European origin and the condition has not been described in the Oriental or South Asian literature. Personal communication with
previous authors has revealed that some of the patients in these series are of Afro-Caribbean descent. Although all our patients have been offered open reconstructive procedures to definitively deal with this condition, the vast majority have elected to have once or twice yearly day case endoscopic procedures. Only a small number of patients have been treated with the novel surgical approach, but the results are promising. In the future, the plan is to use a smaller piece of cartilage in the posterior cricoid split. In addition the team will also be performing pre and post surgical assessment along the lines of the proposed guidelines at the end of this thesis.
5.V Sarcoidosis

5.V.a Introduction

Cesar Boeck of Christiania, Denmark was the first to use the word “sarcoid” and describe the multi-system nature of the disease in 1899 (179, 180). He mentioned the clinical similarity to a previous case described by Jonathan Hutchinson of London in 1898 as Mortimer’s Malady where a female patient, Mrs Mortimer, had generalised skin lesions and swelling of the bridge of the nose. Sarcoidosis has a world-wide distribution and can affect any race, ethnicity, gender or age group. Typically, it is found in patients aged 20-40 years and has a female to male ratio of 2:1, and has a predilection for black African Americans (180). Otolaryngological involvement occurs in <3% of cases and can occur in isolation as the only initial presenting symptom or can represent progression of this systemic disease (181). Laryngeal pathology is often overlooked and many authors have suggested that if actively sought, a high incidence would be found. Laryngeal sarcoidosis thus has a variable incidence reported between 1% and 5% (182-184).

5.V.b Pathogenesis

The pathophysiology behind sarcoidosis remains obscure and numerous infectious, chemical or occupational agents have been postulated as inducing disease. Abnormal auto-immune mechanisms are seen in sarcoidosis such as the inability to mount or maintain delayed type hypersensitivity reactions (185). This forms the basis for a negative tuberculin test that is characteristically seen. Current hypotheses propose sarcoidosis to occur in generally susceptible individuals through alterations in immune responses after exposure to various “triggering” agents. In large case controlled trials, no single cause has been found. Genetic associations have been investigated,
demonstrating HLA DRB1 alleles to be involved (186). Although development of sarcoidosis is likely to be multifactorial, a genetic-environmental interplay appears to be important in disease initiation. Histologically, granulomas are seen arranged in clusters or crops of tubercles typically at the same stage of development. They consist of epithelioid cells, giant cells and various lymphocytes and plasma cells with no evidence of caseation or necrosis. As disease remits, fibrosis occurs around and between granulomas. Fibrous tissue then hyalises, forming a dense scar around the tubercle. Granulomas can completely resolve such that biopsy specimens do not show these characteristic features. Multiple biopsies may be necessary for diagnosis, and even when carried out, may only yield features of non-specific inflammatory infiltrates.

5.V.e Diagnosis

The diagnosis of sarcoidosis depends on the presence of typical clinical features and non-caseating granulomatous inflammation (illustration 5.18) on biopsy of an affected organ with the exclusion of other known causes of granulomas, including tuberculosis, leprosy, syphilis and fungal disease.
The full blood count may be normal or reveal a normocytic anaemia of chronic disease with an elevated erythrocyte sedimentation rate. There may be lymphopenia with a reduction of the CD4 to CD8 T cell ratio. The serum angiotensin converting enzyme (ACE) level is typically elevated, but may be within the normal range. Serum anti-neutrophil cytoplasmic antibody (ANCA) is normal. Biopsy of an affected organ is used to confirm granulomatous inflammation and for specific stains to exclude known infections causes including tuberculosis, leprosy, syphilis, fungi and other granulomatous diseases and vasculitis. A chest X-ray may reveal hilar lymphadenopathy with or without pulmonary infiltrates or evidence of pulmonary fibrosis. In suspected disease, if a chest X-ray is normal, then a CT scan should be requested. Serum calcium may be elevated and a 24-hour urine collection should be obtained to exclude elevated urinary calcium excretion. A Gallium scan may show enhanced uptake in the lacrimal and parotid glands due to granulomatous inflammation. ECG and echocardiogram are usually performed in order to exclude cardiac
involvement. Anatomically, laryngeal sarcoid has a predilection for the supraglottic region, particularly the epiglottis, aryepiglottic folds and arytenoids (illustration 5.19).

Illustration 5.19  Showing diffuse swelling of the supraglottic larynx typical of sarcoidosis

The macroscopic appearance of the supraglottis is diffusely thick, oedematous and characteristically pale or pink in colour. These features are considered pathognomonic for this condition (182). Although exophytic, polypoidal, nodular and granulating lesions have been described, these are less common (184). Isolated involvement of the glottis is exceedingly rare (187). This may be explained by the paucity of lymphatics draining the glottis and the sarcoidosis is a disease of the reticulo-endothelial system (188). Decreased vocal cord mobility is a feature seen with diffuse laryngeal invasion. True vocal cord paralysis can also occur as a result of perineural invasion or multiple cranial nerve polyneuritis (182). Laryngeal disease tends to progress slowly with a relapsing and remitting course. The disease may ultimately “burn out” in later stages. Symptoms are recognised when granulomatous lesions are present; however, they may persist despite remission due to subsequent fibrosis.
5.V.d Clinical Features

The clinical features of laryngeal sarcoidosis have been well described. These include dysphonia, dyspnoea, dysphagia and cough (189). Stridor is a late symptom and an indicator of impending acute airway obstruction. Pain is not a feature of laryngeal lesions as the mucosa remains intact and rarely ulcerates (185). Other constitutional symptoms may be present, the most frequent being fever, weight loss and generalised malaise. Alternatively, patients may be asymptomatic and are diagnosis made on clinical examination.

5.V.e Clinical Evaluation

As 90% of cases of sarcoidosis have pulmonary involvement, patients are often referred to the otolaryngologist by a respiratory physician. These patients therefore need to be managed in a multi-disciplinary setting. The role of the otolaryngologist in this setting is to take a full history and perform a complete ear, nose and throat examination, including examination of the nose and upper aerodigestive tract with a flexible nasal endoscope. The nose may demonstrate congestion or crusting; however, this alone is not diagnostic as one third of the population suffer with some degree of rhinitis. The appearances of the larynx may be pathognomonic, but the diagnosis is still one of exclusion of other disease processes that may mimic sarcoidosis. The otolaryngologist should also confirm that the investigations mentioned above have been performed and the results are collated. If a CT scan of the chest has not recently been performed, then this can be requested to include the neck. This may help with discrimination of soft tissue swelling and cartilaginous abnormalities in the larynx. It may also pick up cervical lymphadenopathy that was not apparent on clinical examination.
Recently, positon emission tomography coupled with computer tomography (PET/CT) has been shown to have an increasing role as a non-invasive imaging tool specifically for extra-thoracic manifestations of sarcoidosis (190). It has also been shown to correlate well with active disease in biopsy proven pharyngo-laryngeal sarcoidosis. The presence and degree of airway obstruction in these patients can be assessed with pulmonary function tests. In upper airway obstruction, flow volume curves show characteristic truncation of peak flow rates.

5.V.f Treatment

Optimum treatment techniques are still debated and various approaches exist, all intending to slow disease progression and/or remove it permanently. The international consensus on sarcoidosis is that corticosteroids are indicated when critical organs are involved or if sarcoidosis is severe (191). Although systemic corticosteroid therapy is initially effective, many patients require long-term low dose steroid treatment to maintain remission, which is not without complications. If symptoms fail to respond or relapse when the Prednisolone is reduced to 10 mg daily, then an additional immunosuppressant is indicated. Hydrochloroquine is given orally in daily doses of 20-400 mg and has been shown to be effective in sarcoid skin lesions. If a steroid sparing agent is required for systemic disease that does not involve the skin, then Methotrexate may be considered. An initial dose of 2.5-5 mg of Methotrexate is increased at 1-2 weekly intervals by 2.5 mg with repeated monitoring of blood count and liver function to a maximum of 15-20 mg once weekly. If tolerated, this can continue long-term while gradually tapering the Prednisolone dosage. Folic acid 5 mg on the day following Methotrexate will also be required. In rare cases when corticosteroids alone or a combination with Methotrexate and/or Hydroxychloroquine fail, then there is a rationale for the use of strategies against human tumour necrosis factor alpha (TNFA) which is
known to be involved in granuloma formation. However, there is very little evidence for or against the use in patients with predominantly upper respiratory tract sarcoidosis. In patients with significant airway compromise, unless specialist shared airway surgical and anaesthetic expertise is available, a tracheostomy may become mandatory (192). Laryngeal sarcoid has been treated previously with intra-lesional corticosteroids via direct or indirect laryngoscopy with moderate success (189, 192). This technique does produce relief and reduction of systemic steroids in many patients, but recurrences are variable and individuals did require multiple injections to control disease. However, a number of patients in these series still required oral steroids. Various techniques of surgical debulking and excision of laryngeal sarcoid lesions have been described. These include open procedures with laryngofissure (192) and laryngectomy (193) which have been used, but are understandably associated with significant morbidity and disability. More recently, minimally invasive direct laryngoscopy with carbon dioxide laser ablation has been shown to improve symptoms, create adequate airways and remove disease (194, 195) although this effect is often temporary (183, 196). Other alternative treatments have included external beam radiotherapy (197, 198). However, this does increase the risk of thyroid malignancies and has not often been utilised.
5.VI Assessing a New Surgical Treatment for Laryngeal Sarcoidosis

Following review of the literature, I did not feel that given the small number of cases of laryngeal sarcoidosis, that a prospective randomised trial comparing laser treatment of laryngeal disease versus steroid injection could be justified in patients who were acutely airway compromised. Lesional steroid injection would be undertaken in these patients based on previous work on airway Wegener’s granulomatosis (161). However, the use of the laser to excise disease in itself had the potential to cause scarring and stenosis. A new technique of laser usage had to be devised. Although pedunculated lesions encroaching onto the airway could be excised “flush” with normal anatomy, circumferential injury in the laryngeal inlet had to be avoided. It is not possible in each patient to determine the extent to which the supraglottic laryngeal swelling is due to scar tissue or active disease, there had to be a technique of reducing tissue bulk in this part of the larynx. It was decided to reduce interstitial tissue bulk using the CO₂ laser in a “pepper pot” fashion as described below.

5.VI.a Methods

Ethical considerations

The following study is a report of the standard treatment for patients undergoing surgery for laryngeal sarcoid at our institution and therefore the Research Committee deemed ethical approval unnecessary. The records of all patients with upper airway stenosis due to laryngeal sarcoid were prospectively collected on a database of adult patients with laryngotracheal stenosis from which this thesis is derived. All the patients were jointly managed within a multi-disciplinary team and the diagnosis of sarcoidosis was based on internationally agreed clinical, radiological and histopathological criteria (191).
Laryngeal sarcoidosis accounted for 2.8% of the units workload at the time of this study (10 out of 353) which included all surgically treated adult airway cases presenting from 2004 to 2008. There were 9 women and 1 man, and the mean (SD) age at presentation was 37 (17) years with a range from 18-62 years. All patients had dyspnoea on presentation. In addition, two patients were stridulous on presentation and 2 were referred to our unit after having received an emergency tracheostomy elsewhere. Six patients presented with isolated laryngeal sarcoid and the remaining 4 patients had multiple systems involvement. Laryngeal subsite manifestation of disease was restricted to the supraglottis. The most common sites (in descending order) were arytenoids, aryepiglottic folds, epiglottis and false vocal folds. One patient had disease in the inter-arytenoid region. There were no cases of macroscopic sarcoid affecting the glottis.

All patients presented with dyspnoea and dysphonia. Five patients presented with stridor, 7 with dysphagia and 2 with a chronic cough. The table 5.3 lists further information about patient and disease characteristics in this series.

**Surgical technique**

Total intravenous anaesthesia was established as described in section 3.II. The airway was secured during induction using a laryngeal mask and following suspension laryngoscopy (Lindholm pattern Laryngoscope, Storz, Germany) supraglottic jet ventilation was established. Where patients did not sustain adequate oxygen saturation, a subglottic jetting catheter was placed during the surgery. The laryngotracheal complex was visualised using laryngoscopy and a combination of microscope and 4 mm 0° Karl Storz endoscope (Karl Storz, Tuttlingen, Germany) were used to visualise and treat the airway.
Laryngeal lesions were identified and a biopsy routinely performed. Variable doses of between 40-120 mg of Methylprednisolone Acetate at a concentration of 40 mg/ml (Pharmacia Ltd, Kent, England) was administered according to lesion size. A standard microlaryngoscopy injection needle or a modified 27 gauge butterfly was used to deliver multiple injections of steroid starting at the base of the lesion and withdrawing the needle to infiltrate as much of the bulk of the lesion as possible. A good indicator of the end point of intra-lesional injection was complete blanching of the lesion. Immediately after complete infiltration of the lesion, laser photo reduction using the carbon dioxide laser was performed at a continuous setting of 8-10 watts. Any pedunculated lesions encroaching on the airway were excised flush to the position of normal anatomical landmarks. Tissue bulk was reduced by lasering spots through the mucosa to a depth of 4-5 mm separated by about 2 mm, thus creating a “pepper pot” effect (illustration 5.20).

**Illustration 5.20** Endoscopic views of laryngeal sarcoid. Preoperative (left) and three weeks post-surgery (right). Peroperative view (middle) demonstrating appearance after steroid injection and “pepper-pot” laser photoreduction.

*Data analysis*

Patient demographics and the nature and timing of treatments were obtained from patient records and the database. Initial presenting symptoms and Medical Research
Council (MRC) dyspnoea scores were obtained pre-operatively, post-operatively and at last follow-up. The MRC dyspnoea outcome assessment instrument has been shown to correlate well with the degree of luminal obstruction and has been validated for adult patients with laryngotracheal stenosis (150). Sites of laryngeal involvement were recorded intra-operatively. Qualitative assessment was via a prospective recorded endoscopic photograph database. A timeline plot was used to illustrate the number and nature of treatment episodes that each patient received. Data were presented either as mean values with standard deviations or binomial percentages where appropriate. Data was analysed and displayed using SPSS software, version 16 for Windows (SPSS Inc, Chicago, Illinois).

5.VI.b Results

Excluding patients with tracheostomy tubes, the median pre-operative and post-operative MRC dyspnoea grade was 3 (range 2-4) and 1 (1-2) respectively. Dyspnoea grading scores improved significantly post-operatively (table 5.3 (p = <0.05 for the Wilcoxon signed-rank test), and patients with tracheostomy tubes were successfully decannulated 5-7 days after the initial operation. The median number of endoscopic treatments was 2 (range 1-4). Illustration 5.21 demonstrates a detailed treatment line for all the patients. The mean (SD) follow-up time was 24 (18) months with no mortalities and no surgical adverse effects reported during that time. Prior to endoscopic surgery, all patients were treated with high dose corticosteroids (>40 mg daily of prednisolone). Post-operatively, 6 patients had a substantial dose reduction in their daily steroid requirements (to <7 mg daily of Prednisolone). Three patients were able to discontinue their systemic corticosteroid therapy following endoscopic treatment (table 5.3)
Illustration 5.21  Showing timeline for individual patients. The preoperative and last follow-up MRC dyspnoea grade appears at the beginning and end, respectively, of each timeline.

<table>
<thead>
<tr>
<th>Patient No./Sex/</th>
<th>Extralaryngeal Sites</th>
<th>Laryngeal Subsites</th>
<th>Presenting Symptoms</th>
<th>MRC Dyspnoea Grade</th>
<th>Systemic Steroid Requirement</th>
<th>Systemic Steroid Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>At Presentation</td>
<td>Last Follow-up</td>
<td>at Last Follow-up</td>
</tr>
<tr>
<td>Sex/Age, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1/F:54</td>
<td>Lungs</td>
<td>E</td>
<td>D&amp;D, stridor, dysphagia</td>
<td>2 (trach)</td>
<td>2 (dexam)</td>
<td>Stopped, with intermittent courses</td>
</tr>
<tr>
<td>2/F:27</td>
<td>None</td>
<td>A, E</td>
<td>D&amp;D, cough</td>
<td>3</td>
<td>1</td>
<td>Stopped, with intermittent courses</td>
</tr>
<tr>
<td>5/F:33</td>
<td>None</td>
<td>A, E, FC (bilateral)</td>
<td>D&amp;D, stridor, dysphagia</td>
<td>2</td>
<td>2</td>
<td>Unchanged, intermittent courses</td>
</tr>
<tr>
<td>4/F:21</td>
<td>None</td>
<td>A, AEF</td>
<td>D&amp;D, stridor, dysphagia</td>
<td>2</td>
<td>1</td>
<td>Reduced to low-dose maintenance</td>
</tr>
<tr>
<td>5/M:60</td>
<td>None</td>
<td>A, AEF</td>
<td>D&amp;D, stridor</td>
<td>1 (trach)</td>
<td>1 (dexam)</td>
<td>Reduced to low-dose maintenance</td>
</tr>
<tr>
<td>6/F:35</td>
<td>Lungs, skin, nose</td>
<td>A, AEF, IA</td>
<td>D&amp;D, stridor, dysphagia</td>
<td>3</td>
<td>1</td>
<td>Reduced to low-dose maintenance</td>
</tr>
<tr>
<td>7/F:19</td>
<td>None</td>
<td>A, AEF, E, FC (Left)</td>
<td>D&amp;D, dysphagia, cough</td>
<td>3</td>
<td>1</td>
<td>Reduced to low-dose maintenance</td>
</tr>
<tr>
<td>8/F:43</td>
<td>Lungs, skin, nose</td>
<td>A, AEF, E</td>
<td>D&amp;D, dysphagia</td>
<td>3</td>
<td>1</td>
<td>Reduced to low-dose maintenance</td>
</tr>
<tr>
<td>5/F:62</td>
<td>Lungs, skin, nose</td>
<td>A, AEF, E</td>
<td>D&amp;D, dysphagia</td>
<td>4</td>
<td>2</td>
<td>Reduced to low-dose maintenance</td>
</tr>
<tr>
<td>10/F:23</td>
<td>None</td>
<td>A, AEF, E</td>
<td>D&amp;D, dysphagia</td>
<td>3</td>
<td>1</td>
<td>Stopped, with intermittent courses</td>
</tr>
</tbody>
</table>

Abbreviations: A, arytenoids; AEF, aryepiglottic folds; D&D, dyspnea and dyschonia; decan, decannulation performed; E, epiglottis; FC, false cord; G, glottis; IA, interarytenoid; MRC, Medical Research Council; SG, subglottis; trach, tracheostomy in situ.

Table 5.3  Characteristics of patients treated for laryngeal sarcoidosis (199)
5.VI.c Discussion

The results of this study are consistent with the other research in this thesis on the management of inflammatory conditions of the laryngotracheal complex such as Wegener’s granulomatosis and post-intubation laryngotracheal stenosis where intra-lesional steroids and laser surgery administered in the active phase of the disease can prevent progression by altering its natural history (section 5.I and 4.VII). This study has found that in those patients with laryngeal sarcoidosis, control of local disease with minimally invasive surgery allowed systemic treatment to be stopped or reduced with associated benefits in terms of reduced exposure to systemic steroids and steroid side effects. This appears to be the largest study undertaken with respect to the management of laryngeal sarcoidosis by a single operator in a single setting using a single treatment philosophy over a short period during which data was systematically and prospectively collected. This study demonstrates the effectiveness of minimally invasive laser surgery and furthermore suggests that laser treatment can be made even safer by the use of a mucosa sparing “pepper-pot” photo-reduction technique as shown in illustration 5.20. The main limitations of this study are the small sample size, which is an inescapable consequence of the rare disease entity that can only be addressed through a prospective multi-centre study. This study also highlights that combining both intra-lesional injection with steroids and laser ablation for debulking can successfully improve symptoms immediately with minimum morbidity. This technique of “pepper-pot” lasering reduces the bulk of underlying sarcoid tissue and allows rapid healing without compromising functional anatomy (illustration 5.20, right). More importantly, this technique reduces the need for systemic steroid administration in most patients.
Chapter 6

6.1 Screening for Laryngotracheal Stenosis

It has already been shown in section 4.III that up to 4 out of 5 cases of post ICU laryngotracheal stenosis are missed. Flow volume loop studies (illustration 1.3) are a good screening tool for upper airway obstruction and also help identify its site and nature. Access to these tests is easy within hospital departments or specialist clinics, but not in primary healthcare clinics. An alternative form of community screening for upper airway obstruction is the Empey index. Empey identified the relationship between peak expiratory flow rate (PEFR) and forced expiratory volume in 1 second (FEV1) (131). The Empey index allows airway stenosis diagnosis through standard spirometry. A modification of the Empey Index is the ratio of FEV1 over PEFR x 100, which provides an expiratory disproportion index. The sensitivity and specificity of this ratio was formally validated using a database at Imperial College London of 10,048 patients undergoing respiratory lung function testing. The diagnosis in all of these patients was known and 200 of these patients had laryngotracheal stenosis. The sensitivity was calculated at 95.2% and the specificity at 94.6% (illustration 6.1). If the expiratory disproportion index (EDI) is greater than 50, then a diagnosis of laryngotracheal stenosis can be excluded. If the index is less than 50, then a patient should be referred for flow volume loop testing. This makes the EDI a very suitable screening tool.
Illustration 6.1 Graph to show sensitivity and specificity of the expiratory disproportion index (EDI). Area under the curve is 0.98. (FEV$_1$= forced expiratory volume in one second, FVC=forced vital capacity, PEFR=peak expiratory flow rate)

A screening test would have to be applied to an ICU patient at the time of discharge from hospital and again at 3 months. This would identify patients with a compromised airway before they leave hospital and also those patients who have a circumferential airway injury that granulates and narrows later, leaving a window to treat endoscopically before significant scaring and contracture takes place (section 4.VII).

The UK National Screening Committee (NSC) define screening as:

“Screening is a process of identifying apparently healthy people who may be at increased risk of a disease or condition. They can then be offered information, further tests and appropriate treatment to reduce their risk and/or any complications arising from the disease or condition”
Wilson and Jungner criteria for screening (200)

- Knowledge of disease:
  - The condition should be important.
  - There must be a recognisable latent or early symptomatic stage.
  - Natural course of condition, including development from latent to declared disease, should be adequately understood.

- Knowledge of test:
  - Suitable test or examination.
  - Test acceptable to population.
  - Case finding should be continuous (not just a "once and for all" project).

- Treatment for disease:
  - Accepted treatment for patients with recognised disease.
  - Facilities for diagnosis and treatment available.
  - Agreed policy concerning whom to treat as patients.

- Cost considerations:
  - Costs of case finding (including diagnosis and treatment of patients diagnosed) economically balanced in relation to possible expenditures on medical care as a whole.

Post-ICU laryngotracheal stenosis, as a condition, meets most of these criteria, except for health economics. Only small numbers of patients develop this condition (130), but the cost of diagnosis would also be small. Individual hospitals could set up screening, however, ICU patients often live at some distance from the hospital in which they were ventilated and it is likely that attendance at follow up clinics (at 3 months) would be poor. Primary health care practitioners could be recruited to review these patients at 3 months with coordination and data collection from a hospital department. These are issues that need to be explored further in future projects.
6.II Proposed Assessment of Patients with Laryngotracheal Airway Compromise

Illustration 6.2 This thesis has researched the anatomy and physiology of airway stenosis, however, future research also needs to be directed towards validating symptom assessment tools and quality of life.

This thesis has looked, in depth, at the anatomy and to some degree the physiology of laryngotracheal stenosis (illustration 6.2). It is possible to accurately calculate the cross sectional area of the airway at the site of a stenosis (section 4.VI) but the most important outcome is the improvement in the patient’s symptoms and also the impact on his or her quality of life. For the purpose of documenting the grade of a stenosis, the Myer-Cotton system will continue to be used.

A simple system for documenting the functional outcome of adult laryngotracheal stenosis is proposed, consisting of four domains of airway (A), providing a description of the status of the airway, dyspnoea (D) which is an adaptation of the Medical Research Council (MRC) dyspnoea grading system, voice (V) and swallowing (S). The last three components are scored by the patient while airway status is documented by
the clinician. All parts of the system have a 1–5 ordinal scale. The airway (A) domain is reported by the surgeon and is as follows:

Airway status (A)

1. No airway prosthesis
2. Intraluminal airway prosthesis (stent)
3. Tracheostomy or T-tube dependent, patient voices
4. Tracheostomy-dependent, patient does not voice
5. Death as a result of a direct complication of airway disease

The dyspnoea (D), voice (V) and swallowing (S) domains are scored by the patient before and after treatment and are shown in illustration 6.3. Outcomes are documented as subscripts, for example A₁-D₂-V₁-S₁ and should not be combined to form a single number. This information can be tabulated or plotted to provide a visual temporal treatment map, charting patient progress through treatment. It can also yield time-dependent variables, e.g. time to the attainment of a prosthesis-free (A₁) or tracheostomy-free (A₁ or A₂) airway from the outset of therapy, for actuarial analysis.

The proposed system provides a simple patient-centred method of assessing the outcome of patients with laryngotracheal stenosis throughout treatment through the use of simple-to-use ordinal scales. The MRC scale which forms the ‘D’ component of the system has been validated for this purpose and is already widely used for evaluating dyspnoea (150, 201). The one difficulty with this MRC dyspnoea scale is its application to patients who have tracheostomies. The ‘A’, ‘V’ and ‘S’ components have been derived through studying other voice and swallowing scales and in consultation with laryngologists and speech and language therapists and still require validation. They are based on the experience of evaluating the range of functional impairments that were
observed in 210 patients with laryngotracheal stenosis who were treated over the first 3 years (level IV evidence) of this study.

Illustration 6.3 The proposed symptom scoring system for the Airway Reconstruction Unit. The Dyspnoea component (top) is based on the Medical Research Council dyspnoea scale and has already been validated for adult airway stenosis (150, 201).
For a more detailed assessment of airway, voice and swallowing symptoms and morbidity the Clinical COPD Questionnaire (CCQ) (202), the Voice Handicap Index-10 (VHI-10) (203) and the Eating Assessment Tool (EAT-10) (204) can be used. These are all validated, 10-item, patient-administered, symptom severity instruments. The Short Form 36 health survey questionnaire (SF-36) can be used to assess changes in patient quality of life in response to airway treatment (205). It is proposed to administer the SF-36 at least six months after the conclusion of airway therapy. It is hoped that this proposed (ADVS scoring) system could lead to a more uniform reporting of airway reconstruction outcomes for easier comparison and combination of treatment results for audit, research and meta-analysis purposes. Table 6.1 lists assessment and outcome measures for all future patients referred to the Airway Reconstruction Unit.

<table>
<thead>
<tr>
<th>Level of Assessment</th>
<th>Outcome Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anatomy</td>
<td>• Myer-Cotton scale for cross-section narrowing</td>
</tr>
<tr>
<td></td>
<td>• Cranio-caudal extent (vertical height) of the lesion</td>
</tr>
<tr>
<td></td>
<td>• Distance from glottis</td>
</tr>
<tr>
<td>Flow Physiology</td>
<td>• Spirometry</td>
</tr>
<tr>
<td></td>
<td>• Flow-volume loop</td>
</tr>
<tr>
<td>Exercise Physiology</td>
<td>• Incremental shuttle walk test</td>
</tr>
<tr>
<td></td>
<td>• Cardiopulmonary exercise testing (CPET)</td>
</tr>
<tr>
<td>Airway Status</td>
<td>• A domain of ADVS</td>
</tr>
<tr>
<td>Symptoms – Dyspnoea and effort intolerance</td>
<td>• D domain of ADVS</td>
</tr>
<tr>
<td></td>
<td>• Clinical COPD Questionnaire (CCQ)</td>
</tr>
<tr>
<td>Symptoms – Voice</td>
<td>• V domain of ADVS</td>
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<td>• VHI-10</td>
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<td>Symptoms – Swallowing</td>
<td>• S domain of ADVS</td>
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<td>• EAT-10 Instrument</td>
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<tr>
<td>Quality of Life</td>
<td>• Short Form 36 Health Survey Questionnaire (SF-36)</td>
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Chapter 7

The Future of Laryngotracheal Stenosis Management

This thesis has shown that it is safe to paralyse and ventilate a patient even with severe laryngotracheal stenosis. These safe anaesthetic techniques have made the exploration of adult benign laryngotracheal stenosis by minimally invasive endoscopic surgery possible. The research in this thesis has:

- Shown that 72% of new cases of post-ventilation airway stenosis can be managed endoscopically, without the need for open surgical procedures and tracheostomies.
- Demonstrated successful surgical approaches to the management of the airway in hitherto difficult to manage inflammatory conditions such as Wegener’s granulomatosis, idiopathic subglottic stenosis and sarcoidosis.
- Pioneered a new approach for managing patients with long length tracheal stenosis.
- Evaluated the possible incidence of this condition and promoted a better understanding of the aetiologies and prevention.

Over the course of this research, following the presentation of some of its findings at national anaesthetic, intensive care, ENT and speech science meetings, there have been changes in medical practice. Colleagues now make balanced decisions in respect of sizing of ventilation tubes rather than ‘largest is best’ and intensivists are moving towards earlier tracheostomies on ICUs. There appears to be a better understanding of the need for regular monitoring of ventilation tube cuff pressures and future designs of tubes will not allow the upper limit of cuff pressure to be exceeded (206).
This thesis has explored the limits of endoscopic techniques for managing laryngotracheal stenosis. However, any piece of research throws up more questions and ideas for future research.

One area of active research and development is in the field of tracheobronchial stents. Stents would be the simplest solution to the immediate management of airway compromise. The ideal stent would be easy to insert and remove, not migrate, cause no airway injury and experience no bio-fouling or risk of obstruction. Unfortunately there is no such stent. The next generation of stents will be reabsorbable (illustration 7.1), or bioengineered in other ways, so that they do not need to be removed. In addition the functional life of the stent could be pre-determined. One concern is that they could degrade non-uniformly, fracture and compromise the airway.

Illustration 7.1 Prototype of a biodegradable airway stent (Qualimed, Hamburg, Germany)

The repair of long lengths of airway defects remains a major problem for clinicians. Up to 6 cm of trachea can be resected (7) in the adult with primary anastomosis. The repair of tracheas beyond this length or where there has been failed previous resective
surgery has proven difficult. Tissue engineering and tracheal allotransplantation are two techniques that are being explored and hold promise for the future. The first clinical transplantation of a tissue engineered airway (207) was reported in 2008. The technique used a decellularised donor tracheal scaffold which was recolonised with the recipient's own cells in a novel bioreactor system. The technique used mesenchymal stem cell derived chondrocytes and the epithelium of the trachea was replaced by culturing samples of the patient's own respiratory epithelium in the laboratory. An area of damaged trachea and adjacent left main bronchus was replaced in a 30-year-old woman who had sustained damage to her airway from a tuberculous infection. The transplant was successful and the patient required no immunosuppressive therapy. The downside of this technique is that the graft requires restoration of the blood supply from adjacent tissues. There is concern that replacing longer lengths of airway runs the risk of some degree of avascular necrosis, even though the metabolic demands of chondrocytes are very low.

Another technique that has been reported (208) uses tracheal allotransplantation without the need for long-term immunosuppressive therapy. In this technique, a donor's trachea was wrapped in the subcutaneous tissue of the recipient's forearm in an orientation to allow revascularisation. Immunosuppressives were initially started and continued until 229 days after completion of airway surgery. During this time, the posterior membranous sheath of the trachea necrosed and was replaced with buccal mucosa from the recipient. At 4 months, the tracheal allograft was found to be fully mucosal lined and with intact cartilaginous rings. This revascularised allograft was dissected with the radial artery and two radial veins and transported as a free flap to the neck where it was used for reconstruction. The allograft was used to repair a 4.5 cm defect in the trachea of a 55-year-old woman. The procedure was reported in January
2010 and there has been no evidence of rejection, despite stopping immunosuppressants. The donor trachea histologically had been surrounded by recipient blood vessels and the mucosal epithelial lining originated from the recipient.

The alternative approach to the two techniques mentioned above is direct organ (laryngeal) transplant with immunosuppresssants. The first such procedure was performed in Cleveland, Ohio in 1998 (209). However, the patient still retains a tracheostomy tube. A more recent composite tissue transplant, performed in California (210) in October 2010, replaced the larynx, thyroid gland and an adjacent length of trachea. This transplant included implantation of the posterior cricoarytenoid muscles with a division of the phrenic nerve (211). It is hoped that abductor motor function to the larynx will be restored to allow decannulation of the patient. A group at the San Vicente de Paul University Hospital in Medellin, Colombia, led by Dr Luis Fernando Tintinago, have claimed several laryngeal and laryngotracheal transplants since the first procedure by the Cleveland Clinic. Unfortunately there are no references in the medical literature of either the short term or long term results in these patients.

Advances in biotechnology may provide the solution to difficult problems such as long length tracheal replacement and tracheomalacia. Biocompatible and biointegratable scaffolds that mimic the mechanical properties of tracheal cartilage could be used to provide shape to muscle flaps for use as tracheal replacements. Biointegratable stents could be a simple solution to airway stenosis. However, the research into these biomaterials is still in its infancy.


34. Winslow J. Reports of cases illustrating our progress in the surgical management of chronic stenosis of the larynx and trachea. Trans Am Laryngol Assoc. 1909;31:177-90.


