

TITLE: Subglottic Stenosis

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Introduction

Subglottic stenosis (SGS) is a congenital or acquired narrowing of the subglottic airway. In the early twentieth century SGS was rare. Most cases occurred in adults. In the 1960s the incidence of acquired SGS began to dramatically increase in the neonatal population. This resulted from the increased survival of low-birth-weight infants and the increased use of intubation in this population. In addition, long term intubation became accepted as an alternative to tracheotomy. As a consequence the management of this condition underwent a revolution in the 1970s and reconstructive surgery was directed towards this population.

Management of laryngotracheal stenosis (LTS) is one of the most challenging problems for the head and neck surgeon to be faced with. Most of these patients are referred to and are treated at large academic centers by physicians specialty trained in this area. Particularly in the pediatric population, a multidisciplinary approach is taken to manage this complex problem.

Anatomy

The subglottis is defined as the area extending from the lower surface of the true vocal cords to the lower surface of the cricoid cartilage. In adults this corresponds to approximately 10 mm inferior to the anterior commissure and 5 mm inferior to the posterior commissure.

The infant larynx differs significantly in size and position when compared to the adult larynx. At birth, the infant larynx is approximately one third the size of the adult larynx, however, the infant larynx is proportionately larger than the adult larynx compared with the remainder of the tracheobronchial system. The vocal process of the arytenoid takes up half the length of the vocal cord in the infant larynx, while it only takes up about $\frac{1}{4}$ of the length of the vocal cord in the adult. The narrowest portion of the airway in the older child and adult is the glottic aperture, while the narrowest part of the airway in the infant is the subglottis. The subglottis in infants measures approximately 4.5 by 7mm. A diameter of 4.0 mm is considered the lower limit of normal in a full term infant and 3.5 mm in a premature infant. One millimeter of edema circumferentially in the subglottis reduces the cross-sectional area by 60%.

The infant larynx is positioned higher in the neck than the adult larynx. The superior border of the larynx of the infant is located at about the level of the first cervical vertebrae with the cricoid positioned at about the fourth cervical vertebrae. In comparison, the adult cricoid rests at about the level of the sixth cervical vertebrae. The structures of the infant larynx are more pliable and less fibrous making the infant airway more susceptible to narrowing from edema and less easily palpable.

Embryology

The respiratory system is an outgrowth of the primitive pharynx. The development of the lower respiratory system begins at 26 days after conception as the laryngotracheal groove at the ventral aspect of the foregut forms.

The laryngotracheal diverticulum becomes separated from the foregut by the tracheoesophageal folds which fuse to become the tracheoesophageal septum. This septum divides the foregut into a ventral laryngotracheal tube and a dorsal esophagus. Failure of the tracheoesophageal folds to fuse during the fourth and fifth weeks can lead to a tracheoesophageal fistula.

The larynx develops from the fourth and fifth branchial arches. The laryngotracheal opening lies between these two arches. This primitive laryngeal aditus is altered to become a T-shaped opening by the growth of three tissue masses. One is the hypobranchial eminence. This mesodermal structure eventually becomes the epiglottis. The second and third growths are two arytenoid masses. As these masses grow between the fifth and seventh weeks, the laryngeal lumen is obliterated. Recanalization occurs by the tenth week. Failure to recanalize may result in atresia, stenosis, or web formation in the larynx. The arytenoid masses are separated by an interarytenoid notch which eventually becomes obliterated. If obliteration does not occur, a posterior laryngeal cleft can result leading to severe aspiration in the newborn

Etiology of SGS

I. *Congenital SGS*

A. Membranous

1. increased fibrous connective tissue
2. hyperplastic submucous glands
3. granulation tissue

B. Cartilagenous

1. cricoid cartilage deformity
 - a. small cricoid
 - b. elliptical cricoid
 - c. large anterior lamina
 - d. large posterior lamina
 - e. generalized thickening
 - f. submucous cleft
2. trapped first tracheal ring

II. *Acquired SGS*

A. Intubation

B. Laryngeal trauma

a. previous airway surgery

- high tracheostomy
- cricothyroidotomy
- prior surgery for respiratory papillomatosis
- prior laser surgery for SGS

b. accidental

1. inhalational (thermal or caustic)
2. trauma (blunt or penetrating)

C. Autoimmune

D. Infection

E. Gastroesophageal reflux (GER)

F. Inflammatory diseases

- a. Anti-neutrophil Cytoplasmic Autoantibodies (C-ANCA)
- b. sarcoidosis
- c. Systemic lupus erythematosus

G. Neoplasms

III. *Idiopathic SGS*

Congenital SGS

SGS may be classified as either acquired or congenital. Although congenital subglottic stenosis is uncommon, accounting for 5% of all cases, it is the third most common congenital airway problem (after laryngomalacia and vocal cord paralysis). Congenital SGS is thought to be secondary to failure of the laryngeal lumen to recanalize properly during embryogenesis. SGS is considered congenital if there is no history of endotracheal intubation or other forms of laryngeal trauma.

Congenital SGS is divided histopathologically into membranous and cartilaginous types. Membranous SGS is usually circumferential and consists of fibrous soft-tissue thickening caused by increased fibrous connective tissue or hyperplastic submucous glands. It may involve the vocal folds as well. The cartilaginous type usually results from a thickened or deformed cricoid cartilage that forms an anterior subglottic shelf that extends posteriorly allowing only a small posterior opening. Other malformations can occur such as an elliptical cricoid leaving a slit-like opening or a trapped first tracheal ring. Membranous SGS is usually less severe than the cartilaginous type.

Congenital SGS is often associated with other congenital malformations. A thorough search for associated anomalies is necessary.

Acquired SGS

Ninety-five percent of cases of SGS are acquired and may be due to a number of causes. The most common cause of acquired SGS (90%) results from endotracheal tube intubation and

the associated inflammatory-type response (see below - pathology). The most important risk factor for the development of laryngotracheal stenosis is the duration of intubation. Other factors include size of the endotracheal tube, movement of the endotracheal tube, traumatic intubation, number of re-intubations, and presence of an infection while intubated.

Other causes of acquired SGS include external and post-surgical trauma, and systemic factors. Laryngotracheal injuries from blunt trauma may result in fractures, dislocations, mucosal lacerations, or cricotracheal separation. Wound healing in these instances occurs as described below with development of granulation tissue and then deposition of fibrous tissue and subsequent scarring which may result in clinically apparent stenosis. Caustic and thermal injuries also cause mucosal injury, ischemia and subsequent remodeling of tissues and may result in LTS.

Post-surgical trauma includes previous tracheotomy (particularly high tracheotomy), cricothyroidotomy, and surgical treatment of airway neoplasms (most commonly recurrent respiratory papillomas and subglottic hemangiomas). The incidence of subglottic stenosis has been reported to be as high as 20% in patient undergoing laser excision of subglottic hemangiomas (Sie, 1994).

Gastroesophageal reflux (GER) has been proposed as a medical condition which may exacerbate the pathogenesis of LTS, may cause re-stenosis after repair, and may be the sole cause of stenosis in patients with no previous history of endotracheal intubation or laryngotracheal trauma. Bain et al. (1983) was the first to suggest that GER may cause SGS. He identified GER in two patients with SGS. Since then animal studies have been performed which have shown that superficial mucosal injury in the trachea and subglottis treated with acid and acid with pepsin result in non healing and inflammation (Koufman, 1991) and may lead to SGS (Little, 1985). Little's study, however, had only one subject in each group and therefore significant results were not obtained. Other studies have shown a high rate of GER in patients with SGS. Walner et al. (1998) retrospectively looked at 74 pediatric patients with SGS and found that they had a three times greater incidence of GER than the general pediatric population. They were unable to draw any conclusions about the relationship between GER and SGS because of the diversity of their patient group. Koufman (1991) found that 72% of 32 patients (11 pediatric and 21 adult) with laryngeal and tracheal stenosis had abnormal lower pH probe results. 67% of those patients had abnormal pharyngeal reflux defined as a single episode of a pH less than 4.0.

The current criteria for diagnosing lower esophageal acid reflux is well documented (a pH of less than 4.0 for more than 10% of the time), however, despite the fact that pH-metry is considered the gold standard for LPR testing, there is no consensus with respect to the number of pH sensors, their location, or the interpretation of results in adults or children (Postma, 2002). Postma suggests four criteria that must be met for an event to be defined as a pharyngeal reflux episode:

- (1) a decrease in the pH level to less than 4.0 (may be increased to 5.0)
- (2) a decrease in the pharyngeal pH level immediately following distal esophageal acid exposure

- (3) no decrease in the pH level during eating or swallowing
- (4) a rapid and sharp decrease in the proximal sensor pH level rather than a gradual one

Pepsin is functional at a pH of 5.0. The laryngopharynx is much more susceptible to the inflammatory effects of acid and pepsin because it lacks the protective mechanisms that the stomach and lower esophagus have. As was shown in Koufman's study (1991), nonhealing ulcers and inflammation resulted in areas of damage to the subglottis as a result of acid and pepsin administration. It is logical to think that exposure to a single episode of LPR in patients who have existing laryngeal or subglottic injury may have significant effects.

Despite the lack of definitive evidence for a cause and effect relationship between GER and SGS, Cotton and O'Connor state that a "reflux workup" is now considered essential to the success of laryngotracheal reconstruction (LTR) (1995). Empirical treatment of GER has been recommended for all patients undergoing LTR (Burton, 1997) even if they do not have symptoms of GER or LPR or documented reflux by pH probe.

Idiopathic subglottic stenosis

Pathology

The pathogenesis of acquired subglottic stenosis is not completely understood but there are several theories that have been proposed. The most accepted theory proposes that subglottic stenosis results from wound healing in the areas of the airway which have undergone compression by an endotracheal tube or the cuff of a tube resulting in necrosis of the underlying mucosa and cartilage. This necrosis is a consequence of ischemia resulting from pressure from the tube or cuff exceeding the capillary pressure of the thin mucosa of the airway. Consequently, the normal mucociliary flow is disrupted which leads to infection in the perichondrium and then extends into cartilage. The cartilage may weaken and collapse, manifesting as tracheomalacia. Healing of the involved segment proceeds by secondary intention. This involves three temporally overlapping stages: an inflammatory stage, a proliferative stage, and a phase of contraction and remodeling. The inflammatory stage begins with the initial injury. It involves active vascular retraction and constriction followed by vasodilation mediated by prostaglandins. Platelets adhere to the exposed collagen forming a hemostatic plug. There are numerous active mediators that are released including adenosine diphosphate, platelet derived growth factor, transforming growth factor, clotting factors and vasoactive substances such as 5-hydroxytryptamine, thromboxane and histamine. The coagulation cascade is activated which lays down the fibrin network. Platelets release proteolytic enzymes that activate the complement system. The complement cascade contributes to bacterial killing and wound debridement and supplies chemotactic signals to effect cells.

Polymorphonuclear lymphocytes (PMNs) enter the wound at about 6 hrs post-injury. They reach their greatest concentration at 24-48hrs post-injury and disappear within 72hrs. The PMNs phagocytize debris and bacteria from the wound and release proteases that lyse devitalized tissue.

T and B cells enter the wound after the PMNs and are most numerous at 6 days after injury. T cells secrete regulatory lymphokines. Helper T-cells are necessary for wound healing. Suppressor T cells down-regulate healing.

Macrophages enter the wound within 48-96 hrs after injury. Large concentrations of macrophages are found in the wound at 3-5 days and can persist for several weeks. Macrophages are the only cells that can function in area of low oxygen tension at the wound center. These cells release many different enzymes but they primarily direct the proliferative and synthetic activity in the wound. This is achieved by interleukin-1 and tumor necrosis factor – alpha. Studies have shown that macrophages are essential to wound healing but PMNs can be absent without impairing the process.

Growth factors secreted by cells in the wound are major regulators of healing. Growth factors are chemotactic, mitogenic, and sometimes have an inhibitory effect on cells involved with wound repair. All growth factors interact with cellular receptors to modify the cells activities. IL-1 directly stimulates fibroblast activity including proliferation and collagen synthesis. IL-2 is produced by helper T cells. It has an indirect effect on wound healing by stimulating lymphocyte and macrophage activity.

Structural components essential to successful wound healing include fibronectin, collagens, glycoproteins and glycosaminoglycans. Fibronectin is secreted by fibroblasts and endothelial cells. It cross-links fibrin and glycosaminoglycans. Several types of collagen are found in the healing wound. The production of collagen by fibroblasts is a complex process. Hydroxylation requires Vitamin B, iron and Vitamin C. Glycoproteins and glycosaminoglycans function in cell-matrix interactions and in controlling wound resilience.

The proliferative phase lasts 10-14 days. It begins with re-epithelization. This process of resurfacing the defect begins at about 12 hrs after injury. The epithelial cells 1-2 mm from the wound edge undergo phenotypic changes. The cells replication rate increase 17 fold.

The next part of the proliferative phase is neovascularization in which blood vessel regeneration begins with the migration of endothelial cells. Macrophages secrete angiogenic factors in response to high lactate levels and low wound oxygen levels. The result of endothelial migration is capillary bud formation. Certain conditions such as diabetes mellitus or radiation therapy impede neovascularization.

Collagen deposition begins when fibroblasts enter the wound at 48-72 hrs. post-injury. The collection of fibroblasts, inflammatory cells and capillary buds is referred to as granulation tissue. Granulation tissue persists until epithelial resurfacing is complete.

The final phase of wound healing is the wound contraction and remodeling phase. Wound contraction begins at 6-7 days after injury and is maximal for 10 days. Wound contraction eventually decreases the defect by 40-60%. Skin flaps and grafts can reduce the amount of wound contraction by 50-70%. Myofibroblasts, a modified fibroblast, provides the contractile force required for contraction. They have many characteristics of smooth muscle cells and are distributed throughout the wound. Wound collagen levels reach maximum at 2-3

weeks after injury, however, tissue strength is still only 5-10% of that of unwounded skin. The wound's neo-matrix is gradually replaced over 6-12 months by stronger interwoven cartilage as Type I collagen displaces Type III cartilage. Remodeling results in a scar with as much as 80% of the involved tissue's original tensile strength.

Diagnosis

There is a wide range of presentation of subglottic stenosis with similarities and differences in the pediatric age group compared to adults. If the stenosis is severe and congenital, the patient will present with airway distress at birth. More commonly, the pediatric patient with SGS will present as a neonate in the intensive care unit who has failed extubation usually multiple times. Occasionally patients will present in clinic with a tracheotomy and the report of some airway obstruction. Infants with mild SGS may present with recurrent croup-like illnesses and poor feeding. Adults usually present with a history of prior intubation with symptoms of progressive shortness of breath and noising breathing.

In the infant or child, a thorough history should be obtained which includes: history of prematurity and associated medical problems and intubation records. A history of noisy breathing and difficulty feeding should lead to suspicion of airway problems. Growth curves should be reviewed and followed to determine if the child has failure to thrive. Particularly the relationship of airway symptoms to feeding is important to elicit in the history. Important characteristics of the intubation include the date of first intubation, duration, size of the endotracheal tube, number of intubations, and if any intubations were traumatic.

In adults, intubation records should be reviewed as well. A complete medical history is taken with particular attention to the patient's cardiopulmonary status, history of diabetes, and any steroid use. History of reflux symptoms should be elicited which may prompt subsequent testing.

Differential diagnosis of laryngotracheal stenosis

I. Congenital

- A. Tracheomalacia
- B. Laryngomalacia
- C. Vocal cord paralysis
- D. Laryngeal cleft
- E. Congenital cysts
- D. External compression from congenital abnormality or lesion
 - 1. Vascular compression
 - a. innominate artery compression (most common)
 - b. right-sided aortic arch with persistent ductus arteriosus
 - c. aberrant left pulmonary artery
 - 2. Mass
 - a. teratoma
 - b. cystic hygroma

c. hemangioma

II. Infectious/inflammatory

- A. Viral laryngotracheobronchitis (croup)
- B. Retropharyngeal abscess
- C. GER
- D. Tracheitis

III. Neoplastic

- A. Subglottic hemangioma
- B. Recurrent respiratory papillomatosis

IV. Traumatic

- External compression
- Foreign body

A complete head and neck exam should be performed on all patients. It begins with observing the patient for any apparent airway symptoms which may include irritability and restlessness in an infant or dyspnea, tachypnea, cyanosis, and stridor in an infant, child, or adult. The classic stridor of subglottic stenosis is biphasic. Voice quality in a child or adult and crying quality in an infant should be evaluated for weakness, hoarseness, breathiness, or complete absence. Flexible fiberoptic nasopharyngolaryngoscopy may be performed at the bedside or in clinic on infants, adults, and some cooperative children if the patient is stable. Vocal cord immobility, reflux changes, immediate subglottic abnormalities, supraglottic sensation, and other glottic and supraglottic abnormalities may be detected.

The gold standard for diagnosis of any laryngotracheal abnormalities is direct laryngoscopy and tracheobronchoscopy under general anesthesia. This should be performed in the operating room with an experienced anesthesiologist. It is important to delay endoscopy for at least two weeks following an acute episode of croup to minimize the risk of postoperative airway obstruction. The potential need for tracheotomy should be discussed with the patient (adults) or patient's family (children) prior to endoscopy. A rigid bronchoscope or a rod lens telescope may be used to assess the airway. The important things to document during endoscopy are as follows: (1) the outer diameter of the largest bronchoscope or endotracheal tube that can be passed through the stenotic segment, (2) the location/subsites (glottis, subglottis, trachea) and length of the stenosis, (3) other separate sites of stenosis, (4) other airway anomalies in infants (clefts, webs, cricoarytenoid joint fixation, neoplasms, etc.), and (5) reflux changes. After removing the sizing endotracheal tube or bronchoscope it is important to observe the stenotic segment for edema which may result in the need for tracheostomy

There are two widely excepted staging systems for classifying subglottic stenosis: Myer-Cotton grading system and the McCaffrey system. Other systems have been described as well, however, none are universally applicable or useful. At this time, no staging system exists that allows comparison of patients treated at different institutions.

The Myer-Cotton staging system is useful for mature, firm, circumferential stenosis confined to the subglottis. It describes the stenosis based on the percent relative reduction in cross-sectional area of the subglottis which is determined by differing sized endotracheal tubes.

Four grades of stenosis are described with this system: **grade I** lesions have less than 50% obstruction, **grade II** lesions have 51% to 70% obstruction, **grade III** lesions have 71% to 99% obstruction, and **grade IV** lesions have no detectable lumen or complete stenosis.

The McCaffrey system classifies laryngotracheal stenosis based on the subsites involved and the length of the stenosis. Four stages are described: **stage I** lesions are confined to the subglottis or trachea and are less than 1cm long, **stage II** lesions are isolated to the subglottis and are greater than 1 cm long, **stage III** are subglottic/tracheal lesions not involving the glottis, and **stage IV** lesions involve the glottis.

Another classification system has been proposed by Lano et al. at Vanderbilt University (1998) for adults. Their system is based on the number of subsites (including the glottis, subglottis and trachea) of involvement: **stage I** lesions involve one subsite, **stage II** involves two subsites and **stage III** involves all three subsites. The authors proposed this classification to better predict patient prognosis (successful decannulation) after reviewing their experience over ten years.

Radiographic tests that may be ordered to evaluate the patient with upper airway problems include plain films, barium esophagram, airway fluoroscopy, magnetic resonance imaging (MRI), and computed tomography (CT). Plain films are more useful in the pediatric population and may be used to diagnose foreign bodies, narrowing of the subglottis and trachea in croup, epiglottitis, retropharyngeal abscess, subglottic cysts, and subglottic hemangioma. They are cheap, easily accessible, and can be done without sedation. If adequate inspiratory and expiratory films cannot be obtained, fluoroscopy may be used. Airway fluoroscopy is dynamic and can show areas of malacia. Barium swallow studies are not useful specifically in the diagnosis of SGS but are indicated when assessing feeding problems in infants and can be used to rule out other anatomic abnormalities such as esophageal compression from vascular anomalies, esophageal masses and may show evidence of reflux. MRI is useful in diagnosing soft tissue masses. CT scanning with thin cuts (1.5) through a stenotic segment of the trachea and/or subglottis can help determine the length of resection that will be needed. CT has not been shown to be useful in diagnosing or characterizing SGS in the pediatric age group but is useful in adults as an adjunct to endoscopy. MRI and CT usually require sedation or general anesthesia in young children and infants.

Management

As previously mentioned, all patients must undergo a complete history, physical examination, flexible nasopharyngolaryngoscopy and +/- radiologic evaluation to make the diagnosis. This is followed by rigid endoscopy to evaluate the larynx, trachea, bronchi, and esophagus and to confirm the diagnosis and characterize the stenotic lesion. The management of the lesion will then depend on its diameter, length, location and the status of the patient.

Medical

Prior to airway reconstruction, it is recommended that all pediatric patients be evaluated for GER with a dual 24hr pH probe (Cotton and Walner, 1999). This is performed with the

consultation of a pediatric gastroenterologist. Different sized pH probes are used depending on the age of the child. Position of the probe should be confirmed with fluoroscopy. In unusual cases the refluxate may be basic in pH. In these patients, diagnosis is made with a nuclear medicine reflux scan. Patients diagnosed with GER should be treated accordingly. Adults are not always subjected to an extensive workup for GER unless symptoms are present. Empiric peri-operative treatment with anti-reflux medications has been recommended by some authors and is practiced by many.

In adults it is important to evaluate the patients general medical condition prior to performing any reconstructive procedures. Many of these patients underwent long periods of intubation secondary to severe medical problems. The decision to perform surgery should be made in consultation with the patient's primary or specialty physician (pulmonary, cardiology, nephrology, etc.). Relative contraindications to LTR in adults are renal failure, diabetes, severe coronary artery disease, severe COPD or restrictive lung disease, obstructive sleep apnea, and systemic steroid use. It is important to consider each patient's case on an individual basis and make the decision to proceed with surgery based on sound judgment.

Observation

Patients (children and adults) with Cotton-Myer grade I and mild grad II subglottic stenosis may sometimes be managed with close observation (Walner and Cotton,1999). In adults, this will depend on the reliability of the patient for close follow-up and their symptomatology. Children may be watched closely if they have only occasional mild stridor without retractions or feeding difficulties and have not required hospitalization for episodes of croup or other airway-related illnesses. Walner and Cotton recommend repeat endoscopy every three to six months to measure the diameter of the airway to ensure that it is enlarging as the child grows. As stated previously, the child should be followed with growth curves by a pediatrician and/or neonatologist.

Surgical treatment options for subglottic stenosis:

- I. Tracheostomy
- II. Endoscopic
 - A. Dilation
 - B. Endoscopic laser excision
- III. Open procedure
 - A. Expansion procedure (one-stage or with stent placement)
 - 1. Anterior cricoid split with or without cartilage graft*
 - 2. Posterior cricoid split with or without cartilage graft*
 - 3. Anterior and posterior cricoid split with cartilage graft
 - 4. Four quadrant LTR
 - B. Segmental resection (cricotracheal resection - CTR)
 - 1. Primary CTR
 - 2. Salvage CTR
 - 3. Extended CTR – CTR with and expansion procedure, arytenoid lateralization, or

arytenoidectomy

* Note: some authors classify laryngotracheoplasty as a cricoid split procedures without cartilage grafting and laryngotracheal reconstruction as a procedure with grafting or segmental resection

Tracheostomy

Tracheostomy is usually required as the initial step, particularly in the pediatric age group with acquired SGS, in the surgical management of patients with SGS. Infants with congenital SGS may forego tracheostomy as they are often treated with primary reconstruction or are observed. Tracheostomy is often not performed in infants with congenital SGS. These patients are either treated conservatively or undergo primary reconstruction and are left intubated for approximately one week. Infants with SGS are often premature or of low birth weight. A tracheostomy allows these patients time to grow before definitive surgical treatment is performed. Cotton and Walner recommend waiting until the infant is at least 10 kilograms before performing airway reconstruction. Delayed reconstruction will also allow for optimization of pulmonary function in patients with bronchopulmonary dysplasia. It is important to note that the mortality rate of laryngotracheal stenosis is primarily due to complications from the tracheostomy of which plugging and accidental decannulation are the most common. The reported mortality rate of tracheostomy in infants and children is 2% to 5% per child per year (Lesperance, 1996).

Tracheostomy may be required in adults if the patient presents in airway distress. More commonly, adults with acquired LTS have progressive symptoms over time and present early enough to allow time to plan for definitive airway reconstruction as the initial treatment with or without tracheostomy.

Once the decision to perform airway reconstruction has been decided upon, the surgeon must choose the most appropriate procedure to perform. The site, grade, and length of stenosis are the major factors in determining which surgical procedure will be used for reconstruction. The goal of all surgical procedures for LTS is to maintain vocal function and allow for early decannulation with subsequent unrestricted activity. Contraindications to reconstruction includes patients who would remain tracheostomy dependent even after adequate laryngotracheal expansion (i.e. patients with severe aspiration or BPD requiring a tracheostomy for pulmonary toilet), children with gastroesophageal incompetence resistant to surgical and medical management, and patients with an absolute contraindication to general anesthesia.

Endoscopic

Mild stenosis (Cotton-Myer grades I and II) can usually be treated with endoscopic techniques such as dilation or CO₂ laser resection. Factors associated with failure of these endoscopic techniques include: previous attempts at endoscopic repair, circumferential scarring, loss of cartilaginous support, exposure of cartilage during laser excision leading to chondritis, severe bacterial infection, posterior inlet scarring with arytenoid fixation, combined laryngeal or tracheal stenosis or vertical scar length >1cm. Endoscopic dilation has had disappointing results,

however, reported success rates with endoscopic laser resection of Grade I and II stenosis range from 66-80%.

Grade III or IV stenoses usually require some form of open surgical procedure. Several techniques have been described.

Anterior Cricoid Split

The anterior cricoid split (ACS) procedure was originally described for a neonate who has had multiple failed extubations instead of performing a tracheostomy (Cotton and Seid, 1980). This procedure is also used for older infants and those who have already been tracheotomized. Indications were later expanded to patients with congenital subglottic stenosis. The lesion responsive to this procedure is a mild anterior subglottic narrowing with extensive fibrosis but a normal cricoid. ACS may also be used to decompress subglottic cysts. Strict criteria for ACS have been established by Cotton and include: extubation failure on two occasions or more due to laryngeal pathology, weight >1500g, no assisted ventilation for 10 days prior to evaluation, O₂ requirements <30%, no CHF for one month prior to evaluation, no acute respiratory tract infection, no antihypertensive medications ten days prior to evaluation. The procedure is performed after direct laryngoscopic and bronchoscopic confirmation of the diagnosis. All other airway pathology must be ruled-out.

A vertical midline incision is made through the cricoid cartilage and first two tracheal rings as well as the lower thyroid cartilage. This allows the cartilages to spring open and allow edematous mucosa to drain, increasing airway size. Prolene stay sutures are placed on either side of the cricoid cartilage and the skin is re-approximated after placement of a drain. The child is then left intubated, sedated and paralyzed in the ICU for 7-14 days. Cotton has guidelines for endotracheal tube sizes for stenting and for duration of stenting based on the infants weight.

Laryngotracheal Expansion Surgery

Laryngotracheal expansion surgery involves scar division with distraction of the edges by interposition of graft material (augmentation) to widen the airway lumen. It is important to avoid removing scar which results in a large surface area of denuded mucosa and leads to restenosis. Cotton recommends augmenting the airway with grafts when the distraction of the laryngotracheal framework must be greater than approximately 3mm. There are several techniques depending on the location and severity of the stenosis. Laryngotracheoplasty can be performed with a tracheostomy and formal stenting or by using the endotracheal tube as a stent, the latter known as a single-stage LTP (SS-LTP). There are a several stents that can be used for LTS including: endotracheal tubes, Silastic sheet rolls, Montgomery T-tubes, and laryngeal stents. Laryngeal stents include: teflon stents [Aboulker stent (short or long), ETS Poirot, Paris], and silastic stents (Montgomery stents: Boston Medical Products, Boston. The primary consideration when deciding on the type of reconstruction and stent material is to provide a safe airway and adequate support for the graft. Success of LTR among, other things, is determined by the surgical procedure, including possible need for stenting; choice of type and length of stent; and duration of stenting. Choosing the appropriate method for stenting requires

considering consistency of stenosis, altered anatomy, size, location and stability of grafts when used for surgical repair and host tissue healing factors (Zalzal, 1988)

Autogenous costal cartilage is the material of choice for grafting. Many other materials have been used for grafting including auricular, hyoid and thyroid cartilage and bone. Cartilage has much less resorption over time compared to bone. Although bone provides good structural support, grafts in the airway do not bear a lot of stress or weight.

Anterior laryngofissure with anterior lumen augmentation

This technique is good for anterior subglottic stenosis or anterior tracheal wall collapse. The lesion should not involve the glottis. Other procedures should be considered if there the cricoid cartilage is deformed or weak. Anterior grafts are made considerably larger and thicker than grafts placed posteriorly. The perichondrium is oriented to the luminal side to allow for epithelialization. The perichondrium is also a good barrier against infection. A large external flange is created to prevent the graft from prolapsing into the airway.

Laryngofissure with division of posterior cricoid lamina

This is indicated for patients with posterior subglottic stenosis, posterior glottic stenosis that extends to the glottis, complete or circumferential stenosis, or if there is significant cricoid deformity. Division of the anterior and posterior cricoid must be carried out for this procedure. If possible, one should avoid a complete laryngofissure to avoid damaging the anterior commissure, however this is often needed for posterior glottic involvement for access. The posterior cricoid cartilage is incised in a manner that is vertically oriented to the cartilage to allow maximal purchase for the graft. The incision is extended superiorly to the interarytenoid area and inferiorly 5 to 10 mm into the membranous trachea. The graft is elliptical in shape. It should not be too thick as it can cause swallowing difficulties and can lead to aspiration. The width of the graft is determined by the desired distraction of the cut edges of the incised posterior cricoid cartilage. 0.05 to 1.00 mm of distraction can be obtained for each year of age, up to 1 cm. It is sutured in place with absorbable suture on a small cutting needle. The knots should be buried so that they remain extraluminal to prevent development of granulation tissue. Long-term stenting is usually necessary (3-6 months).

Laryngofissure and division of posterior cricoid lamina with anterior and posterior grafts

This should be used for patients who have SGS similar to those above but with a significant amount of stenosis posteriorly such that grafting is necessary to maintain the adequate separation.

Once the grafts have been sutured into place in any of the above procedures, the decision must be made on whether it should be single or double-staged. Cotton and Walner (1999) recommend a double-staged procedure for patients with severe stenoses, history of reactive airway, or poor pulmonary function. This should also be considered at institutions with inadequate intensive care facilities. Double-stage procedure implies placement of stent above the tracheostomy tube instead of using an endotracheal tube as the stent (single-staged

procedure). Once this decision is made, the strap muscles are closed to provide blood supply to the outer surface of the anterior graft.

Segmental resection/Cricotracheal resection (CTR) with thyrotracheal anastomosis

The first CTR was performed by Conley in 1953 in a patient undergoing surgery for chondroma of the cricoid cartilage. It was later popularized by Ogura and Powers (1964) as a technique for treatment of traumatic stenosis. In the 1970s it became the treatment of choice in adults with acquired subglottic stenosis from long term intubation. Until recently, surgeons were reluctant to perform this procedure in the pediatric patients because of the risk of anastomotic dehiscence and recurrent laryngeal nerve injury, and disturbing the normal growth of the larynx. The first successful CTR performed in a child was occurred in 1978 (Savary). It wasn't until 1993, however, that the first series of 15 pediatric patients treated with CTR for severe LTS was published. Multiple subsequent series have reported using CTR for severe LTS with good outcomes (Monnier et al., 1995, Monnier et al., 1998, Stern and Cotton, 1999).

This technique is indicated if there is severe deformity of the cricoid making grafting very likely to fail. Most say that there must be at least 10 mm of normal airway below the glottis, however Cotton states that the resection can be up to the vocal folds but to expect prolonged edema. This technique is technically difficult due to the close proximity of the vocal cords and recurrent laryngeal nerves. Stenosis less than 4 cm can be resected by laryngeal release and cervical tracheal mobilization. Stenting is not required and the tracheotomy tube can usually be removed at around 4 weeks.

Post-operative Care

Patients undergoing open laryngeal surgery for SGS require post-operative care in an ICU that has an intensivist and staff familiar with the specialized care these patients require.

Since most of the children undergoing open laryngotracheoplasty have more severe SGS they have usually had a tracheotomy for a while. Children who undergo laryngotracheoplasty with stenting typically only require a few days of care in the hospital to be sure that the parents are educated about tracheotomy care and have all necessary equipment at home. Since they have a stent in place, they should be given antibiotics and antireflux medications should also be continued. The length of time a stent should be kept in place depends on what the airway requires. If stenting is needed only to hold a graft in place while healing, one week may be all that is needed. On the other hand if the stent is used to counteract scar formation and maintain the lumen, months of stenting may be required. Stents should be monitored ever 3 to 4 weeks for displacement and granulation tissue development. Once removed, the patient should undergo repeat endoscopy every 2 weeks until healing is complete at which time decannulation is considered.

Infants and children who undergo either ACS or one-stage LTP require more intense post-operative care in the ICU. They usually stay intubated for 7-14 days with the endotracheal tube acting as a stent. The patient requires heavy sedation with or without paralysis. The patients should be treated with broad-spectrum antibiotics and antireflux medications. Chest

physiotherapy and log-rolling the patient every 4 hrs. is important to prevent atelectasis, pneumonia, and pressure sores. The majority of patients do not need continuous paralysis. The patient undergoes extubation when an air leak develops. An audible air leak at a pressure of 20cm H₂O is a good prognostic indicator for successful extubation. Decadron (1mg/kg) is usually given 12 hours before extubation and for 5 days after.

Most children with LTS have documented GER prior to treatment and therefore are already on an antireflux medical regimen. This should be continued in the peri and postoperative period. Patients (children and adults) without symptoms of reflux prior to treatment and those with a negative reflux workup should be treated in the peri-operative period. Some authors suggest continuing treatment up to three months after surgery in these patients.

Complications are infrequent but can include: atelectasis, pneumonia, malpositioned endotracheal tube, accidental extubation, occluded ET tube, wound infection, granulation tissue, restenosis, and tracheocutaneous fistula. Some complications related specifically to ACS and one-stage LTP that require prolonged intubation with sedation include narcotic withdrawal and transient skeletal muscle paralysis related to the prolonged muscle relaxation.

Outcomes

The goal of management of subglottic stenosis is decannulation. Success rates are dependent on the cause of the stenosis, the number of previous failed attempts, the status of the remainder of the airway, especially the glottis and the severity of the stenosis. Cotton has reported an overall pediatric LTR success rate of 92%, 97% for Grade II, 91% for Grade III, and 72% for Grade IV.

Bailey (1988) reported results of 131 pediatric airway reconstructive procedures. He had a 92% success rate with patients who underwent laryngotracheoplasty procedures (no grafting) and 80% success with patients who underwent LTR (with grafting). He did not report on use of any grading system.

Lano (1998) reviewed 41 cases of LTR in adults. He classified patient lesions with all three previously mentioned grading systems (Cotton-Myer, McCaffrey, and Lano). Over all 80% of patients were decannulated. He found that surgical outcome significantly correlated with the Lano and McCaffrey grading system, however, not with the Cotton-Myer system. He had 94%, 78%, and 20% success rates with Lano stage I, II, and III respectively. Interestingly, the best predictor of surgical outcome was obtained by multiplying the value from the Lano and the Cotton-Myer systems. Lano suggest that the reason for this is that his classification, which grades the extent of the lesion, multiplied by the Cotton-Myer system, which grades the severity of the lesion, provides a three-dimensional rating which is more characteristic of these lesions.

Lano's study was the first to report on the success of LTR with respect to diabetes. 75% of patients with type I or II diabetes who underwent LTR failed decannulation. The most common cause of failure in these patients was exuberant granulation tissue and restenosis with thick scar formation. One had dehiscence of the anastomotic site and required a T-tube to

maintain an airway. Impairment of wound healing secondary to decreased microvascular blood flow and bacterial overgrowth probably account for these findings.

Monnier et al. (1999) has reviewed the experience with CTR at the Department of Otolaryngology at the University of Lausanne, Switzerland. 69 CTRs were performed (48 infants and children and 21 in adults). 95% and 100% of the pediatric and adult patients, all of whom had Cotton-Myer grade III or IV stenosis, were successfully decannulated. Stern and Cotton (1999) reported on 38 pediatric patients who underwent CTR for severe LTS (grade III and IV). 33 patients were successfully decannulated. Complications preventing decannulation in this study included one patient with persistent aspiration, three who restenosed, one with arytenoid prolapse, and one with recurrent laryngeal nerve injury. Overall, 94% successful decannulation has been reported in the literature when CTR is used in pediatric patients with severe LTS (Monnier, 1999).

Grillo (1992) has reported his experience with 80 CTRs. He reported that 97% of patients underwent successful decannulation. He further subdivided patients into groups depending on their voice quality and exercise tolerance. 22.5% had an excellent outcome defined as a normal voice and no activity restriction. 60% had a good outcome in which patients suffered only slight lessening of maximum volume of voice, slight hoarseness that did not impede vocal use, slight weakness of voice after prolonged use, diminished ability to sing, and adequate breathing for all normal activities. 10% had satisfactory results which were those with a hoarse voice and either slight wheezing or shortness of breath on exercise, not sufficient to impair usual activities.

Dysphonia following laryngotracheal reconstruction has not been extensively studied. Many authors report that a functional voice is restored in most patients. MacArthur et al. published a series of 12 patients (average age 6yrs) who underwent LTR. Most patients underwent both endoscopic evaluation and speech analysis. They found that 78% of the children had altered anatomy, 44% had altered function and 100% had decreased voice quality. They concluded that children with high grade subglottic stenosis and a history of multiple prior surgeries are at risk for a poor voice outcome after laryngotracheal reconstruction.

Prevention

Preventative measures used to reduce the likelihood of developing SGS are directed at the those events which are known or postulated to cause or exacerbate this problem. The endotracheal tube (ETT) is well established as the most common cause of SGS. As mentioned before, the size and movement of the tube, multiple and traumatic intubations, high cuff pressures, and duration of intubation all contribute to increase damage to the delicate mucosal lining of the airway. It is therefore important for the primary physician, anesthesiologist and/or intensivist to be aware of SGS as a complication of endotracheal intubation. This starts with education. From there, minimizing the amount of trauma to the airway is key.

Choosing the appropriate size ETT should be determined by the patients age and size. If unsure, a smaller ETT can be inserted and if the leak pressures are too low, a half size larger tube can then be placed. The ideal size tube in children allows an air leak at an inspiratory pressure of

20 cm H₂O. Using this guideline, Cotencin and Narcy (1993) found a very low rate of post extubation stridor in neonates (5/247 patients) with none requiring surgical therapy for stenosis. In adults, a leak should be heard at a peak pressure of 20-25 cm H₂O. In addition, cuff pressure testing by a respiratory therapist should be routine in an intensive care setting. Pressure should be kept below 25 cm H₂O.

Blind intubations should always be avoided if possible. If direct laryngoscopy is difficult, fiberoptic intubation should be attempted. Once a patient is intubated, multiple measures should be taken to prevent the tube from moving. These measures are usually carried out by an anesthesiologist or an intensive care unit respiratory therapist. It is particularly difficult to prevent tube movement in nonparalyzed patients with neurologic injuries or in children. Accidental extubations should be avoided at all costs as these often result in traumatic reintubations. The number reintubations can be minimized by appropriately evaluating the patient with weaning parameters and establishing the presence of an air leak.

There is no definitive safe period for intubation. 5 to 10 days of intubation is generally acceptable in adults after which time a tracheotomy should be considered. Premature infants have much more pliable cartilages allowing for longer periods of intubation. Lesperance and Zalzal (1996) recommend performing a tracheotomy in premature infants after 50 days of intubation.

Most patients who are intubated in the intensive care unit receive intravenous antireflux medications. This is important because these patients are predisposed to reflux. Nasogastric tubes act as a stent and allow gastric contents to breach the upper and lower esophageal sphincters. If possible, the head of bed should be elevated to allow gravity to work for the patient.

In the past 30 years there has been a reduction in the incidence of LTS particularly in the neonates. Seven studies looking at the years of 1971-1979 found an incidence of neonatal SGS of 0.9% to 8.3%. Nine studies looking at the years of 1980 to 1989 reported an incidence of neonatal SGS of 0.0% to 4.2% and 4 studies describe patients cared for between 1990-1999 and reported an incidence of neonatal SGS of 0.0% to 0.63%. Overall the incidence today has been estimated to be 0% to 2% for intubated neonates (Walner, 2001). This compares to incidence estimates in the 1960s of upwards of 22%. This reduction has most likely resulted from better education of physicians and nurses and an increasing awareness of the factors contributing to the development of SGS. Routine use of artificial surfactant and systemic steroids in premature infants as well as the increased use of CPAP when possible has also contributed to the decline in the incidence of SGS.

References

- Bain WM, Harrington JW, Thomas LE, Schaefer SD: Head and neck manifestations of gastroesophageal reflux. *Laryngoscope* 1983; 94:516-519
- Bath AP, Panarese A, Thevasagayam M, Bull PD. Paediatric subglottic stenosis. *Clinical Otolaryngol* 1999; 24(2):117-121
- Burton DM. Gastroesophageal reflux. In: Holinger LD, Lusk RP, Green CG, eds.

- Pediatric Laryngology and Bronchoesophagology. Philadelphia, Pa: JB Lippincott Raven; 1997:317-323
- Conley JJ: Reconstruction of the subglottic air passage. *Ann Otol Rhinol Laryngol* 1953; 62:477-495
- Cotencin P, Narcy P: Size of endotracheal tube and neonatal acquired subglottic stenosis. *Arch Otolaryngol Head Neck Surg* 1993; 119:815
- Cotton RT. Pediatric laryngotracheal stenosis. *J Pediatr Surg* 1984;19:699-704
- Cotton RT, O'Connor DM. Paediatric laryngotracheal reconstruction: 20 years experience. *Acta Otorhinolaryngol Belg* 1995; 49:367-372
- Cotton RT and Andrews TM. Laryngeal Stenosis. In: Bailey BJ, ed. Head and Neck Surgery - Otolaryngology, 2nd ed. Philadelphia: Lippincott-Raven, 1998:1115.
- Cotton RT, Seid AB: Management of the extubation problem in the premature child: Anterior cricoid split as an alternative to tracheotomy. *Ann Otol Rhinol Laryngol* 1980; 89:508
- Gibson FB and Perkins SW. Dynamics of Wound Healing. In: Bailey BJ, ed. Head and Neck Surgery - Otolaryngology, Philadelphia: Lippincott-Raven, 1993: 187.
- Halstead LA. Role of Gastroesophageal Reflux in Pediatric Upper Airway Disorders. *Otolaryngol Head Neck Surg* 1999;120:208
- Koufman JA. The otolarngologic manifestations of gastroesophageal reflux disease (GERD): a clinical investigation of 225 patients using ambulatory 24-hour pH monitoring and an experimental investigation of the role of acid and pepsin in the development of laryngeal injury. *Laryngoscope* 1991; 101(suppl 53):1-64
- Lano, CF et. al. Laryngotracheal reconstruction in the adult: a ten year experience. *Ann Otol Rhinol Laryngol* 1998; 107:92-96
- Lee KJ. Embryology of Clefts and Pouches. In: Lee KJ, ed. Essential Otolaryngology, Appleton & Lange, 1991: 243
- Lesperance MM, Zalzal GH. Assessment and management of laryngotracheal stenosis. *Pediatric clinics of North America* 1996; 43(6):1413-1427
- Little FB, Koufman JA, Kohut RI, Marshall RB. Effect of gastric acid on the pathogenesis of subglottic stenosis. *Ann Otol Rhinol Laryngol* 1985; 94:516-519
- MacArthur CJ, Kearns GH, Healy GB. Voice Quality After Laryngotracheal Reconstruction. *Arch Otolaryngol Head Neck Surg* 1994;120:641
- McCaffrey TV. Classification of laryngotracheal stenosis. *Laryngoscope* 1992:102:335-340
- McCaffrey TV. Management of laryngotracheal stenosis on the basis of site and severity. *Otolaryngol Head Neck Surg* 1993;109(3):468-473
- McCaffrey TV. Management of subglottic stenosis in the adult. *Ann Otol Rhinol Laryngol* 1991;100:90-94
- Monnier PM et al. Cricotracheal resection for adult and pediatric subglottic stenoses: similarities and differences. *Operative Techniques in Otolaryngol-Head Neck Surg* 1999; 10(4): 311-315
- Monnier PM, Savary M, Chapuis G. Cricotracheal resection for pediatric subglottic stenosis: Update of the Lausanne experience. *Acta Otorhinolaryngol Belg* 1995; 49:373-382
- Monnier PM, Savary M, Chapuis G. Partial Cricoid Resection with Primary Tracheal

- Anastomosis for Subglottic Stenosis in Infants and Children. *Laryngoscope* 1993;103:1273
- Myer CM, O'Connor DM, Cotton RT. Proposed Grading System for Subglottic Stenosis Based on Endotracheal Tube Sizes. *Ann Otol Rhinol Laryngol* 1994; 103:319
- Ogura JH, Powers WE: Functional restitution of traumatic stenosis of the larynx and pharynx. *Laryngoscope* 1964; 74:1081-1110
- Postma GN, et al. Laryngopharyngeal reflux testing. *Ear Nose Throat J.* 2002; suppl 2 81(9):14-18
- Sie KCY, McGill T, Healy GB: Subglottic hemangioma: Ten years' experience with the carbon dioxide laser. *Ann Otol Rhinol Laryngol* 1994; 103:167
- Tucker JA, Tucker GF, Vidic B. Clinical correlation of anomalies of the supraglottic larynx with staged sequence of normal human laryngeal development. *Ann Otol Rhinol Laryngol* 1978; 87:636
- Walner DL and Cotton RT. Acquired anomalies of the larynx and trachea. In: Practical Pediatric Otolaryngology. Cotton RT and Myer CM eds. Philadelphia, PA: Lippincott-Raven: 1999:515-537
- Walner DL et al. Gastroesophageal reflux in patients with subglottic stenosis. *Arch Otolaryngol Head Neck Surg* 1998; 124(5):551-555
- Walner DL et al. Neonatal subglottic stenosis-incidence and trends. *Laryngoscope* 2001; 111(1):48-51
- Werkhaven JA, Beste D. Diagnosis and management of pediatric laryngeal stenosis. *Otolaryngol Clin North Am* 1995; 28:797-808
- Zalzal GH. Use of stents in laryngotracheal reconstruction in children: Indications, technical considerations, and complications. *Laryngoscope* 1988; 98:849- 854