The Evolving Management of Children with Complex Airway and Swallowing Disorders

By

Shyan Vijayasekaran

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Breath is life; as breathing fails, life slowly ebbs away. In few situations is this more apt than in the sickly newborn infant whose lungs may be ill-developed, collapsed, or pneumonic, and who fights for his breath and his life through small respiratory passages so easily blocked by spasm and secretions."

McDonald IH, Stocks JG. Prolonged nasotracheal intubation. A review of its development in a paediatric hospital. Br J Anaesth *1965; 37: 161–173*

I certify that this thesis does not incorporate without acknowledgment any material previously submitted for a degree or diploma in any university and the research within will not be submitted for any other future degree or diploma without the permission of Flinders University; and to the best of my knowledge and belief, does not contain any material previously published or written by another person except where due reference is made in the text.

Shyan Vijayasekaran

Contents Page

Research Experience Statement

NAME: Shyan Vijayasekaran

Contact details

Perth ENT Centre

Unit 6, 1 Salvado Road, Subiaco, Australia 6008

+61893280580

+61402040240

shyan@perthentcentre.com.au

Current Positions

1. Clinical Professor, Otolaryngology Head and Neck Surgery, University of Western Australia
2. Surgeon, Otolaryngology Head and Neck Surgery, Perth Children's Hospital, Sir Charles Gairdner Hospital, Royal Perth Hospital, Royal Perth Hospital, King Edward Memorial Hospital, St John of God Hospital Subiaco
3. Surgeon, Perth ENT Centre
4. President, Australia, and New Zealand Society of Paediatric Otorhinolaryngology
5. Adjunct Professor, Kasturba Medical College, Mangalore, India
6. Adjunct Clinical Professor, Curtin University Medical School, Western Australia

Education

1. University of Cincinnati College of Medicine, Cincinnati, Ohio, USA, Division of Pediatric Otolaryngology and Head and Neck Surgery, Cincinnati

Children's Hospital Medical Center, Fellowship in Pediatric Otolaryngology and Head and Neck Surgery, January 2006.

2. Royal Australasian College of Surgeons, Fellowship in Otolaryngology Head and Neck Surgery, December 2003.
3. The University of Western Australia, Bachelor of Medicine and Bachelor of Surgery, March 1994.

Research Experience

Peer-Reviewed publications: 130 (source Google Scholar)

Book Chapters: 12

Presentations as a keynote speaker (national and international): 55

Invited presentations at national and international meetings: 84

Presentations at national and international conferences: 35

Citations: 2805 (source Google Scholar 21/4/24)

H index: 28 (source Google Scholar 21/4/24)

Awards

1. American Society of Pediatric Otolaryngology (ASPO) Charles F. Ferguson Clinical Research Award. Las Vegas, May 2005 (Best research paper).
2. Athelstan and Amy Saw Medical Research Fellowship. University of Western Australia, 2003.

Grants

1. Wesfarmers Centre of Vaccination and Infectious Diseases, Catalyst Grant. (2023). Characterising individual differences in susceptibility and response to tonsil pathogens.
2. Future Health Research and Innovation Fund. Innovation Seed Fund (2022-23) Spritz OM - a nasal vaccine that prevents ear infections: proof-of-feasibility study.
3. WA Child Research Fund (2022): Advancing a Western Australian-led clinical trial to test the safety and tolerability of an anti-biofilm therapy in children with recurrent otitis media.
4. Merck Investigator Studies Program Merck Investigator Studies Program (2021-2023) A cross-sectional observational study on the aetiology of recurrent acute otitis media in Western Australia in the PCV13-era: the WALACE study (Western Australian Aetiology of Acute and Chronic Ear Disease.
5. Telethon Perth Children's Hospital Research Fund (2020) EAR Portal: A randomized waitlist-controlled trial of an urban-based ENT and audiology Referral (EAR) telehealth portal to provide equitable access to specialist ear health services for children.
6. Telethon Perth Children's Hospital Research Fund (2018) Ear Portal in Aboriginal communities of South Metropolitan Perth.
7. Perth Children's Hospital Foundation Grant (2021): Identifying the cause exercise-Induced laryngeal obstruction.
8. Perth Children's Hospital Foundation Grant (2020): Endoscopic Ear Surgery

9. WA Child Research Fund Grant (2019) Could an intracellular bacterial reservoir in the tonsils account for recurrent episodes of strep throat and rheumatic fever.
10. Perth Children's Hospital Foundation Grant (2018) Nasopharyngoscopy for accurate diagnosis.
11. Perth Children's Hospital Foundation Grant (2018): Portable Videolaryngoscopy.
12. Telethon New Children's Hospital Research Fund Grant (2013-18): Infection or Allergy - Understanding the Pathogenesis of Adenotonsillar Hypertrophy
13. Gordon Baron-Hay Grant (2012): Voice Laryngeal Pathology Preterm infants
14. Women's & Infants Research Foundation Grant (2012): Voice disorders in Preterm Infants.
15. SHRAC Grant (2010) Dissolving the glue in glue ear: Assessment of the use of Dornase alfa as an adjunct therapy to ventilation tube insertion.
16. Women and Infants Research Foundation (2010): Voice Disorders in extreme pre-term survivors; a poorly recognized entity.
17. National Health and Medical Research Council (2009): Family Study of Ear Health and Metabolic Diseases in a Western Australian Aboriginal Community.
18. Garnett Passe and Rodney Williams Foundation Research Grant (2003) The role of bacterial biofilm in children with otitis media.

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I would also like to acknowledge the Athelston and Amy Saw research fellowship which funded my training in Cincinnati. Athelston Saw was born in Perth in 1868, studied in Cambridge and was elected a Fellow of the Royal College of Surgeons. In 1895 he was appointed honorary surgeon to the Perth Hospital, subsequently lieutenant colonel in the Australian Army Medical Corps and in 1921 the third Chancellor of the University of Western Australia.

The triumvirate of mentorship represented by Professors Cotton, Rutter, and Choo has not only imparted surgical prowess but has also cultivated in me a profound sense of responsibility and dedication to the medical field. Their influence resonates in every patient whom I treat and every decision I undertake. Their legacy to never stop learning is a beacon that guides me in navigating the complexities of the ever-evolving world of medicine. Under their guidance I undertook the research that led to being awarded the Charles F. Ferguson prize by the American Society of Pediatric Otolaryngology. It is significant that Dr Charles Ferguson was the first full-time paediatric otolaryngologist in the United States. His career at Boston Children's

Hospital spanned four decades. Disorders of the larynx, trachea and bronchi were his principal professional focus, with a specific expertise in bronchoesophagology. He edited the first Paediatric Otolaryngology textbook in 1972 and helped set the foundation for the creation of the American Society of Pediatric otolaryngology.

I am truly humbled for my treasured patients, whose trust is an immense privilege. The role of a doctor is one of profound responsibility, and their faith in me as a doctor has been a driving force. Equally deserving of recognition are the parents who have placed their most precious treasures—their children—under my care. It is with a deep sense of honour that I acknowledge this trust and allow it to fuel my commitment to delivering the best possible care.

However, my gratitude would remain incomplete without a special mention of my anchor—the bedrock of my strength—my family. To my parents, whose unwavering belief in me since my inception has been my foundation, I owe a debt of gratitude that mere words cannot encapsulate. My wife Mel and our children (Harry, Layla, Eddie, and George) have been a source of boundless support in this journey. The children have infused my days with love and light, reminding me of the purpose behind every endeavour.

Their collective understanding, sacrifice, and patience have paved the path to this significant juncture in my career. They have been the driving force behind my accomplishments, a reminder that achievements, no matter how grand, find their true meaning in the embrace of those we love.

Preface

I studied Medicine at the University of Western Australia, completing an MBBS in 1994. I completed my surgical training in otolaryngology and head and neck surgery in 2004 (Fellow of the Royal Australasian College of Surgeons). During my training as an otolaryngologist, I developed a deep curiosity about the airway, breathing, and consequently, feeding and swallowing. The human upper aerodigestive tract begins at the tip of the nose and the lips and extends to the bronchi. Airway, breathing, and circulation are all vital for life, and each is required, in that order, for the next to be effective. Although complete airway obstruction is life-threatening, partial obstruction also results in a significant compromise in the ability to function; this is most dramatically manifested in infants and children. Otolaryngologists are the only medical practitioners whose interests are exclusively focused on the anatomy, physiology, and pathology of the nose, oral cavity, pharynx, larynx, trachea, and bronchi that comprise the human airway. As such, they are uniquely trained to manage disorders of this multiorgan system.

Managing airway disorders became my vocation and passion. After completing my otolaryngology training in Australia, I undertook a fellowship in paediatric otolaryngology (2004-2006) with Dr. Robin Cotton, at Cincinnati Children's Hospital Medical Center (CCHMC), (Cincinnati, Ohio, USA). This institution is considered the global leader in treating airway and swallowing disorders in children. At CCHMC, many significant surgical advances in managing paediatric airway disorders have been made over the last five decades. Also, it is here that the need for a multidisciplinary, patient-centered approach (involving surgeons, physicians, nurses, and allied health professionals) was identified and the very first aerodigestive team (ADT) was formed in 1999 (1). The aim of such teams is to manage patients who

present with complex airway, sleep, and swallowing issues. Over the last 2 decades, such teams have proliferated globally and have been shown to improve patient outcomes, reduce hospitalization and investigations, and reduce costs (2).

Upon returning to Princess Margaret Hospital for Children in 2006, I formed the first multidisciplinary team for the treatment of paediatric airway and swallowing disorders in Australasia. As the senior clinician in the team at Perth Children's Hospital (PCH), I continue to do this (3,4), and multidisciplinary airway teams are now the standard of care at most large children's healthcare facilities globally. More specifically, over the past four years, our ADT has treated 304 patients from Western Australia, Queensland, New South Wales, Victoria, South Australia, Singapore, and Malaysia. (Table 1) Approximately 750 procedures have been performed (Table 2) during this time. These data were presented at the European Society of Paediatric Otolaryngology meeting in 2023 (Liverpool, UK), and the publication is currently undergoing peer review.

Table 1: Patient demographics and diagnoses as seen at the PCH ADT meeting (2018-2022)

Variable	Number of patients (%)
Median age, years (IQR)	2.74 (0.43, 7.71)
Sex, male	155 (51.0)
Premature birth	54 (20.9)
Presenting Issues	
• Sleep	135 (50.8)
○ Obstructive sleep apnoea	91 (34.2)
○ Sleep disordered breathing	23 (8.6)
○ Central apnoea	10 (3.8)
• Airway Obstruction	179 (67.3)
• Feeding	86 (32.3)
Upper Airway Disorders	175 (57.6)
• Tracheomalacia	55 (20.7)
• Laryngomalacia	55 (20.7)
• Laryngotracheal stenosis	35 (13.2)
• Unilateral/bilateral vocal cord palsy	16 (6.0)
• Laryngotracheal clefts	14 (5.3)
• Choanal atresia	4 (1.6)
Pulmonary Disorders	64 (24.1)
• Bronchomalacia	20 (7.5)
• Chronic lung disease	18 (6.8)
• Recurrent lower respiratory tract infection	16 (6.0)
• Bronchopulmonary dysplasia	3 (1.1)
• Other	19 (7.1)
Oesophageal Disorders	58 (21.8)
• Gastroesophageal reflux	25 (9.4)
• Tracheoesophageal fistula	25 (9.4)
• Eosinophilic oesophagitis	4 (1.5)
• Other	9 (3.4)
Cardiac Pathology	46 (17.3)
Secondary Diagnosis	121 (45.5)
• Trisomy 21	27 (10.2)
• Pierre-Robin sequence	13 (4.9)
• Cerebral palsy	8 (3.0)
• CHARGE syndrome	6 (2.3)
• Achondroplasia	4 (1.5)
• DiGeorge syndrome	3 (1.1)
• Congenital central hypoventilation	3 (1.1)
• Crouzon syndrome	3 (1.1)
• Other	54 (20.3)
Tracheostomy Dependent	21 (7.9)
• At time of consult	17 (6.4)
• Prior to consult	4 (1.5)
Failure to Thrive	17 (6.4)
Obesity	25 (9.4)

Table 2: Procedures conducted on the patients seen at the PCH ADT (2018-2022)

Interventional Surgical Procedures	n
Tracheoesophageal fistula repair	
• Open	17
Laryngotracheal cleft repair	
• Open	7
• Endoscopic	23
Laryngotracheal reconstruction	14
Tracheostomy formation	17
Slide tracheoplasty	5
Open suture lateralisation of vocal fold	1
Supraglottoplasty	50
Epiglottopexy	5
Adenoidectomy	92
Tonsillotomy	36
Tonsillectomy	24
Adenotonsillectomy	22
Turbinate reduction (turbinoplasty / cautery / turbinectomy)	22
Cleft palate repair	15
Tongue base reduction	10
Insertion of mandibular distractor	10
Aortopexy	6
Laparoscopic Nissen fundoplication	3
Tracheopexy	1
Balloon dilation of	
• Laryngotracheal stenosis	70
• Oesophageal strictures	15
• Pyriform aperture stenosis	4
• Narrow nasal tract	2
• Choanal stenosis	1
Injection to	
• Laryngeal scar or granulation tissue	62
• Inter-arytenoid notch	39
• Salivary glands	17
• Nasal scar or granulation tissue	10
• Laryngotracheal clefts	7
• Vocal folds	6
• Laryngeal cysts	3
• Nasal vestibule	2
• Cricopharyngeus	1

This thesis accounts for a personal journey taken over nearly two decades and aimed at developing novel approaches and techniques to improve survival, outcomes, safety, and quality of life of children treated within a multidisciplinary team setting. I aimed to achieve these results by early diagnosis and definitive intervention in a spectrum of conditions from the nose to the bronchi in children that presented with breathing and feeding difficulties.

Summary

Stridor, stertor, snoring, feeding difficulty and obstructed breathing are common presentations to neonatologists, paediatricians, respiratory physicians, and general practitioners. Typically, affected patients are referred to a paediatric otolaryngologist for evaluation and treatment. A wide range of pathology affecting the nose to the bronchi causes obstructed breathing and feeding difficulties, and the assessment and treatment of these conditions are constantly evolving. In this thesis, my aim has been to collate the body of relevant academic work that I have undertaken. It is my hope that I have contributed to ongoing changes aimed at improving treatment algorithms and increasingly achieving positive outcomes.

Methods

This thesis is a compilation of 37 publications spanning over 17 years (2006 to 2023). The 11 chapters include peer reviewed articles, book chapters, and video journal publications that focus on a variety of upper aerodigestive tract pathologies in the child. The publications include histopathological studies of the larynx, animal studies, case series, novel surgical techniques, assessment of surgical outcomes, international consensus documents, literature reviews, and book chapters.

Conclusion

Although the breadth of the publications is wide, they reflect a number of common themes, including principles of treatment and early diagnosis of infants and children with complex aero-digestive problems, multidisciplinary management of these children, minimising adverse events, and continuous assessment of the outcomes.

Many of the interventions described in these publications remain the only publications from Australian and New Zealand institutions on these topics.

List of Publications that comprise this thesis

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Chapter 1

BACKGROUND

1. Development of the Upper Aerodigestive Tract
2. Synopsis of Upper Aerodigestive Tract Pathology in the Child

Development of the Upper Aerodigestive Tract

Branchial Apparatus

The cranial region of the human embryo during the fourth week resembles a fish embryo at a comparable stage of development, when the neural crest cells migrate into the future head and neck region. During the fourth and fifth embryologic weeks, the primitive pharynx is bounded laterally by bar-like branchial arches-hence, the use of the word branchial from the Greek word "branchia" meaning "gill". Each arch consists of a core of mesenchyme covered externally by surface ectoderm and internally by endoderm. The mesenchymal core of each branchial arch contains numerous neural crest cells that migrate into the branchial arches and proliferate to form the distinct swellings that demarcate each arch. Each branchial arch has an artery, cartilage, a nerve, and a muscular component. The external arches are separated by branchial grooves. Internally, the arches are separated extensions of the pharynx (pharyngeal pouches). A branchial membrane is formed where the ectoderm and the endoderm meet. The pharyngeal pouches, branchial arches, grooves and membrane together form the branchial apparatus. (5)

Branchial Arches

The first branchial arch develops to form the mandibular and maxillary prominences. The mandibular prominence forms the mandible, whereas the maxillary prominence forms the maxilla, zygoma, and squamous part of the temporal bone. The second arch forms the hyoid bone.

The arches support the lateral walls of the foregut (primitive pharynx). The stomodeum is a depression in the surface ectoderm separated from the pharynx by the buccopharyngeal membrane, which ruptures at about 24 days to bring the foregut into communication with the amniotic fluid. (Table 3)

Table 3: Derivatives of the Branchial Arches

Arch	Nerve	Muscles	Skeletal Structures	Ligaments	Vessels
First	Trigeminal (principle sensory nerve of the skin of the face and mucosal structures of the mouth and nose; also supplies the muscles of mastication)	-Muscles of mastication -Mylohyoid -Anterior belly of digastric -Tensor tympani -Tensor veli palatini	Malleus Incus	Anterior ligament of the malleus Sphenomandibular ligament	Maxillary artery External carotid artery
Second	Facial	-Muscles of facial expression -Stapedius -Stylohyoid -Posterior belly of digastric	Stapes Styloid process Lesser cornu and upper part of the body of the hyoid	Stylohyoid ligament	Stapedial artery
Third	Glossopharyngeal	Stylopharyngeus	Greater cornu and the lower part of the body of the hyoid		Common carotid Internal carotid arteries
Fourth and sixth	Superior laryngeal Recurrent laryngeal	-Cricothyroid -Levator veli palatini -Constrictors of the pharynx -Striated muscle of the oesophagus	Thyroid Cricoid Arytenoid Corniculate Cuneiform cartilages		Left 4th: Aortic arch Right 4th: Right subclavian artery Left 6th: (proximal part)Left pulmonary artery (distal portion) ductus

					Right 6th:(proximal part) – Right pulmonary artery Distally degenerates

Pharyngeal Pouches

The primitive pharynx is derived from the foregut. It widens cranially to join the primitive mouth and narrows caudally to join the oesophagus. The pharyngeal pouches are diverticulae on the internal aspect of the branchial arches. (Table 4)

Table 4: Derivatives of the Pharyngeal Pouches

Pouch	Derivatives
First	Eustachian tube, middle ear and mastoid cavity, tympanic membrane
Second	Intra-tonsillar cleft around which the mesenchyme differentiates into lymphoid tissue to form the tonsils
Third	Separates from the pharynx and forms Inferior parathyroid glands and thymus
Fourth	Superior parathyroid glands

Branchial Grooves

With exception of the first groove the rest of the grooves degenerate. The first branchial groove forms the external auditory meatus and in conjunction with the first branchial membrane meet the first pouch to form the tympanic membrane. (Fig 1-3)

Fig 1-3 Branchial Arches (Ben Pansky. Review of Medical Embryology.

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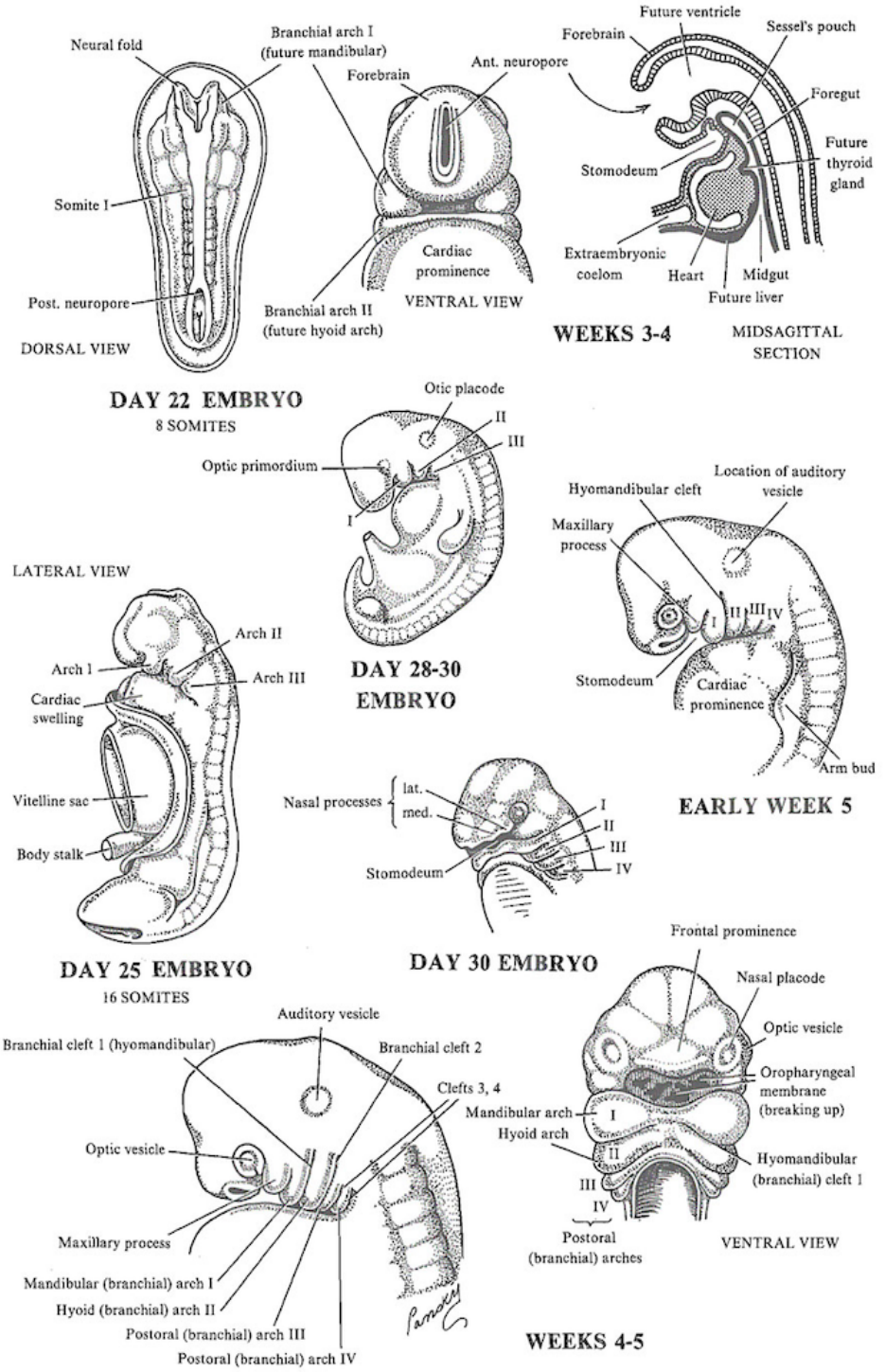
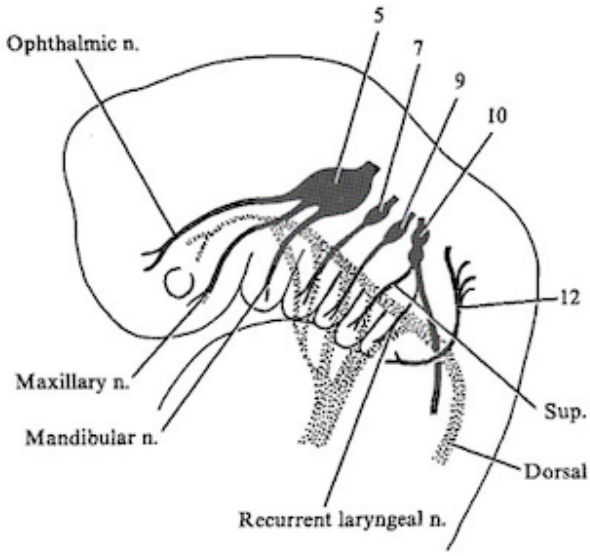
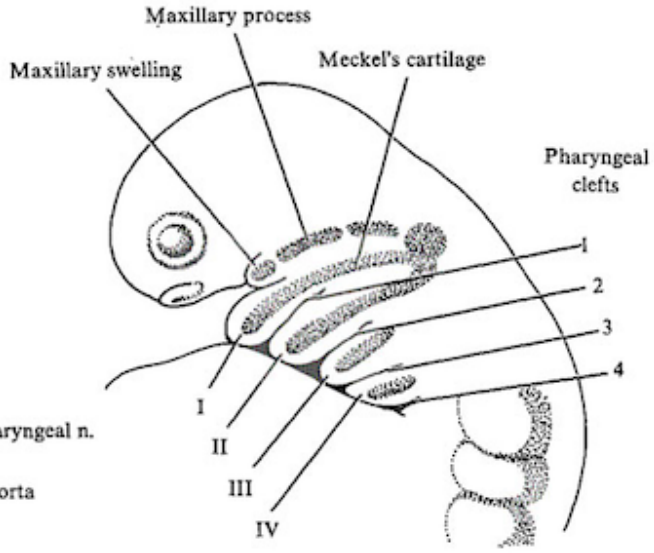
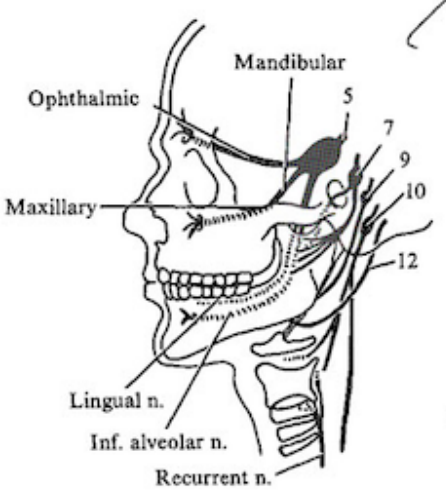
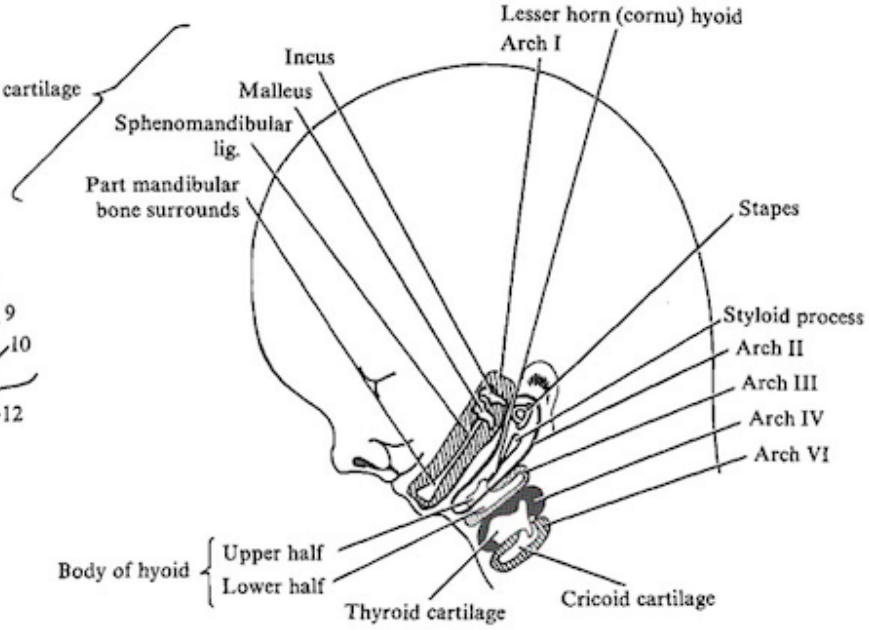




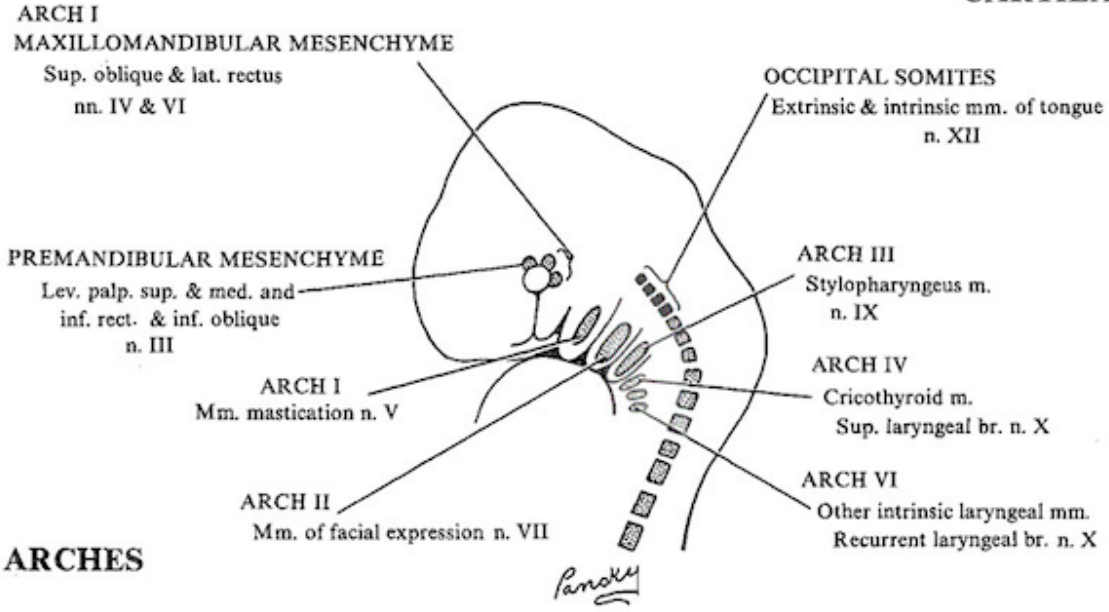


PHARYNGEAL ARCH NERVES

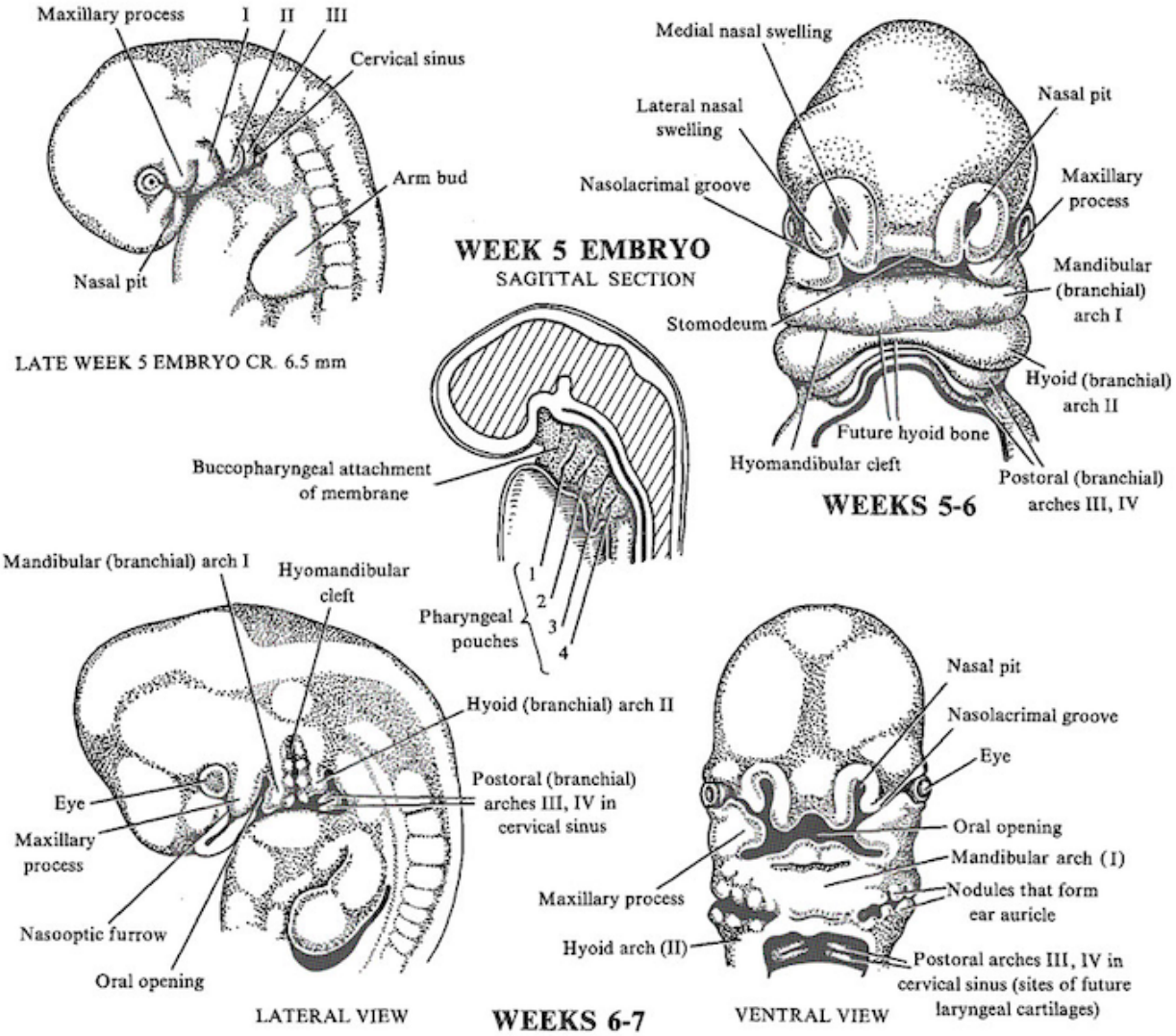


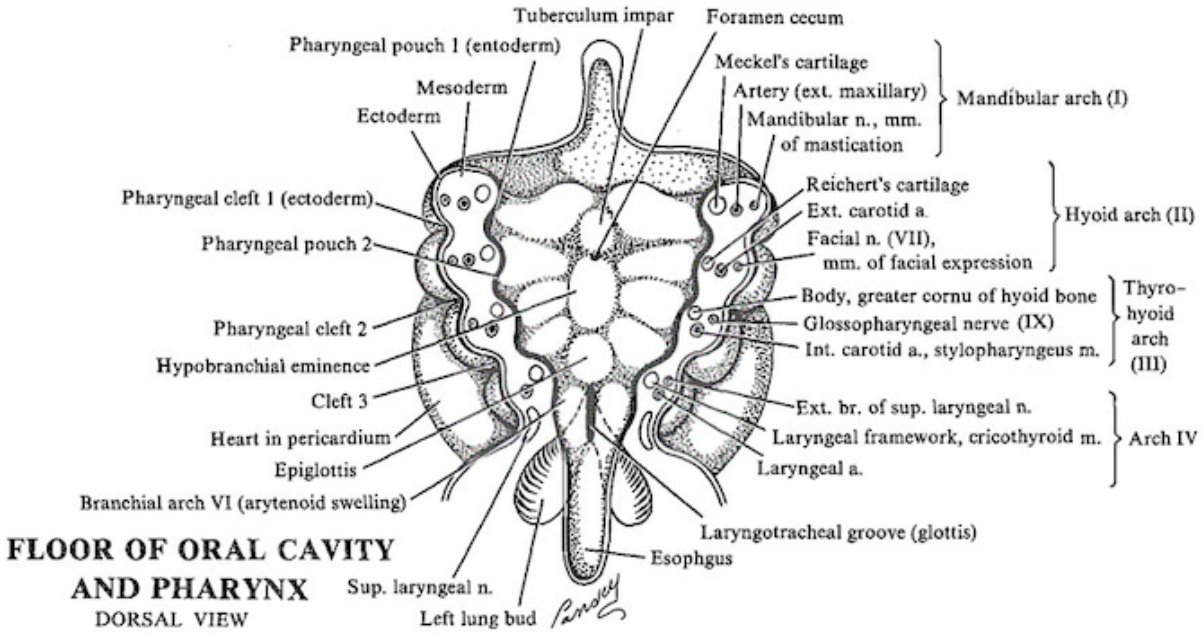


CARTILAGES



ARCHES


Maxillary process
I
II
III
Cervical sinus
Arm bud
Nasal pit
LATE WEEK 5 EMBRYO CR. 6.5 mm
WEEK 5 EMBRYO
SAGITTAL SECTION
Medial nasal swelling
Lateral nasal swelling
Nasolacrimal groove
Nasal pit
Maxillary process
Mandibular (branchial) arch I
Stomodeum
Hyoid (branchial) arch II
Future hyoid bone
Hyomandibular cleft
Postoral (branchial) arches III, IV
WEEKS 5-6
Buccopharyngeal attachment of membrane
Pharyngeal pouches
1
2
3
4
Mandibular (branchial) arch I
Hyomandibular cleft
Hyoid (branchial) arch II
Postoral (branchial) arches III, IV in cervical sinus
Eye
Maxillary process
Nasooptic furrow
Oral opening
LATERAL VIEW
WEEKS 6-7
Nasal pit
Nasolacrimal groove
Eye
Oral opening
Mandibular arch (I)
Nodules that form ear auricle
Maxillary process
Hyoid arch (II)
Postoral arches III, IV in cervical sinus (sites of future laryngeal cartilages)
VENTRAL VIEW


Tuberculum impar
Foramen cecum
Pharyngeal pouch 1 (entoderm)
Meckel's cartilage
Mesoderm
Artery (ext. maxillary)
Ectoderm
Mandibular n., mm. of mastication
Mandibular arch (I)
Pharyngeal cleft 1 (ectoderm)
Reichert's cartilage
Ext. carotid a.
Pharyngeal pouch 2
Facial n. (VII), mm. of facial expression
Hyoid arch (II)
Body, greater cornu of hyoid bone
Pharyngeal cleft 2
Glossopharyngeal nerve (IX)
Int. carotid a., stylopharyngeus m.
Thyro-hyoid arch (III)
Hypobranchial eminence
Cleft 3
Ext. br. of sup. laryngeal n.
Heart in pericardium
Laryngeal framework, cricothyroid m.
Arch IV
Epiglottis
Laryngeal a.
Branchial arch VI (arytenoid swelling)
Laryngotracheal groove (glottis)
Esophgus
FLOOR OF ORAL CAVITY AND PHARYNX
DORSAL VIEW
Sup. laryngeal n.
Left lung bud

Development of the Tongue

Anterior Two-Thirds of the Tongue

At the end of the fourth week, a triangular elevation on the floor of the primitive pharynx forms the median tongue bud. This is followed by two distal oval tongue buds on each side. These mesenchymal proliferations arise from the ventro-medial parts of the first pair of branchial arches. The distal tongue buds overgrow the median tongue buds, and the midline sulcus of the tongue represents the plane of fusion.

Posterior Third of the Tongue

Fusion of ventro-medial parts of the second and third arches caudal to the foramen caecum results in an elevation of tissue called the hypobranchial eminence; this forms the posterior third of the tongue.

The mesenchyme of the first and third branchial arches forms the connective tissue, lymphatics, blood vessels, and sensory nerves of the tongue. The nerve supply of the anterior two-thirds of the tongue is provided by the lingual branch of the mandibular (CN V) for sensation and the chorda tympani branch of the facial nerve for taste (CN VII). The nerve supply of the posterior third is the glossopharyngeal nerve (CN IX) for sensation and taste. The muscular elements of the tongue arise from occipital myotomes, while the hypoglossal nerve (CN XII) provides motor function to the entire tongue.

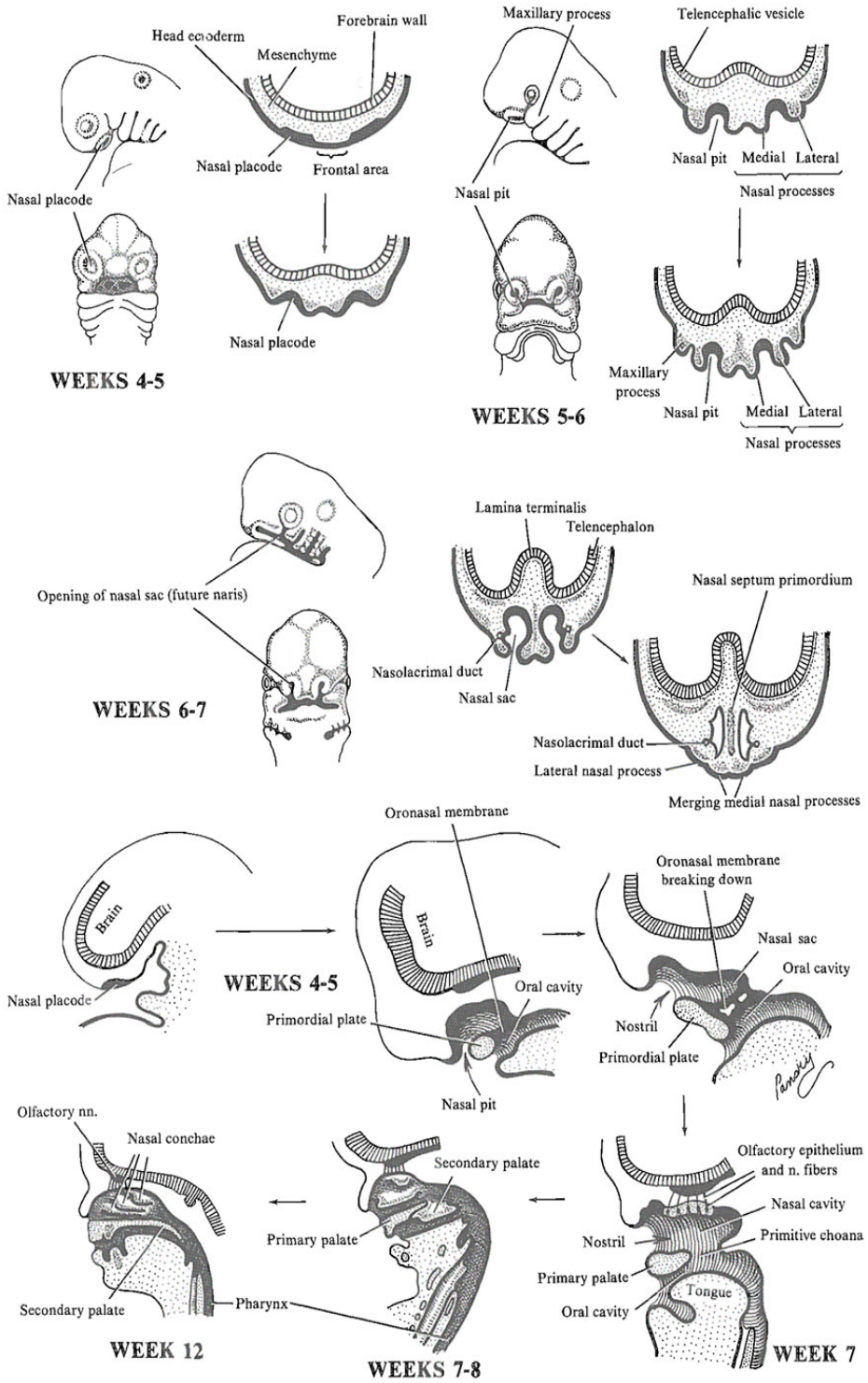
Development of the nose

At the end of the fourth embryologic week, bilateral oval prominences on the surface ectoderm form the nasal placodes on each side of the frontonasal prominence. The mesenchyme proliferates at the margins of these placodes, producing horseshoe-shaped elevations referred to as the medial and lateral nasal prominences. The

nasal placodes depress to form the nasal pits. The maxillary prominences enlarge and grow medially towards each other and the medial nasal prominences. This forces the median nasal prominences towards each other. During the sixth and seventh weeks of gestation, the medial nasal prominence forms the philtrum of the lip, the septum and premaxilla. The maxillary prominence forms the lateral part of the upper lip, maxilla, and palate. The frontonasal prominence forms the dorsum of the nose, and the lateral nasal prominences form the alae of the nose.

The nasal pits grow dorsally to form sacs initially separated from the oral cavity by the bucconasal membrane. This ruptures and the oral and nasal cavities come into communication. The palate then grows and pushes the choanal opening into the pharynx further distally. (Fig 4)

Figure 4. Development of the Nose (Ben Pansky. Review of Medical Embryology. Copyright Life LifeMap Sciences, Inc)



The nasolacrimal duct develops as an ectodermal thickening that gets buried in the mesoderm between the maxillary and lateral nasal prominences and eventually canalizes from superior to inferior.

Facial clefts, clefts of the lip and palate, and bifid nose are the result of impaired mesenchymal migration and fusion during this phase of development. Other abnormalities such as piriform aperture stenosis, choanal atresia, and arrhinia, result from excessive merging of these processes. Several regulatory genes have been associated with nasal development, including PTPN14, TBX22, and CHD7. Mutations of the PTPN14 gene are associated with choanal atresia, CHD7 is a cause of CHARGE syndrome, and TBX22 is linked with orofacial clefts. (6-8)

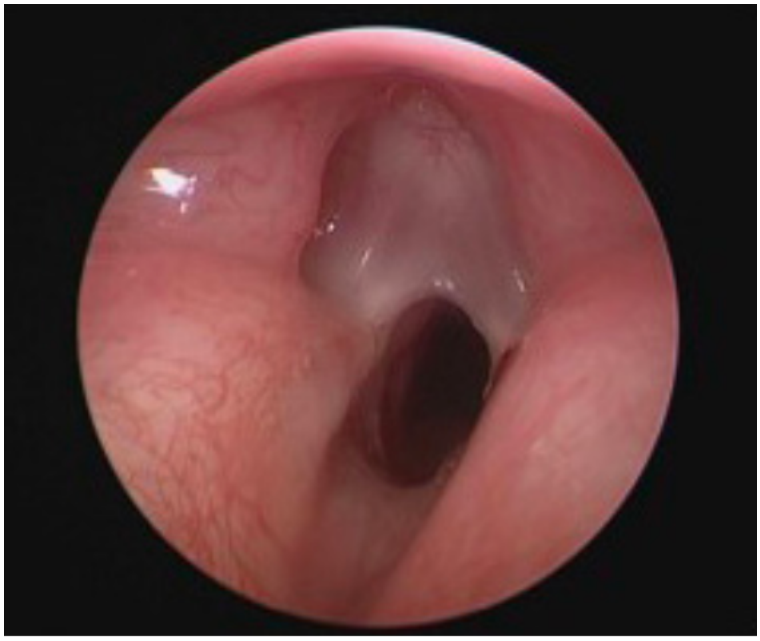
Development of the Pharynx, Larynx and Trachea

The first sign of the developing respiratory system is an epithelial thickening and out-pouching along the ventral aspect of the primitive foregut; this is known as the laryngotracheal diverticulum (LD). The LD appears at the end of the fourth week of gestation and is separated from the hepatic diverticulum by the septum transversum. This structure develops into the central tendon of the diaphragm. As the diverticulum grows, it forms a lung bud at its distal end. The LD becomes separated from the primitive pharynx by longitudinal tracheo-oesophageal folds, which form a septum. This septum divides the foregut into a ventral portion, the laryngotracheal tube (structures that will become the larynx, trachea, and lungs) and a dorsal part (that forms the oesophagus). The molecular mechanisms driving this early partition include the localized expression of Nkx2-1 (Tif1) in the ventral wall of the anterior foregut, while Sox2 expression predominates dorsally. Patterning of Nkx2-1/Sox2

expression is signalled by the expression of Bmps, noggin, Fgfs, Shh, and Wnts in the surrounding mesenchyme. (9)

The epithelium of the larynx arises from the endoderm of the cranial end of the laryngotracheal tube. The cartilage structures of the larynx are derived from the fourth and sixth branchial arches. The mesenchyme proliferates rapidly to form the arytenoid swellings, which grow towards the tongue, converting the slit-like glottis into a T-shaped opening and reducing the lumen into a slit. Due to rapid proliferation of the laryngeal epithelium, the lumen becomes occluded. Recanalisation occurs by gestational week 10. During this time the vocal folds, vestibular folds, and the laryngeal ventricles form. The epiglottis develops from the caudal part of the hypobranchial eminence (see Development of the Tongue).

The laryngeal muscles develop from the myoblasts of the fourth and sixth branchial arches. Laryngeal webs or atresia result from the incomplete canalization of the larynx at week 10 of gestation.

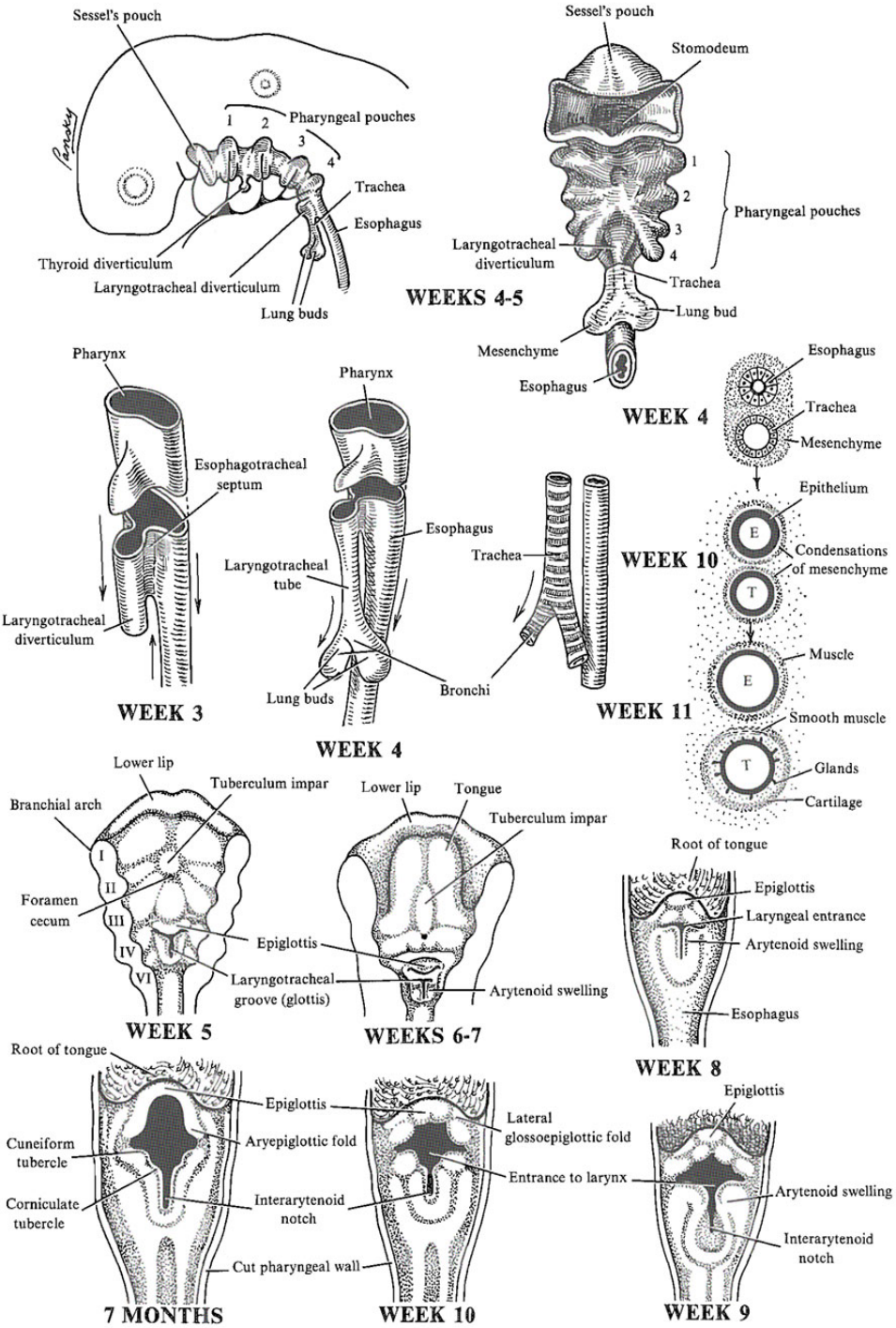


Clinical photograph 1: Laryngeal Atresia (partial)

The trachea develops from the endoderm of the distal part of the laryngotracheal tube. The cartilage, connective tissue and muscles are derived from the surrounding splanchnic mesenchyme. The development of smooth muscle posteriorly and cartilage anteriorly at regular intervals is guided by differential expression of Fgf10 and Shh (9). Likewise, Fgf10 plays an essential role alongside Fgfr2 in the branching morphogenesis of the lung buds. (10) Mesenchymal differentiation within the oesophagus results in a muscular layer of striated muscle in the upper one-third and smooth muscle in the lower two-thirds of the tube.

Laryngotracheal clefts and tracheoesophageal fistulas arise from incomplete division of the cranial part of the foregut into respiratory and digestive portions during gestational week 4 or defective fusion of the tracheoesophageal folds in the formation of the tracheoesophageal septum (11). Tracheal stenosis probably results from unequal partitioning of the foregut into the trachea and oesophagus. In rare cases, there can be complete atresia of the trachea.

Fig 5: Development of the Larynx and Trachea (Ben Pansky. Review of Medical Embryology. Copyright LifeMap Sciences, Inc.)



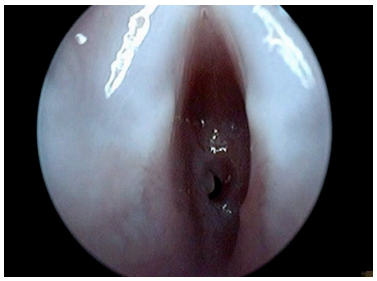
Synopsis of Upper Aerodigestive Tract Pathology in the Child

The obstetrician, neonatologist, paediatrician, or family physician may initiate a referral of a neonate with upper aerodigestive tract symptoms to an experienced paediatric otolaryngologist. The source of the referral may indicate the type and severity of the pathology. This synopsis discusses the presentation of a variety of airway and feeding disorders in an age chronological order from foetal presentations to school age presentations. The chapters in the rest of the thesis are organised in an anatomic fashion from cephalad to caudad.

Referral from the obstetrician is usually for an airway lesion identified at antenatal foetal ultrasound. Foetal magnetic resonance imaging (MRI) is also sometimes indicated. Severe cases may present with congenital high airway obstruction syndrome (CHAOS). These patients usually require an extrauterine intrapartum treatment (EXIT) procedure for delivery. This procedure entails securing the airway by intubation or tracheostomy while the foetus is still on placental oxygenation (12).

Patients with airway obstruction referred from a neonatal ICU may have primary pathology (ie, pathology of the nose, oropharynx, larynx, or trachea) or pathology caused by intubation. The latter is most frequently glottic or subglottic oedema or stenosis. Primary pathology is still most likely to be laryngomalacia, which is the most frequent cause of obstructed breathing and feeding difficulty in the newborn. Subglottic stenosis (SGS) may also present as a congenital lesion but is usually acquired following intubation trauma. The diagnosis is confirmed by microlaryngoscopy.

Mild stenosis (Cotton-Myer grade 2 or low grade 3) may be treated with endoscopic therapy only. This usually involves the use of balloon dilation with or without endoscopic cricoid split.(13-15) More severe stenosis requires a tracheostomy with delayed laryngotracheal reconstruction (LTR). In the absence of multiple comorbidities, primary LTR is performed to avoid the need for a long-term tracheostomy and its associated risks. This procedure often utilizing thyroid alar cartilage has largely replaced the open anterior cricoid split. (16-18)



Clinical photograph 2: Acquired Subglottic Stenosis

Laryngomalacia may present with feeding difficulties, failure to thrive, and/or symptoms consistent with obstructive sleep apnoea. In neonates with severe laryngomalacia, early intervention with supraglottoplasty to release short aryepiglottic folds and excision of redundant arytenoid mucosa has allowed earlier feeding and discharge. Previously, many of these neonates experienced repeated bouts of airway obstruction and feeding difficulty. In some cases, a tracheostomy is indicated. Patients with underlying neurological disease are more likely to require a tracheostomy (19).

Vocal cord paralysis or fixation is the next most likely diagnosis. These patients are investigated by awake nasendoscopy followed by microlaryngoscopy and bronchoscopy. Bilateral vocal fold fixation or paralysis presents with airway obstruction. The traditional approach was to perform a tracheostomy for the more

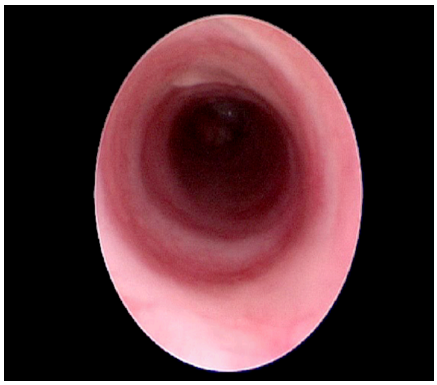
severe cases and manage others with close observation. Imaging of the brain is indicated to exclude lesions in the posterior fossa such as Arnold–Chiari malformation. The differential diagnosis includes posterior glottic stenosis and cricoarytenoid joint fixation. As with subglottic stenosis, there has been a trend towards managing these patients with primary surgical interventions to avoid a tracheostomy. This involves a posterior cricoid cartilage split and a costal cartilage graft placement via an endoscopic or an open approach to widen the glottic space and abduct the vocal folds (20, 21). Unilateral vocal cord paralysis is usually iatrogenic, following cardiac or oesophageal surgery and usually presents with aspiration and choking rather than airway obstruction (22).

Less frequently, lesions that affect the nose, such as choanal atresia or pyriform aperture stenosis, also cause respiratory distress in the newborn.
Choanal stenosis/atresia, a posterior nasal obstruction, is seen in approximately 1 in every 5000 to 7000 births, and, with utilization of high-definition prenatal ultrasound, it is increasingly diagnosed antenatally. Choanal atresia is a hallmark of CHARGE syndrome (23). In cases of bilateral choanal atresia, surgical intervention is mandatory in the perinatal period. Due to obligate nasal breathing, neonates with total bilateral nasal obstruction need immediate intervention. Those with partial nasal obstruction require less emergent intervention but may have significant feeding issues.

In rare cases, a nasolacrimal duct cyst or nasal mass may present as nasal obstruction and must be ruled out by a computed tomography (CT) scan during the evaluation process.

Congenital nasal pyriform aperture stenosis differs from choanal atresia in that the obstruction occurs anteriorly at nasal bony inlet. Its diagnosis carries a genetic significance, as it is associated with holoprosencephaly, hypopituitarism, and septo-optic dysplasia. Surgical intervention is more likely in cases in which the pyriform aperture width is <6 mm, as determined by CT (24).

Distal tracheal lesions (tracheomalacia, complete tracheal rings) may be encountered. In the case of complete tracheal rings, the typical C-shaped cartilage is fused posteriorly and lacks the posterior membranous trachea. CT or MRI, along with angiography may be used to further evaluate the stenosis as well as evaluate for vascular malformations/anomalies and extrinsic compression. Bronchoscopy remains the gold standard for diagnosis to assess the length of involvement. Less severe stenosis may be monitored, although treating associated gastro-oesophageal reflux is crucial. Respiratory illness may require steroids and close monitoring. Tracheal clearance may be affected, leading to recurrent pneumonia, necessitating culture-directed antibiotic therapy. Slide tracheoplasty, with the assistance of temporary cardiac bypass, is the procedure of choice for severe lesions (25, 26)



Clinical photograph 3: Complete tracheal rings

Chronic aspiration also presents with breathing and feeding difficulty. This may be seen in structural (such as laryngeal clefts or tracheoesophageal fistulae) or

neurological disease. Aspiration of the child's feeds can be addressed by treating the underlying anatomical anomaly, modifying oral intake, or delivering nutrition directly to the stomach. Aspiration of gastric reflux is managed similarly or can be addressed by fundoplication. Salivary aspiration can be challenging to control in these patients, leading to chronic cough, recurrent respiratory infections, and chronic lung disease. Managing chronic salivary aspiration is therefore an essential function of the complex airway team (27, 28).

Lesions of the tongue base, such as lingual thyroglossal duct cysts, lingual thyroid tissue, and vallecular cysts may all cause acute airway obstruction in the neonate. These lesions may all be treated surgically and have an excellent prognosis (29-31). Community physicians may refer patients with pathology that presents later in in infancy, such as milder cases of laryngomalacia, nasolacrimal duct cysts, choanal stenosis, and tongue-base pathology. Subglottic hemangiomas as well as mild cases of tracheomalacia or tracheal stenosis may present to a family physician when they become symptomatic several weeks post-delivery. Likewise, patients with less severe subglottic stenosis may be identified by their local medical facility in infancy, rather than in the neonatal period, with recurrent croup or exertional dyspnoea.

The most common causes of airway obstruction in older children include adenotonsillar hypertrophy and inferior turbinate hypertrophy. Adenoidectomy, adenotonsillectomy, and medical or surgical treatment of turbinate hypertrophy are well-established and usually successful in reducing the airway obstruction (32). Nevertheless, some children present with symptoms that are refractory to commonly utilized treatments. (33). The obstructed breathing in these patients may be due to septal deformity, tongue- base obstruction, or less commonly, laryngomalacia. This

usually calls for less conventional treatments such as supraglottoplasty, epiglottopexy, lingual tonsillectomy, and midline posterior glossectomy (34-37).

Chapter 2

Overview of the Management of Paediatric Airway Disorders

1. **Vijayasekaran S**, Lioy J, Maschhoff K. Airway disorders of the fetus and neonate: An overview. Semin. Fetal Neonatal Med. 2016;21(4):220-9.

2. **Vijayasekaran S**. Pediatric airway pathology. Front Pediatr. 2020;8:246.

***Publications 1 and 2*:** Two review articles in which I was the primary author discuss the anatomy, physiology, and pathology of the paediatric airway and summarise the management of paediatric airway disorders. One of these publications (Sem Fetal Neonat Med, 2016) focuses on disorders affecting the foetus and the neonate. It was coauthored by two neonatologists from the Children's Hospital of Philadelphia. The second publication in this chapter focuses on pathology affecting the neonate and infant. This was published in Frontiers of Paediatrics (2020) and serves as a guide for paediatricians or general otolaryngologists regarding contemporary management strategies for paediatric airway disorders.

Chapter 3

Nose and Paranasal Sinuses

3. **Vijayasekaran S**, Elluru RG, Prunty S. Congenital Malformations of the Nose and Paranasal Sinuses. In: Paparella MM, da Costa SS, Fagan J. Paparella's otolaryngology head and neck surgery
4. Wormald R, Hinton-Bayre A, Bumbak P, **Vijayasekaran S**. Congenital nasal pyriform aperture stenosis 5.7 mm or less is associated with surgical intervention: A pooled case series. Int. J. Pediatr. Otorhinolaryngol. 2015;79(11):1802-5.
5. Pollaers K, Herbert E, Giblett N, Thompson A, **Vijayasekaran S**, Herbert H. Re-thinking congenital piriform aperture stenosis: Modern imaging demonstrates narrowing of the full nasal cavity length. Int. J Pediatr Otorhinolaryngol. 2022;158:111184.
6. O'Neil LM, Pollaers K, Sale P, **Vijayasekaran S,** Herbert H. The utility of balloon dilation for piriform aperture stenosis: A first line surgical treatment. Int. J Pediatr Otorhinolaryngol. 2023:111654.
7. Ha J, **Vijayasekaran S**. Congenital choanal atresia and pyriform aperture stenosis. Int. J Pediatr Otorhinolaryngol. Extra. 2011;6(4):265-8.
8. Ha J, Lee F, **Vijayasekaran S**. Congenital Nasolacrimal Duct Cysts in Infants: Case Series and Literature Review. Surg Res Pract. 2018;2(1):16-20.

***Publication 3*: A Summary of Congenital Nasal Malformations**

This publication "Congenital Malformations of the Nose and Paranasal Sinuses" summarises congenital nasal deformities that often present with airway obstruction. This chapter was published in the 2-volume textbook entitled Paparella's Otolaryngology: Head and Neck Surgery and is the most recent of several chapters that I have published on this topic.

***Publications 4-7:* Congenital Nasal Piriform Aperture Stenosis (CNPAS)**

CNPAS is a rare condition, first described by Douglas in 1952 (38). The piriform aperture (PA) is the anterior limit of the bony nasal cavity. It is bound inferiorly by the maxillary process of the maxillary bone, laterally by the frontal processes of the maxillary bone, and superiorly by the nasal bones. The first radiological description of piriform aperture stenosis was in 1988 (39), and the first clinical case series was published the following year (40).

Early diagnosis and management are essential for this potentially life-threatening condition. Given that neonates are obligate nasal breathers, narrowing can significantly impact them.

Nasal obstruction can affect primary airflow and the suck-swallow-breathe reflex of affected infants. Patients present on a spectrum of shortness of breath when feeding, failure to thrive and nasal congestion, to persistent nasal obstruction leading to oxygen desaturations, apnoeas, and cyanosis. They can be managed non-operatively or operatively. The aim of management is to utilise the least invasive approach to increase the width of the aperture and nasal cavity to enable breathing and feeding while allowing the patient to grow. In some cases, medical management can be sufficient, achieved by reducing soft tissue oedema and keeping the nasal

airway clear. This approach includes the use of intranasal decongestants, intranasal steroids, and saline, in conjunction with periodic nasal suction. Surgical treatment is usually reserved for patients who fail non-operative therapy. Traditional surgical treatment was to perform an open sublabial approach to widen the piriform aperture (40).

Publication 4: The aim of this study was to provide a radiologically measured pyriform aperture (PA) width that predicts the need for surgical intervention. Objective measurement using CT of the piriform aperture width is usually performed to make the diagnosis. Based on a multi-institutional pooled case series (including a case series with my patients), we identified that a piriform aperture width of <5.7 mm is an indication for surgical intervention. This article has been cited 41 times, and for the first time, provided a measurement for surgeons trying to decide if surgical intervention is indicated. It is the most extensive series of patients with CNPAS published to date.

Publication 5: Subsequently, further evaluation of imaging data made it clear that it was not just the piriform aperture but rather, the entire length of the nasal cavity that is narrowed in CNPAS. A case-control study was undertaken to evaluate 14 of our cases and 100 matched controls. Results showed that the bony nasal cavity was narrower at the piriform aperture and at 25%, 50%, and 75% along its length between the piriform aperture and the choana. Traditional surgical treatment for piriform aperture stenosis addressed only the anterior aspect of the nasal stenosis. Dilation of the piriform aperture has been described in the literature, with Wine et al. reporting a case series of 4 patients in whom Hegar cervical dilators were utilised.(41) In this cohort, 2 patients required repeat dilation and none required drill-out or nasal stents. The use of balloon dilation has also been described by Gungor et

al., who reported a single case with an excellent clinical outcome with balloon dilation and post-dilation insertion of a nasal stent. (42)

Publication 6: In 2017, I performed a balloon dilation of the nose on a patient with CNPAS. This child required only a single, minimally invasive procedure. Since then, I have treated 3 other children with CNPAS, performing balloon dilation as the initial procedure. My colleagues at Perth Children's Hospital have treated 3 more cases. All patients underwent general anaesthesia and endotracheal intubation. Topical 1:10,000 adrenaline was used to vasoconstrict the nasal mucosa. Sinoscopy was performed with a 1.9 mm paediatric rigid nasendoscope to assess the nasal cavity size. A 6 – 7mm balloon was used to dilate the nasal cavity. The balloon was held at pressure for 60 seconds. The dilation was repeated twice under the same general anaesthetic. Whilst dilating one nasal cavity, a 3.0 endotracheal tube was placed in the contralateral nasal cavity to apply counter pressure to prevent septal deflection. In patients who required a stent, a 3 mm ivory Portex endotracheal tube (Smith Medical, USA) was fashioned into a nasal stent, which enabled securing around the posterior septum and at the columella. Patients who underwent steroid injection had triamcinolone acetonide (40mg/1mL – Kenacort A40) injected submucosally. Post-operatively all patients were given Xylometazoline and saline drops, with regular suction of the stents if placed. All patients were followed up regularly, and decisions for further management were based on clinical response to interventions. Four of the six patients were managed with balloon dilation only. Two patients required an open surgical drill out. The patients requiring multiple interventions and a drill-out were medically complex, with significant comorbidities.

Publication 7: An extremely rare case of choanal atresia and congenital nasal piriform aperture stenosis that presented to the Princess Margaret Hospital for

Children was reported and published in 2011. This case study highlighted that these two rare anomalies can occur simultaneously.

Over the last decade these articles have defined the point of CNPAS at which surgical intervention is indicated (most patients with an aperture < 5.7mm) and found that in patients with CNPAS, the narrowing is not limited to the piriform aperture, but involves the entire length of the nasal cavity. As such, balloon dilation, which addresses the entire length of the nasal cavity, may have an advantage over the traditional open approach of widening the piriform aperture alone and is an effective treatment for uncomplicated cases of CNPAS.

Publication 8: **Nasolacrimal Duct Cysts**

Nasolacrimal duct cysts are a rare and often missed cause of airway obstruction in neonates (43, 44). In this publication, we described a series of infants with congenital unilateral or bilateral nasolacrimal duct cysts (NLDC) and intranasal mucoceles who presented at different stages of infancy with intermittent respiratory distress. All four patients required surgical intervention for symptomatic disease. One hundred fifteen cases of congenital NLDC with significant nasal extension were reported in the literature of which 93 cases were reported to have symptomatic respiratory distress. The majority (87%; n=100) of the cases underwent some form of surgical intervention. We concluded that although cases of congenital NLDC causing nasal obstruction are rare, they should nevertheless be considered in the differential diagnosis of infants with symptoms of upper airway obstruction. Surgery is the definitive treatment and results in an immediate resolution of symptoms.

Chapter 4

Pharynx

9. Zhen E, Locatelli Smith A, Herbert H, **Vijayasekaran S**. Midline posterior glossectomy and lingual tonsillectomy in children with refractory obstructive sleep apnoea: factors that influence outcomes. Aust J Otolaryngol. 2022;5:24.

Adenotonsillar hypertrophy is recognised as the most common cause of upper airway obstruction in children, and frequently leads to sleep disordered breathing. Less commonly, in children, macroglossia and glossoptosis result in OSA. In patients who fail adenotonsillectomy and management of nasal obstruction, the tongue base is the most frequently identified pathology causing OSA. (45) Our recent retrospective review of 41 patients who underwent drug-induced sleep nasendoscopy (DISE) was presented at the European Society of Paediatric Otolaryngology meeting in 2023 (Friedland Y, Blokland R, Vijayasekaran S). We also identified the tongue base as the most common site of obstruction and the site that has the most severe degree of obstruction.

(Table 5 and Figure 6)

Figure 6: Anatomic Sites of Obstruction (% of cases) (Friedland, Blokland and Vijayasekaran, 2023).

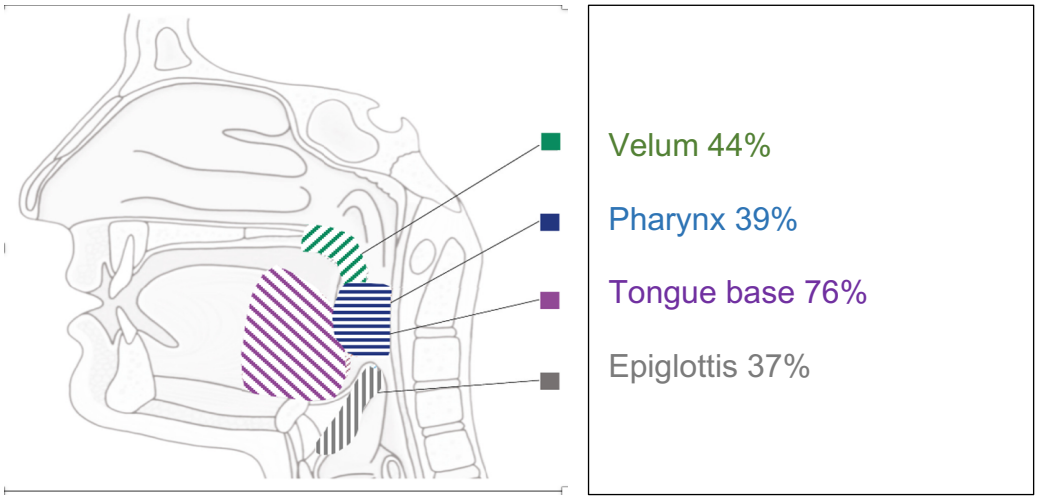


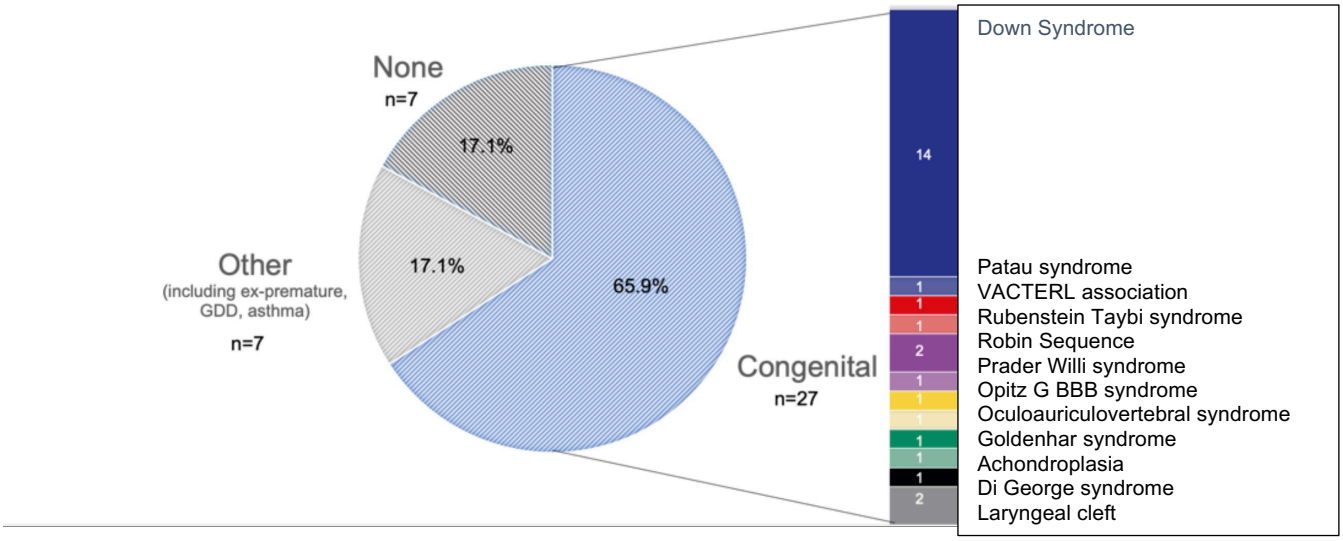
Table 5. Patient Demographics, Findings, and Procedures

PATIENT CHARACTERISTICS	n	%	Mean	± SD
Age at DISE (years)			6.2	4.1
Gender				
Female	17	41.5		
Male	24	58.5		
BMI (kg/m^2)			18.2	4.8
BMI percentile*				
Underweight (<5%)	4	9.8		
Normal range (5-85%)	22	53.6		
Overweight (85-95%)	4	9.8		
Obese (>95%)	11	26.8		
Comorbidities				
Yes	34	82.9		
No	7	17.1		
Surgical history				
Surgically naïve	13	31.7		
Previous adenoidectomy/tonsillectomy	28	68.3		
Anatomical obstruction site				
Multiple sites	34	82.9		
Single site	7	17.1		
Adenoid	1	14.2		
Supraglottis	1	14.2		
Tongue base	5	71.4		
Adenoid/tonsillar hypertrophy**				
Adenoid grade				
0	12	29.3		
1	10	24.4		
2	12	29.3		
3	5	12.1		
4	2	4.9		
Tonsil grade				
0	21	51.1		
1	4	9.8		
2	7	17.1		
3	9	22		
4	0	0		
Surgical intervention following DISE				
Yes	33	80.5		
No	8	19.5		
Polysomnography				
Preoperative	37	90.2		
OAHI*** (events/hour)			11.0	17.6
SpO_2 nadir ****(%)			81.9	11.4
Postoperative	24	58.5		
OAHI (events/hour)			7.4	9.5
SpO_2 nadir (%)			84.9	12.4

*based on CDC guidelines; **using Brodsky grading scale 1-4 where 0 = no tissue present OAHI*** – obstructive apnoea/hypopnoea index. SpO_2 nadir **** (lowest oxygen desaturation)

Management of the tongue base in children is evolving. The tongue-base issues that cause obstructed breathing in children with mandibular growth disorders (e.g., Robin sequence) or congenital syndromes associated with macroglossia (e.g., Trisomy 21, Beckwith Wiedemann syndrome) may result in infants who present with airway obstruction, often despite adenotonsillectomy. Diagnoses identified in our case series are presented below (Figure 7).

Figure 7: Diagnoses identified (Friedland, Blokland and Vijayasekaran, 2023)



Publication 9: Although adenotonsillectomy is a successful treatment for paediatric obstructive sleep apnoea (OSA), success rates in certain groups of children are much lower and refractory OSA (rOSA) my persist. Based on works of other teams we know that this group of children often present with airway obstruction at the level of the tongue base. Tongue base reduction (TBR) by lingual tonsillectomy (LT) or midline posterior glossectomy (MPG) are utilised to treat the tongue base. The tongue base was also the most common site of airway obstruction in our DISE series (discussed above). Hence, the aim of this study was to assess the efficacy of midline posterior glossectomy (MPG) to treat refractory OSA (rOSA). There is very little published on this topic. This article describes a single surgeon, single institution

audit of outcomes. It is one of only four studies reporting on the use of TBR to treat macroglossia and glossoptosis in children with rOSA.

Other authors include Propst et al. who conducted a retrospective study of 13 children with Down syndrome. They found a statistically significant reduction in mean AHI (apnoea-hypopnoea index, a marker of OSA severity) in non-obese children following MPG (36). Totham reported on robot-assisted lingual tonsillectomy (LT) and MPG in 9 patients and Wooten et al. in 17 cases (46, 47). Most patients in these two studies had multilevel surgery, so it is difficult to comment on the success of MPG alone. More recently, Ulualp conducted a retrospective study of 10 children who underwent MPG and found a statistically significant reduction in AHI in all children, with the greatest improvement in children of normal weight (48). Only 51 cases of MPG performed in children have been reported in the literature. A systematic review published in 2017, included MPG and LT (114 patients from 11 studies). However, only 24 of the 114 patients who were assessed had an MPG. The AHI, when considering all 114 patients, by improved by 48.5%. As expected, there was a more significant improvement in the AHI for non-syndromic children than for syndromic children. Children with Down syndrome had the smallest improvement in AHI. A confounder is that the group with Down syndrome had the highest BMI compared to both children with other syndromes and non-syndromic children(47, 49).

In our study, 15 patients with moderate to severe OSA underwent TBR using LT (3/15) MPG (9/15) and MPG with LT (3/15). The surgery was tailored to the patients' anatomical anomalies. Eleven patients were diagnosed with a syndrome and 7 had a history of cardiopulmonary disease. One third of the patients were obese (BMI ≥95th percentile). Ten patients (66.7%) demonstrated complete resolution of rOSA after

TBR (33.3% patients who underwent MPG with LT, 66.7% patients who underwent MPG alone, and all patients who underwent LT alone)

Children with preoperative BMI <95th percentile had significant improvements in OAHI (*P* = 0.008) compared to those with BMI ≥95th percentile (*P* = 0.465). Hence, we concluded that in children with rOSA who have a BMI < 95th percentile, TBR is likely to be successful in managing macroglossia and glossoptosis.

Chapter 5

Larynx

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Stridor is a common presenting complaint in children with laryngeal and tracheal pathology. Its prevalence in newborn patients ranges from 0.17 to 5.8% (50). Most patients younger than age 1 who present with this symptom have a structural problem, and in many of these patients, the abnormality causing stridor is laryngomalacia (50).

Laryngomalacia

Publication 10: Laryngomalacia is the most common cause of airway obstruction in neonates (51), The most common indications for surgery in affected patients are feeding difficulty and failure to thrive. This publication (experience of a single surgeon at a single institution) utilized polysomnography to accurately determine the severity of obstruction in patients who presented with laryngomalacia (LM) causing obstructive sleep apnoea (OSA). The outcomes of surgery (supraglottoplasty) for this group of patients with laryngomalacia was assessed. Of 46 patients who underwent surgery to treat LM, 10 were suitable for inclusion in the study. Exclusion criteria included patients who presented with recurrent episodes of cyanosis and desaturation whilst awake, and those who presented with failure to thrive and feeding difficulty as the indication for surgery. Further exclusion criteria included patients undergoing revision supraglottoplasty, cases with secondary airway lesions, and cases in which supraglottoplasty was performed in combination with other procedures such as adenoidectomy or adenotonsillectomy.

In this case series, the mean age at first presentation with laryngomalacia was 2 months and 19 days (range 30–134 days). Statistically significant improvements occurred in mean values for total sleep time (P = 0.049), Lowest Oxygen Saturation

Levels (LSAT) (P = 0.006), Obstructive Apnoea Hypopnoea Index (P = 0.009) and respiratory disturbance index (RDI) (P = 0.002), following supraglottoplasty.

Two other publications in 2006 and 2008, respectively, described the outcomes of early supraglottoplasty for laryngomalacia presenting with OSA (50, 51). This study was the third publication describing the benefits of supraglottoplasty in patients with OSA.

Subsequently two meta-analyses have been published on this topic. Our article was one of only eleven articles to be included in one meta-analysis and one of four studies in another metanalysis (52, 53). Both reviews found that supraglottoplasty is an effective treatment modality for most patients with laryngomalacia presenting with OSA, albeit with some patients having incomplete resolution of symptoms.

Neonatal intubation is a medical procedure performed on newborns who require assistance with breathing or airway management. It involves the insertion of an endotracheal tube (ETT) into the infant's trachea through the mouth or nose. This procedure is performed to secure the airway and ensure proper ventilation in infants who cannot breathe adequately. It is commonly carried out in situations such as respiratory distress syndrome, meconium aspiration, prematurity, birth asphyxia, and other conditions that compromise a baby's ability to breathe effectively. Complications of intubation include laryngeal oedema, cricoarytenoid joint fixation, subglottic cysts, posterior glottic stenosis, and SGS.

Cricoarytenoid Joint Fixation

Publication 11: Vocal fold immobility can be due iatrogenic, idiopathic, neurologic, or traumatic causes (54), and treatment is based on symptoms. Unilateral vocal fold immobility presents with dysphonia and aspiration, whereas bilateral immobility presents with stridor and respiratory compromise. When the cause of immobility is idiopathic or neurologic, observation before definitive surgery is recommended to allow time for spontaneous resolution. In cases where immobility is caused by scarring or joint pathology, spontaneous resolution is unlikely to occur, and hence, early surgical intervention can be implemented. Electromyography of the laryngeal musculature is one way to approach to the assessment of neurological function. (54, 55)

In my publication (publication 11 of this thesis) of the histopathology of post-mortem specimens of the cricoarytenoid joint (CAJ) we showed that in previously intubated children, reduced vocal fold mobility is not always due to paralysis of the recurrent laryngeal nerve. (22) It may be due to inflammatory arthropathy, leading to CAJ

fixation. (56) This can be easily misdiagnosed as vocal cord paralysis. Laryngeal specimens from infants intubated for prolonged periods demonstrate evidence of bleeding, infection, inflammation, and fibrosis within the CAJ. In cases where we found normal CAJs, the infants had been intubated for a mean (median) duration of 6 days (range, 1-20 days). In cases where abnormal CAJ histopathologic findings were seen, infants had a mean intubation duration of 21 days (range 14-30 days). In the cited study, I found a significant difference in mean intubation times between the group with normal CAJ histologic findings and the group with abnormal CAJ histologic findings (P=.02). This has implications for treatment, because if CAJ fixation (rather than vocal cord paralysis) is the cause of vocal cord immobility, early surgery rather than observation, non-invasive ventilation, or tracheostomy is an acceptable course of action. Whereas in cases of neurological vocal fold immobility, reconstructive surgery is usually delayed whilst waiting for nerve regeneration. I undertook this research during my fellowship at Cincinnati Children's Hospital Medical Centre (Cincinnati, Ohio, USA), and it is important to note that this is the only study in the literature that examines the CAJ in intubated infants. This research was awarded the Charles Ferguson Award for the best presentation at the American Society of Pediatric Otolaryngology meeting, 2005.

Subglottic Stenosis

As a result of long-term intubation for dependence on mechanical ventilatory assistance, which was first introduced in the 1960s (57), the incidence of acquired subglottic stenosis in neonates has increased Currently, up to 10% of intubated neonates develop this disorder (58, 59).

The standard treatment of airway obstruction, including SGS, has been the tracheostomy. Although this procedure was first described by Chevalier Jackson in 1909 (60), given its relatively high associated morbidity and occasional mortality rates in neonates, there has been an impetus to find alternatives for treating SGS. Various endoscopic and open surgical options were advocated in the 1970s. (61-64) These included dilation, steroid injection, various ablative procedures, anterior cricoid split (ACS), posterior cricoid split, Laryngotracheoplasty, and laryngotracheal reconstruction using costal cartilage grafts.

Laryngotracheal reconstruction (LTR) is a procedure using an autologous cartilage graft to enlarge the calibre of the larynx and proximal trachea as a treatment for SGS to improve the airway. My mentor, Dr. Robin T. Cotton, first described LTR in the 1970s. (61) It is now the most widely used procedure for the treatment of SGS in children.

Prior to the use of LTR, endoscopic therapy or ACS were the only treatment options. After the advent of LTR, initially, a tracheostomy was created and delayed reconstruction was performed once the child reached a certain weight (10kg and subsequently, revised down to 4kg). (65) The patient's tracheostomy is subsequently removed at a later date. This procedure was known as a double-stage LTR.

The subsequent development of single-stage LTR, in which the patient is decannulated at the reconstruction, has led to the options of reducing tracheostomy dependence, reconstruction at a younger age, and the ability to treat SGS without performing a tracheostomy. (17, 66-70) The efficacy of laryngotracheal reconstruction in avoiding a tracheostomy in infants and neonates with SGSs has been of particular interest to me.

Publications 12 and 13 reported the results of the use of LTR in neonates and infants younger than 1 year of age. This research has significantly advanced the surgical paradigm so that selected younger children and those weighing less than 5kg (the traditional benchmark) can undergo reconstruction without requiring postoperative tracheostomy.

Publication 12: This publication, written with colleagues from Cincinnati Children's Hospital Medical Centre (Cincinnati, Ohio, USA), is a case-control study with a cohort of patients who underwent ACS compared to a cohort of patients who underwent LTR. Twenty-one infants younger than 6 months of age who underwent single-stage LTR as an alternative to tracheostomy were compared with 11 infants who underwent ACS as an alternative to tracheostomy. The operation-specific success was defined as extubation without subsequent tracheotomy or revision of the open-airway procedure. We found that infants who underwent LTR had a greater number of grade 3 SGS (*P*=.02). The mean age of patients was similar: 3.7 months in the LTR group vs. 2.8 months in the ACS group (*P*=0.12). The operation-specific success rate was 81% in the LTR group and 27% in the ACS group (*P*=0.006), even though the LTR group had more severe stenosis. We concluded that single-stage LTR should be considered as the first alternative to tracheotomy when SGS is the primary airway lesion.

Publication 13: This publication describes a case series of patients younger than 12 months of age who underwent single-stage LTR for SGS at Princess Margaret Hospital over a 3-year period. Nine patients had a diagnosis of acquired SGS and 1 had congenital SGS. The median birth gestation of these patients was 26 weeks (range, 23-41 weeks), and the median birth weight was 0.87 kg (range, 0.59-3.2 kg). The median corrected age at which patients underwent surgical repair was 8 weeks

and 3 days, and the median weight was 3.05 kg (range, 2.2-9.0 kg). Significant comorbidities were present in 9 of 10 patients. Prematurity and prematurity-related lung disease were most commonly seen. The mean intubation period after surgery was 6.8 days (range, 5-9 days). Nine of 10 patients had complete resolution of their airway symptoms. We concluded that LTR is a safe and effective alternative to long-term tracheostomy for young infants weighing less than 5 kg.

In addition to LTR, another procedure for treating severe SGS is cricotracheal resection (CTR), which is reserved for cases in which the stenosis is too severe to perform LTR.

Publication 14: CTR is a procedure that involves resection of the anterior cricoid arch and thinning of the posterior cricoid plate. The transected normal trachea is then telescoped into the posterior cricoid plate and anastomosed to the posterior laryngeal mucosa and thyroid cartilage (71, 72).

The youngest age at which CTR can be successfully performed has been controversial. Research coauthored during my fellowship with colleagues at Cincinnati Children's Hospital shows that with an experienced team, even in children younger than age 2 years, a CTR that enables decannulation without prolonged tracheostomy tube dependence can be performed (73).

Subglottic Cysts

Publications 15 and 16: Although subglottic cysts (SGCs) are rare, they are an important cause of stridor in neonates (74, 75). They can present with significant airway obstruction and potentially have lethal consequences. Although laryngeal cysts can be congenital (rare) or acquired, most SGCs follow a period of intubation.

Two publications report the rare presentation of a congenital SGC and investigate the aetiology of acquired SGC's.

Publication 15 is a case report on the very rare entity, congenital subglottic cyst, and reports on the presentation and management of this lesion.

Publication 16 is a case control study investigating acquired SGC's. We looked at several variables in 2 matched groups of intubated patients who underwent airway evaluation for various reasons and found no difference in the size of the endotracheal tube (ETT), number of re-intubations, or duration of intubation between the cases with and those without (control group) SGC's. There was, however, a significant difference between cases and controls in the endotracheal tube suction (7.3 vs 3.7) events per day. Even though we could not account for the increased suction frequency in cases as compared to controls, we hypothesised that this may be due to infection or gastro-oesophageal reflux. Whether these conditions caused the cysts or whether the trauma caused by manipulation of the ETTs caused the cysts requires further investigation.

Preventing Intubation Injury

Although significant progress has been made over the past few decades in managing the adverse consequences of neonatal intubation, avoiding these negative consequences while preserving life and providing adequate oxygenation and ventilation is equally important. Although the reported incidence of SGS in the neonatal population ranges from 0% to 11%, it is generally thought to be between 0% and 2%. The main risk factors for severe acquired SGS are low birth weight, low gestational age, longer duration of intubation, traumatic intubation, multiple number of intubations, a large diameter endotracheal tubes (ETT) and infant activity level.

(58, 76-79) In view of these factors, together with the Neonatology, Intensive care, and Anaesthesia Departments at Princess Margaret Hospital, we undertook a collaborative project to better identify the aetiopathogenesis of severe SGS and to reduce the risk of laryngeal injury in intubated neonates.

Publication 17: Over nine years (January 2006 to December 2014) 50 infants for whom I performed surgical intervention to treat SGS were identified from the ENT surgery database. During this period 2913 infants were intubated and ventilated in the neonatal intensive care unit (NICU). Congenital SGS was the diagnosis in 7 of the 50 (14%) patients, and 43 of 50 (86%) had acquired SGS (ages 2 weeks to 13 years). Of the 43 patients with SGS, 37 had previously been intubated during the neonatal period (7 patients were intubated after leaving the NICU). Thirty-five cases were born at less than 30 weeks' gestation. Seven patients had grade 2 stenosis, 23 had grade 3 stenosis, 1 had grade 4 stenosis, and 4 were not classified on the Myer-Cotton Classification Scale. (80) Eleven patients underwent an initial tracheostomy at a median age of 47 weeks; all but 3 of these patients subsequently underwent LTR at a median corrected age (CA) of 15.5 months (range 5–36 months). The median time from tracheostomy to LTR was 15.5 months. Of the 32 who underwent LTR, the procedure occurred at a median CA of 10.5 months (range 0–88 months CA).

This surgical group was compared to a matched control population of 70 patients identified from the total number of intubated patients. The incidence of SGS in surviving children who had required ventilation in the neonatal period was 27/2913 (0.93%). Incidence was higher in infants <28weeks' gestation (3.8%) compared to infants who were ≥28weeks' gestation (0.13%; *P*=0.0001). On univariate analysis,

risk factors for SGS were 1) a higher number of intubations (P<0.001); 2) longer duration ventilation days (P<0.001); 3) unplanned extubation (P=0.007); 4) traumatic intubation (P=0.003) and 5) oversized endotracheal tubes (ETTs) (P=0.001). On multivariate analysis, risk factors for SGS were: 1. Sherman ratio >0.1 (ETT size/ gestational age), 2. more than five previous intubations and 3. traumatic intubation. The results suggest that more intubations, prolonged intubation, unplanned extubation, traumatic reintubation, and oversized uncuffed tubes (identified by a Sherman ratio >0.1) were independent risk factors for developing SGS.

These findings led to a proposed change in management, and a randomised control study was completed by the same multidisciplinary team to compare cuffed (smaller) ETT versus uncuffed ETT with respect to the incidence of SGS. The primary outcome was the achievement of optimal ETT leak in the target range (10%–20%). The secondary outcomes included reintubations, ventilatory parameters, ventilatory complications, post-extubation complications, and long-term follow-up. There was no difference in the primary outcome, though the percentage time spent in the optimal leak range was significantly higher in the cuffed ETT group. Cuffed ETTs enable the team to better manage ventilator leaks (leaks result in poor ventilation and hence increase the risk of atelectasis), reducing the need for reintubations to optimise ETT size and episodes of atelectasis. The outcome suggested that cuffed ETTs may be a feasible alternative to uncuffed ETTs in this group of patients (81).

Both of these publications were part of Dr. Rebecca Thomas' (Neonatologist, Perth Children’s Hospital) Master’s thesis.

Subglottic Haemangioma

Publication 18: The use of beta-blockers to reduce the size of subglottic haemangiomas has dramatically revolutionised treatment outcomes for patients with these lesions (82). Nonetheless, 12% of subglottic haemangiomas are not responsive to medical therapy (beta-blockers and corticosteroids) (83). In these cases, as shown in publication 18 (a retrospective case series and literature review), open resection is a highly effective option to avoid the traditional approach of tracheostomy and waiting for involution. This study included 22 children ranging in age from 2 to 42 months (median age, 5 months) who underwent open excision of subglottic hemangioma over a 10-year period. Twenty-one patients were treated with single-stage procedures, with postoperative endotracheal intubation for an average of 5 days. Cartilage grafts were inserted in 10 patients. None of the patients developed SGS. Twenty-one patients reported good voice and no airway symptoms after a mean follow-up period of 42 months. One patient, who remains minimally symptomatic, developed an anterior glottic web. Also, 1 patient required a 6-month course of steroids after surgery to treat residual glottic hemangioma.

Laryngeal Atresia

Publication 19: 22q11.2 deletion syndrome (22q11.2DS) is a chromosomal disorder with a multisystem set of symptoms varying in clinical expression. Patients are at increased risk of airway anomalies, with partial laryngeal atresia (PLA) also called glottic webs, being one of the most common. This article reports a series of my patients (from 2009-2020) with partial laryngeal atresia and a diagnosis of 22q11.2 deletion. It documents diagnosis, surgical options, outcomes, and proposes an approach in which early intervention is carried out so to avoid long-term tracheostomy, even in severe cases. Cohen classified the degree of atresia as I-IV

depending on the degree of stenosis (84). The Cohen classification is as follows: type I, less than 35% obstruction; type II, between 35% and 50% obstruction; type III, between 50% and 75% obstruction with subglottic extension and involvement of the anterior cricoid; and type IV, glottic stenosis up to 99%, with associated SGS. Surgical management of the airway secondary to PLA varies according to the severity of the airway obstruction and comorbidities.

Ten patients between 4 days and 17 months of age were identified and 8 underwent surgery to treat atresia. The main presenting symptoms were stridor (75%), dysphonia (62%), and dysphagia (85%). Comorbidities were cardiac pathology (75%), craniofacial anomalies (50%), global development delay (62.5%), palate defects (75%), and immunodeficiency (50%). Classification: 33% Cohen type I, 11% type II, and 56% type III. Surgical procedures included endoscopic web division (n=3), laryngotracheal reconstruction (LTR) with anterior cartilage graft (n=4), and slide thyro-crico-tracheoplasty (n=1). Three patients required a peri-operative tracheostomy. At last clinical assessment, all patients were sized with an age-appropriate airway and were free of tracheostomy. Dysphonia and dysphagia are common in this group. While children with mild laryngeal obstruction are successfully treated with an endoscopic procedure, patients with severe obstruction typically require open airway reconstruction. Compared with previous reports (85, 86), our population was significantly younger and no patient required tracheostomy before LTR, suggesting that open airway reconstruction may be a safe option for young patients with 22q11.2 DS laryngeal atresia to avoid the complications of a long-term tracheostomy. This once again highlights the role of early definitive intervention to treat the neonate with airway stenosis, thereby avoiding tracheostomy.

Tracheostomy

Publication 20: Not all patients can avoid the need for a tracheostomy, and the procedure is not without associated risks. The most common serious complication of tracheostomy is accidental decannulation. Paediatric tracheostomy with Maturation Sutures was published in the surgical video journal c-surgeries.com (https://doi.org/10.17797/2020081101). This is an instructional video of the recommended technique for paediatric tracheostomy with the use of maturation sutures (a well recognised, but not universally practiced technique), which improve the safety of the procedure (87).

Chapter 6

Trachea

21. Jackson C, **Vijayasekaran S**, Orford J. Exomphalos and type IV laryngeal cleft: a surgical challenge. Eur J Pediatr Surg 2009;19(2):124-5.

22. Sim G, **Vijayasekaran S**. Novel use of coblation technology in an unusual congenital tracheal stenosis. J Laryngol Otol. 2014;128(S1):S55-S8.

23. Rutter MJ, **Vijayasekaran S**, Salamone FN, Cohen AP, Manning P, Collins MH, et al. Deficient tracheal rings. Int J Pediatr Otorhinolaryngol. 2006;70(11):1981-4.

24. Quick ME, **Vijayasekaran S**. Open cervical surgery for congenital H-type tracheo-esophageal fistulae (TOF). Open access atlas of otolaryngology, head & neck operative surgery. [Internet]. Cape Town. University of Cape Town. 2017. http://www.entdev.uct.ac.za

25. Quick ME, Giblett N, Uwiera TC, Herbert H, **Vijayasekaran S**. A novel approach in managing challenging tracheoesophageal fistulae. Int J Pediatr Otorhinolaryngol. 2020;138:110261.

Laryngotracheoesophageal Clefts (LTEC)

Publication 21*:* Laryngotracheoesophageal clefts were first described by Richter in 1792, and the first successful repair of this anomaly was reported in 1955 (88). These clefts are classified according to the extent of the cleft between the trachea and oesophagus:

Type 1: supraglottic inter-arytenoid cleft, sparing the cricoid cartilage extending to the level of the vocal fold.

Type 2: Partial cricoid cleft remains above the cricoid lamina.

Type 3*:* Total cricoid cleft, with or without extension into the cervical trachea.

Type 4: Laryngoesophageal cleft, extending into the thoracic trachea and may extend as far as carina or bronchi (89).

Given that there is an absence of formation of the posterior tracheal wall in Types 3 and 4 clefts, using an ETT for ventilation can be quite difficult; this is due to the potential for a large air-leak around the ETT. Publication 21 identifies a technique in which a laryngeal mask can be used to ventilate patients who present with a laryngeal cleft and in whom ventilation with a traditional endotracheal tube has failed. Incidentally this patient also had a previously unreported combination of anomalies, exomphalos and type 4 laryngeal cleft,

Tracheal Stenosis

Publication 22*:* This case report is the first to document the use of an ultrafine Coblation ™ (bipolar radiofrequency plasma ablation, Smith + Nephew, UK) to treat short-segment tracheal stenosis. Minimally invasive coblation resection of the stenotic segment was used to avoid an open tracheoplasty (90). Subsequent

publications have documented the use of the same technology in adult patients for various types of tracheal stenoses (91).

***Publication 23**:* Although slide tracheoplasty is an established procedure for the treatment of congenital tracheal stenosis (92, 93), the use of this technique in the management of absent tracheal rings (a rare condition) had not been previously documented. Deficient cartilaginous rings are a sporadic intrinsic tracheal defect that causes severe tracheomalacia. We described 3 patients who presented with this unusual defect who were successfully managed with slide-tracheoplasty.

Tracheoesophageal Fistula

Publications 24 and 25: Management of H-type and recurrent tracheoesophageal fistula.

H-type tracheoesophageal fistula (TOF) is a rare anomaly accounting for 1 in 87,000 births (94). Publication 24 is a chapter published in the open access Textbook of Otolaryngology (https://health.uct.ac.za/entdev/guides/open-access-atlas-otolaryngology-head-neck-operative-surgery). It presents an overview of the approach to diagnosis and treatment of H-type TOFs. Article 25 describes a unique anterior approach (not previously described in the literature) to tracheoesophageal fistulae and a series of my patients who were successfully managed by this novel technique. Given that this approach is via an extended tracheostomy, it avoids extensive extraluminal tracheal dissection and reduces the morbidity of surgery, especially potential injury to the recurrent laryngeal nerves. Such an injury has been shown to be the most common serious complication of H-Type TOF repair (95). This

article also reports the successful use of slide tracheoplasty for the treatment of recurrent TOFs, first described by Provenzano in 2014 (96).

Chapter 7

Voice

26. Reynolds V, Meldrum S, Simmer K, **Vijayasekaran S**, French N. Laryngeal pathology at school age following very preterm birth. Int J Pediatr Otorhinolaryngol. 2015;79(3):398-404.

27. Buckland A, Jackson L, Ilich T, Lipscombe J, Jones G, **Vijayasekaran S**. Drilling speaking valves to promote phonation in tracheostomy-dependent children. Laryngoscope. 2012;122(10):2316-22.

***Publication 26*:** Although intubation can be a life-saving manoeuvre in the treatment of airway obstruction and respiratory pathology in preterm infants, the possibility of longer-term manifestations of laryngeal injury should be kept in mind. (97) Few long-term studies have examined structural changes and the relationship of these changes to voice outcomes (98-101). This study reports the results of prospective laryngeal function examinations of a cohort of 20 very preterm children born between 23 and 29 weeks gestation, all of whom presented with significant dysphonia at school age. Eighteen of these infants were intubated in the neonatal period. Working collaboratively with Dr. Victoria Reynolds (a speech pathologist at the Princess Margaret Hospital for Children Voice Clinic), we assessed laryngeal structure and function using an angled 70-degree rigid laryngoscope or flexible nasendoscopy. (Dr. Reynolds included the data gathered in her PhD dissertation.) We found that 70% of children presented with a chink in the posterior glottis and all children demonstrated at least a mild degree of supraglottic hyperfunction. The 2 children who were not intubated showed vocal fold nodules and a vocal fold cyst respectively. Other common findings included arytenoid prolapse and vocal fold immobility. Voice quality of very preterm children is affected by both laryngeal structure and function.

***Publication 27*:** Not all patients with airway obstruction can avoid a tracheostomy. One of the disadvantages of this procedure is loss of the ability to vocalise. Although this can be helped with the use of a speaking valve, phonation can be difficult when there is a stenosis above the stoma and high intrathoracic pressures are generated on expiration − leading to poor tolerance of the valve. This modification to the speaking valve was devised initially by my mentor, Dr Rutter. However, publication 27 was the first peer reviewed research paper to show a series of patients who could

be helped to vocalise by a simple modification to the speaking valve. More specifically, up to two 1.6-mm holes drilled in the side of the valve enabled better tolerance of the valve despite proximal airway obstruction.

Chapter 8

Airway Surgery in the Era of SARS-CoV-2

28. Pollaers K, Herbert H, **Vijayasekaran S**. Pediatric microlaryngoscopy and bronchoscopy in the COVID-19 era. JAMA Otolaryngol Head Neck Surg. 2020;146(7):608-12.

29. Hendriks T, **Vijayasekaran S**. Microlaryngoscopy, bronchoscopy and supraglottoplasty in the Covid 19 Era. C-Surgeries. [Internet]. Little Rock Arkansas. 2020 Apr 09. Video: 3:02. Available from: https://doi.org/10.17797/2020040901

Publication 28 and Video Journal Publication 29: The SARS-CoV-2 pandemic presented unique challenges for otolaryngologists. These articles were the very first publications in the literature identifying the aerosol limiting techniques for microlaryngoscopy during the COVID 19 era. Article 28, published in the earlier days of the pandemic when hospital staff were at high risk from aerosolization of viral particles during airway interventions. We discuss a technique to safely perform microlaryngoscopy whilst minimising the risk to healthcare workers and the patient. A video describing supraglottoplasty with a modification to minimise aerosol generation was also published in April 2020 (https://doi.org/10.17797/2020040901). Subsequent publications have used these principles to refine or modify the procedure (102, 103).

Chapter 9

Swallowing Disorders, Drooling, and Aspiration

30. Pollaers K, **Vijayasekaran S**. Surgical treatment of paediatric drooling. Open access atlas of otolaryngology, head & neck operative surgery. [Internet]. Cape Town. University of Cape Town. 2017. http://www.entdev.uct.ac.za

31. **Vijayasekaran S**, Unal F, Schraff SA, Johnson RF, Rutter MJ. Salivary gland surgery for chronic pulmonary aspiration in children. Int J Pediatr Otorhinolaryngol. 2007;71(1):119-23.

32. Noonan K, Prunty S, Ha JF, **Vijayasekaran S**. Surgical management of chronic salivary aspiration. Int J Pediatr Otorhinolaryngol. 2014;78(12):2079-82.

33. Herbert H, **Vijayasekaran S**. Paediatric swallowing disorders. In: Tanya S, editor. XVI IAPO Manual of pediatric otorhinolaryngology. Brazil: Interamerican Association of Pediatric Otorhinolaryngolgy. 2018. p. 90-7.

***Publications 30-32*:** Drooling and chronic aspiration (saliva, oral liquids, and solids) in the neurologically impaired child is associated with considerable morbidity and occasional mortality (28, 104). Hospitalization, physician visits, and health costs associated with the sequelae of aspiration are considerable (105). This section includes a chapter in the open access Textbook of Otolaryngology on the treatment of anterior and posterior drooling (article 30) and 2 publications on the efficacy of salivary gland surgery in the treatment of chronic posterior drooling, which may lead to pulmonary salivary aspiration and chronic lung disease.

Publication 31 is a review of salivary gland surgery in children who underwent a heterogenous combination of surgical procedures. These procedures included submandibular duct ligation, submandibular gland excision (SMGE), and unilateral or bilateral parotid duct ligation (PDL) and were all used to treat the complications of chronic salivary aspiration. Two outcome measures were assessed: the rate of lower respiratory tract infection and baseline oxygen saturation. We found that children with cerebral palsy (CP) showed no improvements in either measure, whereas children younger than age 3 years showed improvements in both measures.

In publication 32, we focused specifically on patients who underwent a combination of SMGE and PDL. We found that in this cohort of neurologically impaired children, these procedures together were effective in reducing hospital admissions for aspiration pneumonia.

In a systematic review that looked at 3186 studies, only 21 articles met the inclusion criteria set out by the authors. Two of these were those listed as publications 31 and 32 in this thesis. Only 6 of the 21 studies looked at the rates of lower respiratory tract infection (our paper being one). The review found that using SMGE for patients with chronic sialorrhea, very good control of symptoms and reduced rates of lower

respiratory tract infection was achieved. There was no additional benefit when parotid duct rerouting or PDL was performed as a concurrent procedure (106).

Publication 33 is a chapter summarising the swallowing disorders that typically present to a complex airway/aerodigestive multidisciplinary team. It was published in the XVIth manual of Inter-American Association of Pediatric Otolaryngology.

Chapter 10

Animal studies

34. Stacey J, Heard AMB, Chapman G, Wallace CJ, Hegarty M, **Vijayasekaran S**, et al. The ‘can't intubate can't oxygenate’ scenario in pediatric anesthesia: a comparison of different devices for needle cricothyroidotomy. Paediatr Anaesth. 2012;22(12):1155-8.

35. Prunty SL, Aranda-Palacios A, Heard AM, Chapman G, Ramgolam A, Hegarty M, **Vijayasekaran S** et al. The ‘can't intubate can't oxygenate’ scenario in pediatric anesthesia: a comparison of the Melker cricothyroidotomy kit with a scalpel bougie technique. Paediatr Anaesth. 2015;25(4):400-4.

36. Prunty SL, Heard AM, Chapman G, Challen A, **Vijayasekaran S**, von Ungern-Sternberg BS. “Cannot intubate, cannot oxygenate”: A novel 2-operator technique for cannula tracheotomy in an infant animal model—a feasibility study. Paediatr Anaesth. 2021;31(12):1298-303.

Publications 34-36: In an emergent setting in which there is a "Can't intubate, can't oxygenate" (CICO) scenario, little evidence exists to guide the management of the paediatric patient. To address this, I played a key role in developing a post-mortem rabbit model of the infant airway (comparable to a 1-year-old infant in size). Our research group subsequently evaluated the success and complication rates of needle tracheotomy, comparing 14- and 18-gauge cannulae. Furthermore, cannula tracheotomy using the Quicktrach Child™ device was also performed. We found that cannula tracheotomy with a 14- and 18-gauge cannula appear to offer similar performance. Successful aspiration is the key predictor of appropriate cannula placement. The Quicktrach Child™ was not used successfully in this model.

A second study using the same animal model was undertaken to compare the COOK Melker cricothyroidotomy kit (CM) with a scalpel bougie (SB) technique. CM had an overall success rate of 100% compared to a 75% success rate for SB. The success rate for the first attempt was dependent on the level of the tracheotomy, and greater complication rates were seen with the SB technique. Research in this area continues.

In a systematic review published in 2018 (107) from 144 potentially eligible studies, only five were included and articles 34 and 35 were amongst those five. The most recent article using the same animal model (publication 36 of this thesis) reported on a cannula tracheotomy, comparing direct and indirect aspiration. This study found that there was a very high risk of posterior trachea injury utilising both techniques, suggesting that more research was required to identify the optimal approach for managing the infant with an acute airway emergency.

These techniques have subsequently been investigated by others. Mann et al published their results using cannula tracheostomy and various ventilation devices

(108). Both and colleagues found that the post-mortem rabbit model was a good training model for paediatric airway intervention. It facilitated rapid skill acquisition under realistic anatomic conditions to perform an emergency tracheostomy in children younger than 2 years (109).

Chapter 11

International Consensus Statements

37. Karthik Balakrishnan, MD, MPH; Douglas R. Sidell, MD; Nancy M. Bauman, MD;Gaston F. Bellia-Munzon, MD, MHSA; R. Paul Boesch, DO; Matthew Bromwich, MD, FRCSC;Shelagh A. Cofer, MD; Cori Daines, MD; Alessandro de Alarcon, MD, MPH; Nöel Garabedian, MD;Catherine K. Hart, MD; Jonathan B. Ida, MD, MA; Nicolas Leboulanger, MD, PhD;Peter B. Manning, MD; Deepak K. Mehta, MD; Philippe Monnier, MD; Charles M. Myer III MD;Jeremy D. Prager, MD, MA; Diego Preciado, MD, PhD; Evan J. Propst, MD, MSc, FRCSC;Reza Rahbar, DMD, MD; John Russell, MB, BSc, MCh, FRCS(ORL); Michael J. Rutter, FRACS;Briac Thierry, MD; Dana M. Thompson, MD, MS; Michele Torre, MD; Patricio Varela, MD; **Shyan Vijayasekaran, MBBS, FRACS;** David R. White, MD; Andre M. Wineland, MD, MSCI;Robert E. Wood, PhD, MD; Christopher T. Wootten, MD, MMHC; Karen Zur, MD;Robin T. Cotton, MD. Outcome measures for pediatric laryngotracheal reconstruction: International consensus statement. Laryngoscope. 2019;129(1):244-55.

***Publication 37*:** I was the only Australasian paediatric otolaryngologist to be included in the 2019 international consensus document on outcome measures of laryngotracheal reconstruction. The objective of this study was to define consensus outcome measures, including those pertaining to the patient, operation, disease, and associated complications. Using the Delphi method, we sought to integrate the experience of an international multidisciplinary panel of airway surgeons to generate future hypotheses and improve communication of results across institutions.

Chapter 12

Conclusions

The otolaryngologist plays a distinctive role in managing disorders of the upper aerodigestive tract, particularly those involving breathing and swallowing difficulties in children. Over the past two decades, this field has been my primary focus, inspired by mentors who motivated me to establish the region's inaugural aerodigestive team upon my return to Australia in 2006.

The research endeavours presented here underscore my contributions to advancing paediatric otolaryngologic practices, with the goal of refining existing management strategies for severe upper aerodigestive tract conditions. These publications cover a wide array of topics, including insights into congenital nasal pyriform aperture stenosis, such as optimal parameters that determine the need for surgery, nasal cavity characteristics in CNPAS, and innovative balloon dilation techniques. Additionally, they explore rare occurrences like the coexistence of CNPAS and choanal atresia. Moreover, this thesis delves into various subjects, such as midline posterior glossectomy for refractory obstructive sleep apnoea, histological evaluations of the crico-arytenoid joint of intubated neonates, and interventions aimed at reducing tracheostomy dependence in cases of laryngeal atresia, subglottic stenosis and hemangioma through early laryngotracheal reconstruction or cricotracheal resection. My research also investigates risk factors for acquired subglottic stenosis, subglottic cysts, and the use of cuffed ETT’s to mitigate these risks. Additionally, it includes video publications aimed at enhancing the safety of tracheostomy with maturation sutures and explores alternative ventilation methods using laryngeal masks for rescue in cases of laryngeal clefts.

Furthermore, body of research addresses innovative treatments for absent tracheal rings, tracheal stenosis, and tracheoesophageal fistula. In addition, this group of publications includes discussions on voice and laryngeal pathology in intubated infants and improvements through speaking valve modifications. Publications on dysphagia focus on the surgical outcomes for managing sialorrhea and aspiration. Techniques to tackle challenges posed by SARS-CoV-2, animal studies focusing on paediatric airway emergencies, and international consensus efforts in paediatric airway reconstruction are also highlighted.

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