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Welcome to Volume 8 Issue 1 of Journal of ENT Masterclass 2015

After seven years, the ENT Masterclass® team presents the Eighth Annual Journal with a new Editorial board.

The Journal is the core product of the Masterclass educational platform. Over the past 11 years, I am proud to have been regularly involved as a lecturer in its various courses and as a previous Rhinology section editor for this journal.

It is a great honour to follow on from Professor Pat Bradley as the Chairman of the Editorial Board of the Journal of ENT Masterclass®. Pat has worked very hard over the last seven years to develop the journal to its current high standards. I will strive to continue with the editorial team to maintain these standards and hope to develop new ideas for the journal.

I would like to welcome Mr Michael Kuo as the new Paediatric Otolaryngology section editor. He replaces Mr Haytham Kubba who steps down from his position this year. I thank Haytham for his outstanding contribution to the previous editions. I also welcome two new members to the Editorial Board, Professor Nirmal Kumar and Mr Amit Prasai, who will undoubtedly complement the wealth of expertise in the board. Professor Kumar is the current honorary secretary of ENT-UK and shall be the ex-officio ENT-UK representative on our Editorial Board. This has been after the ENT-UK executive expressed their desire to collaborate with ENT Masterclass® in educational ventures and has endorsed the Journal and the Annual Consultants' Revalidation ENT Masterclass®.

The editorial team has been busy producing the journal in its eighth edition. We continue the same format with articles that cover the subspecialties of Paediatrics, Otology, Rhinology and Head & Neck. For the eighth edition the subeditors have selected 26 high quality articles from the UK and abroad. The breadth of subjects covered and their quality is impressive. We thank the contributors for the high standards of the work they have produced.

The process of making this journal continues to evolve, and we are exploring new ideas, commensurate with new technology. We hope that the journal will, in the future, be indexed on Medline. We are open to all suggestions and happy to receive your comments and ideas to further develop our work.

Meanwhile, the Academic arm continues to expand with free ENT Masterclasses® in UK, Australia, China and Europe. The ENT Masterclass Academic Travelling club had its maiden trip to India in December, 2014 and the next one is scheduled for Cape Town, South Africa in April 2017. The 4th Edition of the popular Cyber textbook, a collection of over 350 surgical videos is due in Jan 2016.

With the goodwill and generosity of the faculty, delegates and volunteers we hope to continue to develop this free training platform into a high quality international educational resource.

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November 2015.

Anaesthetic considerations in paediatric ENT

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Abstract

Between a third and a half of the total volume of work for ENT surgeons involves paediatric patients [1]. Challenges to the anaesthetist arise from the physiological changes in the age range, from neonates to teenagers; potential and significant co-morbidities; and the particular difficulties presented by the shared airway in a child. Successful practice relies on good communication and an understanding of each specialty's requirements. In addition to the relevant past medical history, routine pre-operative assessment of a child should include associated syndromes, history of failure to thrive, current or recent respiratory infections, sickle cell status, fasting times and known behavioural issues which may require play specialist input. Particular pre-operative, peri-operative and post-operative attention in relation to ENT is focused on several areas. This article reviews some of the general and specific considerations in paediatric ENT anaesthesia.

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Airway and cervical spine considerations

The Mallampati score used to predict ease of intubation in adults can be useful as a common and recognised reference point. However it is unclear as to its predictive value in children and has never been validated in paediatric practice[2]. Previous difficult or traumatic intubation should be noted, as well as prolonged intubation on an intensive care or neonatal unit. Unexpected difficult intubation is rare in paediatrics[3]. The incidence of difficult intubation is estimated at 1.35% and is commonly associated with specific features such as micro/retrognathia, or specific syndromes which include Hunter, Hurler, Treacher Collins, and Goldenhar syndromes; Pierre Robin sequence; congenital head and neck masses including lymphatic malformations, as well as acquired conditions including infections (quinsy, retropharyngeal abscess, epiglottitis) and burns[4]. Fibreoptic endoscopy and devices such as the Glidescope (Figure 1) effectively facilitate intubation in the child with difficult airway access.

Airway obstruction may present with symptoms of stertor (pharyngeal obstruction) or stridor (laryngotracheal obstruction). Flow through the airway is normally laminar and is governed by the Hagen –Poiseuille law. Flow is proportional to the fourth power of the radius, with a halving of the radius resulting in a 16-fold reduction in flow. Therefore, children who present with stridor and obstruction may already have a significant reduction in their airway diameter and small changes in the airway diameter in infants can lead to a significant reduction in flow. Table 1 illustrates common causes of upper airway obstruction in children. Assessment of the cervical spine is integral to airway management, intubation and positioning for surgery. Reduced movement, immobilisation or disease of the cervical spine increases the difficulty in intubation[5]. Operations such as tonsillectomy require extension of the neck. Thus positioning of the patient with cervical spine disease or potential instability (e.g. Down syndrome or

Figure 1: *Glidescope*

Table 1: Common causes of upper airway obstruction in children presenting for ENT surgery	
Congential	**Acquired**
Syndromes associated with retrognathia Pierre Robin Treacher Collins Goldenhar	Physical Obstruction: Foreign Body Adenotonsillar hypertrophy Trauma Thermal or chemical burns Angio oedema
Choanal atresia (CHARGE syndrome)	Infections: Croup/ Epiglottitis Quinsy Tracheitis Retropharyngeal abscess
Macroglossia Downs syndrome Beckwith-Wiedemann Mucopolysaccharidoses (Hurler, Hunter, Morquio)	Tumours Lymphatic malformation Vascular malformation Post intubation: Subglottic stenosis Cysts
Larynx: Laryngomalacia Laryngeal web Laryngeal cleft Vocal Cord palsy Subglottic stenosis Haemangioma / Cysts	Neurological or myopathy Depressed consciousness Pharyngeal hypotonia Brainstem lesions Vocal cord palsy (previous cardiac surgery)
Tracheal: Tracheomalacia Tracheal stenosis	
Vascular Rings	

Morquio disease) once anaesthetised will require careful consideration, especially for prolonged surgery.

Obstructive Sleep Apnoea (OSA)

Characterised by intermittent partial or complete obstruction of the upper airway whilst asleep, OSA has a wide clinical spectrum from mild snoring at night in otherwise healthy children to significant OSA in children with syndromes or significant co-morbidities such as myopathies or neurodegeneration. Polysomnography is the gold standard for OSA assessment, but it is rarely used in the UK[6]. These studies are useful when the diagnosis is unclear or if there are significant co-morbidities. Paediatric OSA can be stratified into mild, moderate, severe categories as illustrated in table 2 below[7]. Patients with significant OSA and prolonged periods of obstruction may require an ECG and echocardiography to assess right heart function and presence of pulmonary hypertension. Mild to moderate OSA usually does not warrant a change in anaesthetic protocols. Severe OSA implies increased sensitivity to anaesthesia and a higher risk of respiratory complications. Anaesthesia and administration of drugs with a respiratory depressant profile, such as opioids, need to be carefully titrated[8]. Postoperative care may require high dependency unit or intensive care and involve prolonged intubation or BiPAP / CPAP. Adenotonsillectomy is the commonest operation associated with OSA. The consensus document from the Royal College of Anaesthetists (RCoA) recommended that the majority of patients can be treated in a District General Hospital and included a guideline for stratification of 'at-risk' groups of children that should be referred to a Tertiary centre for management – see appendix 1[9].

Appendix 1: Children at risk from respiratory complications unsuitable for DGH adenotonsillectomy
Age <2 years
Weight <15 kg
Failure to thrive (weight <5th centile for age)
Obesity (BMI >2.5SDS or >99th centile for age and gender)
Severe cerebral palsy
Hypotonia or neuromuscular disorders (moderately severely or severely affected)
Significant craniofacial anomalies
Mucopolysaccharoidosis and syndromes associated with difficult airway
Significant comorbidity (e.g. congenital heart disease chronic lung disease, ASA 3 or above)
ECG or echocardiographic abnormalities
Severe OSA (described by polysomnographic indices including Obstructive index >10, Respiratory Disturbance Index >40 and Oxygen saturation nadir <80)

Table 2: Grading of SRBD severity based on overnight pulse oximetry [7]

SRBD severity	Baseline oxygen saturations	No. of drops <90%	No. of drops <85%	No. of drops <80%	Other criteria
Normal /inconclusive for OSA oximetry	Normal with mean saturation >92%	<3	0	0	< 3 clusters of desaturations and saturations >95%
Mild SRBD	Clusters of desaturations (≥3) with increase in heart rate	≥ 3	≤ 3	0	3 or more clusters of desaturation events
Moderate SRBD	Clusters of desaturations (≥3) with increase in heart rate	≥ 3	>3	≤3	3 or more clusters of desaturation events
Severe SRBD	Clusters of desaturations (≥3) with increase in	≥ 3	>3	>3	3 or more clusters of desaturation events

Neonatal surgery

Neonatal physiology poses specific anaesthetic challenges in this age group and in small infants[10]. A high basal metabolic rate (up to three times that of an adult) coupled with different relationship of respiratory physiological parameters (functional residual capacity vs lung closing volume and chest wall compliance) result in rapid desaturation when ventilation is inadequate, obstructed or apnoeic. The sympathetic system is immature compared to the parasympathetic system at birth, resulting in bradycardia in situations of stress, for example stimulation with laryngoscopy and/or hypoxia. High surface area to body weight ratio causes exposed neonates and infants to be prone to hypothermia. This is especially true in preterm neonates who have reduced brown fat and non-keratinised skin. During a procedure care with exposure, providing a warm environment and active heating is necessary to prevent temperature loss. Neonates, especially preterm, are prone to hypoglycaemia, as a result of reduced glycogen stores and immature gluconeogenesis pathways. Prolonged starvation may lead to hypoglycaemia and dextrose containing intravenous fluid is required perioperatively along with blood glucose monitoring. Normal starvation policy in children is 6 hours for food or formula milk, 4 hours for breast milk and 2 hours for clear fluids[11].

Cardiac considerations

Deafness can be associated with long QT syndromes (Jervell and Lange-Nielsen syndrome). No specific anaesthetic technique is advantageous although total intravenous anaesthesia (TIVA) possibly prolongs the QT interval less. Beta blockade should continue perioperatively if it is part of the patient's current treatment. Autonomic sympathetic stimulation should be avoided as much as possible (consider premedication and avoid adrenaline containing solutions), and avoid drugs which prolong the QT interval (e.g. ondansetron). Development of an unstable cardiovascular arrhythmia will require cardioversion and intravenous magnesium may be beneficial. Postoperatively, continuous ECG monitoring should be used.

Neonates with a cardiac murmur, have cyanosis, a difference in pre and post ductal saturations, midline defects or a syndrome associated with cardiac anomalies (e.g. CHARGE) should raise concerns for intraoperative cardiac complications and have appropriate pre-operative cardiac assessment and investigation.

Specific considerations for tonsillectomy

Even with newer methods of surgery, tonsillectomy is an operation associated with significant post-operative pain and nausea. Pain relief is multimodal. Intraoperative analgesia is predominantly opioid based. Post-operative analgesia was traditionally achieved with regular paracetamol and ibuprofen (NSAIDs) with breakthrough pain treated with codeine. The withdrawal of codeine from use in children with OSA as a result of concern with accumulation, genetic determined rate of acetylation and possible link with postoperative deaths has dictated the need to explore alternatives for breakthrough pain[12]. Oral morphine (0.05-0.1 mg/kg) is routinely used by many centres, with careful titration in patients with significant OSA. Tramadol may be an alternative[13]. Pre-emptive treatment for postoperative nausea and vomiting (PONV) includes prevention of dehydration with preoperative clear fluids up to 2 hours prior to surgery, peri-operative intravenous fluids, 5HT antagonists (ondansetron) and steroids (dexamethasone). One report suggested that dexamethasone at a dose >0.15 mg/kg potentially could slightly increase the risk of bleeding[14].

Assessment of blood loss and resuscitation requires understanding of the normal paediatric haemodynamic parameters. Table 3 outlines normal physiological parameters. A child's blood volume is approximately 80ml/kg. Blood loss of greater than 20% is probably required before a child shows signs of decompensation. Hypotension is therefore a late sign.

Earlier signs/symptoms of post-tonsillectomy haemorrhage are: altered consciousness (AVPU) or quiet child, excessive swallowing, pallor, tachycardia and decreased capillary refill greater than 2-3 seconds. Initial resuscitation should include administration of oxygen and fluid resuscitation with crystalloid (initially Hartmann's solution 10 ml/kg). Blood replacement may be required if haematocrit is less than 25% or haemoglobin less than 7 g/dl, or ongoing blood loss after 50mls/kg of crystalloid have been used in

Table 3: Normal Paediatric Physiological Parameters

Age Group	Heart Rate (bpm)	Respiratory Rate/min	Blood Pressure Systolic/ Diastolic (mmHg)	Blood Volume (mls/kg)
Neonate	130-180	30-40	80/40	70-90
Infant	80-150	20-30	90-100/40-50	70-80
3-12 years	70-120	15-20	90-100/40-50	70-80
12+ years	60-100	15-16	100-120/60-80	70-80

volume resuscitation. Anaesthesia in this setting will be difficult and there is no agreement as to the safest anaesthetic technique (rapid sequence and cricoid pressure vs inhalation induction in left lateral head down position).

Airway Endoscopy (Shared Airway)

In the setting of an airway emergency, the ventilating bronchoscope can be used to bypass an upper airway obstruction to allow oxygenation, and also an aid in difficult intubation. Both ventilating bronchoscopy and tracheostomy are included as rescue techniques for 'Can't Intubate, Can't Ventilate' (CICV) scenario as per the difficult airway algorithm published by the Association of Paediatric Anaesthetists of Great Britain And Northern Ireland[15]. During airway endoscopy, the commonest technique is to maintain spontaneous respiration with a nasopharyngeal airway (NPA) as an airway adjunct and maintain anaesthesia using a volatile agent (sevoflurane), total intravenous anaesthesia (propofol), or a combination of both. Atropine or glycopyrrolate (anticholinergic agents) can be used as a drying agent to improve conditions and reduce incidence of bradycardia.

Lignocaine (<8 mg/kg) is sprayed on the glottis, vallecula and trachea to reduce airway reactivity.

Airway oedema can be managed intraoperatively with topical adrenaline (on neuro-patties or nebulized) and intravenous dexamethasone (0.25-3 mg/kg). Subsequent doses may be repeated every 6-8 hours. Prophylactic nebulized adrenaline in recovery or as an emergency can be administered (0.5 ml/kg 1:1000 adrenaline).

Postoperative fluid management

Fluid management in children in the postoperative phase can be difficult[16]. Following surgery, release of ADH with the retention of free water occurs. Cases of hyponatraemia have led to the NPSA to issue a statement that hypotonic solutions should not be used postoperatively. However there is no ideal intravenous solution, Hartmann's solution containing dextrose is thought by many to be most suitable but is not commercially available in the UK. Consequently, no consensus has been reached as to the most effective regime. The standard formula for calculating fluid requirement per hour is 4ml/kg for first 10 kg body weight, followed by 2 ml/kg the next 10 kg body weight and 1 ml/kg for remainder weight in kg - the '4/2/1 regime'. For example: a 15 kg child's full maintenance will be calculated as 50 ml/hour – 40mls/hr for their first 10 kg and 10ml for their next 5 kg. A common regime is to prescribe 0.45% saline/5% dextrose without added potassium at 50-75% maintenance and replace losses ml for ml (most often nasogastric losses) with an isotonic solution such as 0.9% saline with 10mmols of potassium added to a bag. Daily electrolytes should be checked in patients who continue on intravenous fluids as hyponatraemia can occur with any fluid regime. Symptoms and signs of hyponatraemia are non-specific and can result in a change in behaviour, sleepiness or fitting. Diagnosis is usually only reached if clinical suspicion results in electrolytes being checked. Confirmation of hyponatraemia should result in prompt correction.

Anaesthesia and the developing nervous system

Preclinical trials have shown anaesthetic agents potentially can cause dose-dependent harm to the developing brain. A considerable range of anaesthetics are implicated; volatile anaesthetics, ketamine and propofol. Drugs such as local anaesthetics, opioids and clonidine do not cause significant changes. Medical advances and improved care for complex congenital conditions result in younger children and babies being exposed to multiple operations, and as a result, multiple anaesthetics. Epidemiological studies suggest a slight increase in learning difficulties with early exposure to surgery and anaesthesia, whereas retrospective cohort studies show that single exposure causes no harm[17]. It is not known at what age the risk is reduced. There are currently several prospective trials which may answer these questions but all are years away from any results because several years of detailed follow up to document neurological development is needed. A balanced approach to clinical practice is necessary rather than a sea change. Urgent surgery or treatment should not be postponed if harm is done with its delay. If the treatment is considered non-urgent, discussion with parents and relevant clinicians to delay to surgery should be considered to at least one year or possibly three years of age.

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Management and treatment of patients with first, second, third or fourth branchial pouch anomalies: an update

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Abstract

Objective: To review the best available evidence from the past five years to provide an update on treatment strategies for first and second cleft, and third and fourth pouch anomalies to prevent the occurrence of recurrence.

Data sources: PubMed, EMBASE and the Cochrane Library.

Results: In the treatment of pre-auricular sinus and –fistulas (1st branchial clefts) the use of the: Supra-Auricular Approach (SAA), radiofrequency and microscope to detect the anatomical tract, resulted in lower disease recurrence rates. In the treatment of third- and fourth pouch anomalies, comparable success rates of surgical tract excision and cauterization were reported.

Conclusions: Branchial anomalies are the second most common (20%) neck lesions in children. Correct diagnosis and management are essential to avoid repetitive procedures, due to occurred recurrence after inadequate initial surgery. For each specific branchial cleft anomaly specific tailored treatment strategies should be applied.

Conflict of interest:

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Key words:

Branchial pouch sinus(es), branchial cleft anomaly, branchial cysts, fistulas

Introduction:

Branchial cleft and pouch anomalies are the second most common head- and neck congenital lesions in children and represent 20%[1] of the anomalies encountered in the paediatric population. The embryological remnants frequently consist of cysts, fistulas, sinuses or cartilaginous remainders.

Four types of branchial anomalies exist: first and second cleft, and third and fourth pouch anomalies[1]. Second branchial cleft pouches are the most common and account for 95%[1] of the lesions. Between 5–25% of the lesions consists of first cleft anomalies[1,2,3] and third and fourth pouch anomalies are the least frequently identified. A distinction between the latter two remnants is based on the relationship to the superior - and recurrent laryngeal nerves and can therefore, only be made by surgical confirmation of the anatomical location[4]. Their respective prevalence is reported to range between 2–8% and 1–4%[5-7].

Branchial anomalies result from incomplete obliteration of branchial clefts and pouches during embryogenesis[8, 9]. By the fourth week of embryonic life, six branchial arches can be identified. Five pairs of ectodermal grooves (or clefts) and five endodermal branchial pouches separate these six arches, with a membrane located at the interface between the pouch and the cleft[10]. However, many alternative developmental theories exist: branchial apparatus theory, cervical sinus theory, thymopharyngeal theory and inclusion theory[11].

The embryonic origin of each type of branchial anomaly defines both its presentation and surgical treatment. Accurate history taking, physical examination and clinical awareness are essential to suspect and identify a specific branchial anomaly[1]. In case of patients presenting with a newly developed or recurrent pre or periauricular infectious mass, neck mass or abscess, branchial anomalies should be suspected. Due to the fact that branchial lesions do not regress spontaneously and lesion recurrence frequently occurs[12], surgical excision of all types of branchial lesions is essential. Surgical timing is controversial and depends mainly on the patient's age and infection history[13]. Recurrences are most frequently identified in first, third and fourth branchial cleft and pouch anomalies[2]. Recurrence rates are especially elevated when the patient suffered from multiple preoperative infections and when after excision, no histopathological epithelial lining can be identified[14].

Historically, treatment of all types of lesions has been by complete surgical excision of the entire tract. However, a wide range of ideal and new treatment strategies has been suggested for the management of branchial anomalies. Considering high reported recurrence rates (ranging between 2-13%[1]) subsequent to initial surgical treatment, we aim to provide an update from recent literature on new treatment strategies in preventing recurrence in patients with first, second, third or fourth branchial cleft and pouch anomalies.

A literature search was performed in the PubMed, EMBASE databases and the Cochrane Library on the 1st of March, 2015. A search strategy specifically constructed for three branchial anomalies was applied. The third- and fourth branchial were combined in one search syntax as the intraoperative distinction between the two types is not relevant in terms of surgical treatment. Only studies reporting original study data were selected. Case reports were excluded due to possible high risk of bias (RoB). To provide an update on the most recent literature, articles published in the last 5 years were selected for the current review. Both abstract and full text of the selected articles was critically appraised for both directness of evidence (DoE) and risk of bias (RoB) (by two authors independently L.S.M.D. and H.B.). All articles were required to have a high DoE to be selected to answer our research queries.

To compare the outcomes, recurrence rates after applied surgical treatments were retrieved from selected articles. Identified recurrence rates are provided in the Results section. Tables are provided separately for each independent branchial anomaly, whereas results from third and fourth branchial pouch anomalies surgery are combined. Success rates of treatments were defined as prevention of a recurrence within the time of follow-up provided in the study.

First cleft anomalies

The anatomical location of first cleft anomalies can vary between a lesion in the retroauricular- and parotid region to a lesion presenting in the cervical region below the mandible and above the hyoid[15]. Presenting symptoms depend on the lesions' anatomical location: patients with a retroauricular or parotid lesion might present with a painful mass, surrounded by erythema and swelling[13], whereas patients with a cervical lesion more commonly present with a pit-like (possibly infected) indentation. Due to the fact that the external appearance of a first cleft anomaly in most cases suggests a minor abnormality, clinicians could underestimate the extent of the disease[1]. Frequently, a significant cutaneous tract exists that should be removed to prevent recurrence occurrence. Particularly if the branchial cleft anomalies lie medial to the facial nerve, an increased risk of persistent disease exists[16].

To accurately classify and appropriately treat first cleft anomalies, several classifications have been suggested. In 1971, Arnot[17] developed a classification, followed by Work[18] in 1972, Aronsohn[19] in 1976 and finally, Olsen et al.[3] in 1980. The Work[18] and Olsen[3] are the most widely applied classifications. Work[18] classified first branchial cleft anomalies into two groups based on both histological- and clinical symptoms. Type I lesions are rare ectodermal lesions, that typically present in young children as a cystic mass protruding in the external auditory ear channel. The histological differentiation is based on the fact that type II lesions contain not only ectodermal tissue, but mesoderm (cartilage) in addition. The latter lesions are comparatively more common, may be associated with the parotid gland, but are most frequently associated with conchal or external auditory canal fistulae as well as fistulous neck openings. Disease presentation is frequently later in childhood as a cysts, sinus or fistula[20]. Olsen[3] simplified the classification into: cysts, sinuses and fistulas.

Historically, the optimal treatment for first cleft anomalies was a superficial parotidectomy approach with facial nerve exposure[1]. Especially when a patient has suffered from multiple preoperative infections or incomplete surgical excisions, facial nerve injury can occur and therefore, intraoperative facial nerve monitoring is essential[21]. A wide range of more new surgical treatments has been developed to treat first cleft anomalies, and especially frequently seen pre-auricular sinuses and -fistulas.

Table 1. Surgical outcomes (recurrence rates) of different pre-auricular sinus removal techniques.					
Authors	**Study design**	**N. of ears**	**Surgical technique**	**Recurrence**	**p-value**
Bae *et* al. (2012)[22]	RCS	1 – 89 2 – 12	1 – SAA without drain 2 – SAA with drain	No recurrence in both groups.	–
Bajwa *et* al. (2010)[24]	RCT	1 – 30 2 – 30	1 – SAA Cold steel 2 – SAA Radiofrequency	1 – 23% 2 – 3%	p=.016
Gan *et* al. (2013)[23]	RCS	1 – 114 2 – 94	1 – Microscope 2 – Methylene blue dye	1 – 0.9% 2 – 4.3%	p=.037
Huang *et* al. (2013)[25]	RCS	1 – 48 2 – 31 3 – 30	1 – Sinusectomy 2 – Local wide excision 3 – Figure-8 excision	1 – 2.08% 2 – 22.58% 3 – none	–

When assessing the most recent literature, we identified four studies with a high DoE, presenting newer surgical strategies for pre-auricular sinus removal (Table 1). The supra-auricular approach (SAA) resulted in no recurrence in the study of Bae et al.[22] The use of a drain did not affect disease recurrence rates[22]. Use of radiofrequency during SAA, compared to cold steel surgery, showed to significantly lower (p=0.016) recurrence rates in the study of Bajwa et al.[24]. Use of a microscope during sinectomy to detect the anatomical course of the pre-auricular sinus tract, resulted in significantly lower (p=0.037) recurrence rates in the study of Gan et al.[23]. Ultimately, in pre-operatively highly inflamed tissue, Huang et al.[25] showed that the use of a figure-of-8 incision to remove the pre-auricular sinus resulted in no cases of recurrence. In their study population, a sinusectomy was used in patients with preoperative mildly inflamatory tissue, which resulted in a recurrence percentage of 2.08%[25] (Table 1). Combining results of aforementioned, recently published studies, a SAA seems to provide the lowest recurrence rate ompared to sinectomy, specifically combined with using radiofrequency dissection compared to the use of cold steel alone. In addition, Gan *et al*[23] reported that resecting cartilage and microscope use are essential in preventing recurrence when sinectomy is elected over SAA. Resecting cartilage during surgery seems to be essential in preventing recurrence from occurring.

Second cleft anomalies

Sinuses are the most frequently reported second cleft anomalies, followed by cysts and least commonly, fistulae are observed[10, 26]. Similar to all other types of branchial cleft anomalies, second cleft sinuses and/or fistulas need to be completely excised to prevent disease recurrence[14]. A common surgical approach is to apply a horizontal incision encompassing the external sinus opening and to dissect the sinus tract entirely[1]. The length of the incision can be minimised by using a stepladder approach in longer sinuses or fistulae (Figure 1). Injury to both the hypoglossal- and vagus nerves should be carefully prevented[8]. Goff et al.[13] reported that second branchial anomalies are more likely to be found on the right side (89%), whereas third and fourth branchial pouch are more likely to be retrieved on the left side (reported left-sided incidence rate by Nicouar et al.[6, 7] of 93.5%).

Third and fourth anomalies

The treatment of third and fourth branchial pouch anomalies consists of two stages. Patients usually present themselves with a (recurrent) neck abscess or acute suppurative thyroiditis (Figure 2a). This occurs on the left side almost exclusively but the embryological reason for this is not known. The diagnosis can be confirmed by barium swallow, which shows a tract from the pyriform fossa down to the upper pole of the thyroid (Figure 2b). This must be treated first by incision and drainage of the abscess. As this is only a temporary treatment with a high recurrence rate, 94% and 89% in third and fourth branchial pouch sinuses, a more definite treatment must follow around six weeks after the initial infection[6, 7]. There are two second-stage treatment methods for third and fourth branchial pouch sinuses: the conventional method consisting of surgical excision of the entire sinus or fistula tract, with or without simultaneous thyroid lobectomy[7,27], and endoscopic cauterization of the opening of the sinus

Figure 1: *Stepladder incision for excision of a long second branchial arch sinus.*

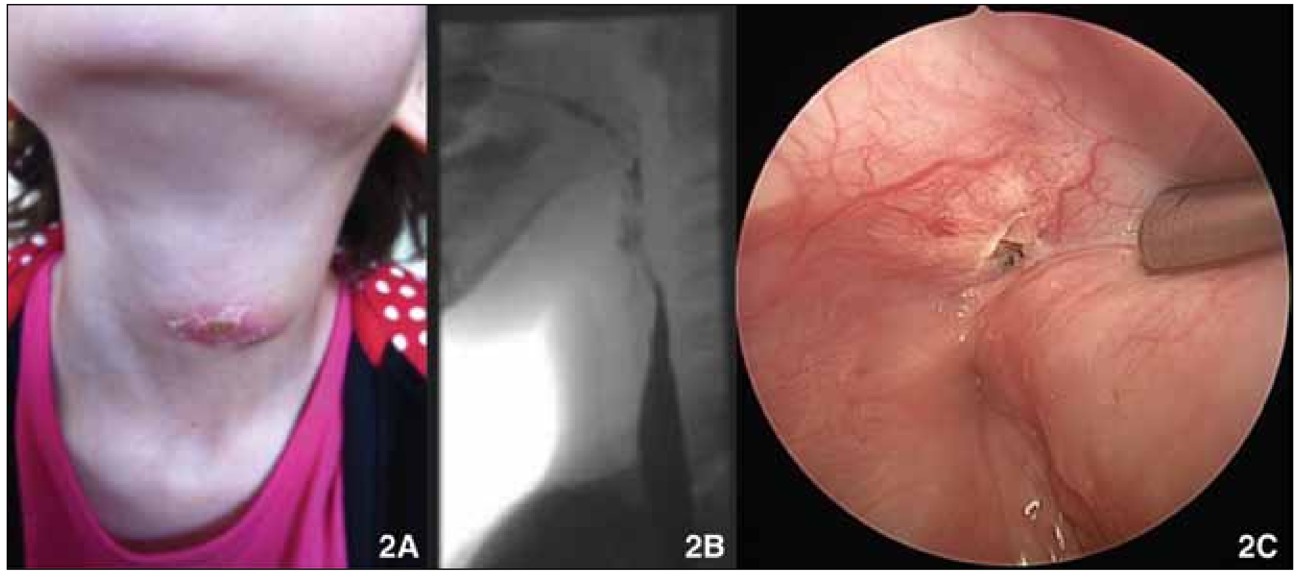

Figure 2a: *Left acute suppurative thyroiditis associated with a III/IVth branchial pouch anomaly.*
Figure 2b: *Barium swallow showing III/IVth branchial pouch anomaly.*
Figure 2c: *Opening to III/IVth branchial pouch anomaly in left pyriform fossa following endoscopic cautery.*

tract, originating in the pyriform sinus. Due to the anatomical course of the third-and fourth anomaly tracts, complete resection has previously shown to be extremely challenging[28, 29]. Endoscopic cauterization is a more recent technique that appears to be successful in preventing recurrence with a low post-operative complication rate[30,31] (Figure 2c). The theory behind the effect of cauterization is that obliteration of the sinus tract opening prevents the bacterial flora of the pharynx to enter the sinus tract. Different methods for cauterization of the sinus tract opening have been described: chemo-cauterization by application of trichloroacetic acid (TCA), silver nitrate or fibrin glue in the sinus tract opening, and electrocauterization of the opening with a monopolar diathermy[13]. There is no consensus as to what is the superior method of cauterization.

Recently, Nicouar et al.[6,7] conducted two large systematic reviews, which included reviews, original studies and case reports. Altogether, authors compared surgical outcomes of 105 patients treated with cauterization and 535 patients receiving surgery. Authors[6,7] reported a success rate for cauterization of 82% and 85% for third- and fourth branchial pouch sinuses respectively, and of 85% for surgical removal for both type of sinuses. This is comparable to the success rate reported in even more recent literature (Table 2).

Due to the low prevalence of these anomalies the best available evidence consists of retrospective cohort studies, showing a comparable success rate of surgical tract excision and cauterization[6,7]. Goff et al.[13] suggested in their surgical algorithm to apply cauterization only in the case of pyriform sinus location of the lesion. However, we

Table 2. Reported success rates for both applied surgical- and cauterization treatement strategies in third- and fourth branchial cleft anomalies.							
Study	**Study design**	**N.of patients**	**Treatment method**	**(Cumulative) success rate**		**Mean follow up, months (range)**	**Complication rate**
				1st treatment	**2nd treatment**		
Cha et al. (2013)[32]	RCS	44	Chemo-cauterization: TCA	77.3%	93.2%	113.5 (18 – 226)	0%
Sun et al. (2014)[15]	RCS	23	Electro-cauterization	91.3%	95.7%	88.6 (1 – 153.6)	0%
Wong et al. (2014)[33]	RCS	3	Electro-cauterization	–	–	27.6 (12 – 48)	33.3%
			Surgical excision + simultaneous electro-cauterization	–	–		33.3%
			Surgical excision	–	–		0

suggest a slight favour consists towards cauterization as the primary treatment method of choice for all lesions independent of their anatomical location, due to lower complication rates because of the minimally invasive character of this treatment method.

Conclusions:

Branchial anomalies are the second most common (20%) neck lesions in the paediatric population. Four types can be distinguished: first and second cleft, and third and fourth pouch anomalies. Both correct identification and surgical management are essential to avoid repetitive procedures, due to recurrence after inadequately selected initial surgical strategies. We provide an overview of new views on treatment strategies that could be selected to treat all four types of branchial cleft anomalies.

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Syndromic craniosynostosis and their implications for an ENT surgeon

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ABSTRACT:

Patients with syndromic craniosynostosis present with complex anomalies involving multiple organ systems. Provision of care for these patients requires effective multidisciplinary planning and delivery of treatment in a timely manner in a regional centre equipped with the expertise required. The aim of this paper is to highlight the general features of syndromic craniosynostosis along with the more specific ENT manifestations associated with these difficult conditions.

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INTRODUCTION

Craniosynostosis describes a group of craniofacial anomalies arising as a result of premature fusion of one or more of the cranial sutures resulting in an abnormal head shape, the nature of which depends on the type of suture affected. They were first described by Otto in 1830[1] and have a prevalence of around 1 in 2,500 live births[2]. Around 80 to 85% present as an isolated sporadic single suture synostosis. In around 15 to 20% of cases, they present with a complex group of multi-system anomalies or with well-defined features identified as part of specific syndromes. These patients are grouped as syndromic craniosynostosis. They arise as a result of specific gene mutations. Over 60 different mutations occur, with the majority of them occurring at the Fibroblast Growth Factor Receptor (FGFR) 2 gene[3]. Over 70 different syndromes associated with craniosynostosis have been described[4]. The most common are Crouzon, Apert, Pfeiffer, Muenke and Saethre-Chotzen syndromes.

The purpose of this article is to provide a brief description of each of the common types of syndromes, provide details of their ENT manifestations and their multidisciplinary management.

CROUZON SYNDROME

First described by a French Neurosurgeon, Louis Crouzon, in 1912[5], this is the most common type of syndromic craniosynostosis with an incidence of around 1 in 25,000 live births[6]. It is caused by a mutation in the FGFR 2 gene[7] and is transmitted via autosomal dominant inheritance. Patients have a range of clinical presentations because of variable penetrance. The classic features (figure 1) of Crouzon syndrome are[4,6,8]:

- Brachycephaly secondary to bicoronal craniosynostosis
- Shallow orbits with exorbitism
- Hypertelorism
- Mid face or maxillary hypoplasia resulting in class III malocclusion
- Crowded and high arched palate with reduction in AP dimension of the palate
- Parrot beaked nose
- Short upper lip
- Relative mandibular prognathism/overjet
- Conductive hearing loss secondary to middle ear anomalies
- Normal intelligence

Figure 1: *Showing the characteristic features of a patient with Crouzon syndrome.*

In spite of normal intelligence they can have several abnormalities of the central nervous system including chiari malformations (cerebellar tonsillar descent)[9]. Cervical spine fusion is noted in 18%[10] and stiffness of the joints can occur, especially at the elbow joints.

ENT manifestations of Crouzon syndrome are as follows:

Airway Manifestations:

Patients with Crouzon syndrome can present with airway problems - some of these patients can present with a solid cartilaginous trachea[11]. Furthermore, the midface hypoplasia can result in airway obstruction. The use of a nasopharyngeal airway, as shown in Figure 1, may be helpful.

Auditory Manifestations:

Over 50% of patients with Crouzon syndrome present with hearing loss[12] secondary to inner ear anomalies. 10 % of cases can present with external auditory canal atresia[13].

APERT SYNDROME

Eugene Apert[14], a French Neurologist (1906), described this syndrome with an incidence of 1 in 65000 live births. This syndrome also arises as a result of a mutation in the FGFR 2 gene[15] and is transmitted with autosomal dominant inheritance with complete penetrance. The common features (figure 2) of patients with Apert syndrome[7,16] are:

- Bicoronal synostosis with large fontanelle sometimes extending from the glabella to the posterior fontanelle resulting in turribrachycephaly
- Bilateral symmetric syndactyly of the fingers and toes (Figure 3)
- Down slanting palpebral fissures, hypertelorism
- Shallow orbits resulting in proptosis
- Midface hypoplasia resulting in class III malocclusion with anterior open bite
- Trapezoid shaped lips and high arched, cleft palate (30%)[17]

Figure 2: *Showing the characteristic features of a patient with Apert syndrome.*

Figure 3: *Showing the complex syndactyly in a patient with Apert syndrome.*

The other manifestations include acneiform lesions, excess sweating, skin dimples[18] and variable intelligence with more than 50% of patients presenting with intellectual ability classed as moderate or less[19].,20.

ENT manifestations of this syndrome are as follows:

Airway Manifestations:

The airway manifestations in Apert syndrome patients are secondary to midface hypoplasia. This can be to varying degrees, ranging from severe cases where tracheostomy is required during infancy to moderate cases, which present with obstructive sleep apnoea. This can require a range of interventions from non-invasive methods of management including adenotonsillectomy and at later stages midface advancement procedures.

Auditory Manifestations:

Hearing loss has been reported to be as high as 90% in Apert syndrome patients because of recurrent otitis media secondary to obstruction of the epipharyngeal space and cleft palate, and also due to inner ear anomalies during development[21]. Although only 6% of these patients present with conductive hearing loss in infancy, the incidence of permanent mild to moderate hearing loss is around 56% due to persistent otitis media[22].

PFEIFFER SYNDROME

In 1964, Rudolph Pfeiffer, a German geneticist first described this rare type of syndromic craniosynostosis. It is transmitted via autosomal dominant inheritance as a result of a mutation in the FGFR[2] gene in 95% of cases and the FGFR[1] gene in 5 % of cases[23]. The classic diagnostic features of patients with Pfeiffer's syndrome are[24] :

- Turribrachycephaly secondary to craniosynostosis most commonly involving multiple sutures

Figure 4: *Showing the characteristic features of a patient with Pfeiffer syndrome.*

- Broad thumbs and big toes
- Partial syndactyly of hands and toes.

The other features (figure 4) noted in patients with Pfeiffer syndrome are ocular proptosis secondary to shallow orbits, a small nose with depressed nasal bridge and midface hypoplasia. Hydrocephalus secondary to aqueductal stenosis can prove difficult to manage and can eventually result in chiari malformation[25] .

The possible ENT malformations in patients with Pfeiffer syndrome are as follows:

Airway Manifestations:

Patients with Pfeiffer syndrome have anomalies that affect both the upper and lower airways.

Upper airway: Severe midface (maxillary) hypoplasia, choanal stenosis or atresia and macroglossia. This can result in sleep apnoea and feeding difficulties.

Lower airway: Tracheal cartilaginous sleeve[26] presents as a continuous cartilaginous trachea with no rings as a result of abnormal fusion of the rings. This can extend from 5 rings to beyond the primary bronchi[27].

Type	Morphological features
Type 1	"Classic Pfeiffer's" - Brachycephaly, midface hypoplasia, broad thumbs and big toes. Normal mental development. Good prognosis
Type 2	Trilobated (clover leaf) skull resulting in limited brain growth, severe midface hypoplasia, and severe ocular proptosis resulting in visual impairments. Also presents with skeletal anomalies involving elbows (ankylosis), fingers and toes. Prognosis is poor with poor intellectual development and short life span
Type 3	Similar to type 2 without cloverleaf skull. Prognosis is poor with short life span.

Table 1: *Cohen (1993)[24] classified Pfeiffer syndrome into three types based on the severity of the phenotype and their prognosis.*

Figure 5: *Showing the characteristic features of a patient with Muenke syndrome.*

Auditory Manifestations

Children with Pfeiffer syndrome may present with varying degrees of conductive and sensorineural hearing loss depending on the degree of structural anomalies. These include atresia of the external auditory canal or hypoplasia of the middle ear canal ossicles[28].

MUENKE SYNDROME

Muenke syndrome is the second most common syndromic craniosynostosis with an incidence of 1 in 30,000 births as a result of a pro250Arg mutation in the FGFR[3] gene. It is characterised by[29,30] (figure 5).

- Craniosynostosis, most commonly of the coronal suture leading to a brachycephalic head shape
- Carpal and/or tarsal bone fusion
- Thimble shaped middle phalanges
- Developmental delay
- Hearing loss

ENT malformations of Muenke syndrome are as follows:

Airway manifestations:

Midface hypoplasia is an uncommon feature of patients with Muenke syndrome, therefore they do not have any significant airway concerns.

Auditory manifestations:

This is a common feature and presents as bilateral symmetrical sensorineural hearing loss to mid to low frequency patterns in almost all cases[30].

SAETHRE CHOTZEN SYNDROME

First described by a Norwegian Psychiatrist Haakan Saethre[31] in 1931 and a year later by a German Psychiatrist F. Chotzen[32], this is a rare type of syndromic

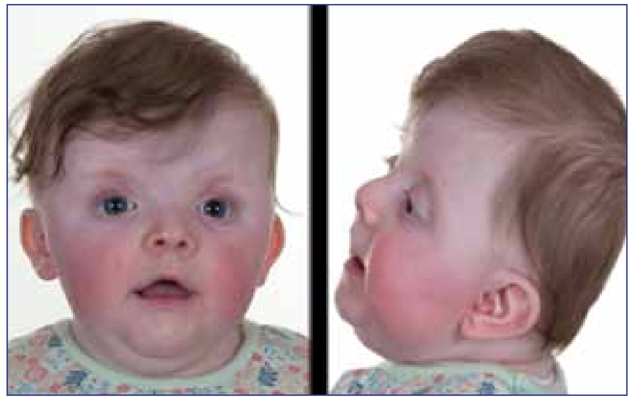

Figure 6: *Showing the characteristic features of a patient with Saethre-Chtotzen syndrome.*

craniosynostosis arising as a result of an autosomal dominant mutation at the TWIST-1 gene located on chromosome 7p21.1[33]. It occurs in around 1 in 25,000 to 50,000 live births[7] with craniosynostosis affecting commonly both coronal sutures. There can be varying degrees of other sutures affected, most commonly sagittal. This results in a brachycephalic head shape with or without turricephaly. The anterior and posterior cranial fossae are general small and dysmorphic, resulting in ear anomalies as described below.

The other classic features are as follows (figure 6):

- Flat forehead with low hairline
- Broad indented nasal bridge
- Eyelid ptosis with occasional hypertelorism
- Facial asymmetry

Some cases may present with high arched palate and rarely with palatal cleft, external ear anomalies involving prominent crus helices extending through the conchal bowl or a small rounded pinna. Skeletal anomalies include varying degrees of syndactyly, clinodactyly, broad toes and rarely radio ulnar synostosis and vertebral fusions[34]. There is some phenotypic overlap of this syndrome with Muenke syndrome[35]. However, detailed clinical examination can differentiate the two syndromes from one another. For example, anomalies of the external ear are characteristic of Saethre–Chotzen syndrome, while extremely rare in Muenke syndrome (Fig. 5).

The ENT malformations linked with Saethre-Chotzen syndrome are as follows:

Airway manifestations:

Patients with Saethre-Chotzen do not usually present with significant airway anomalies requiring intervention during early childhood. The high arched/cleft palate and mild midface hypoplasia may present with difficulties during anaesthetic airway management[36]. They may have a deviated nasal septum, which is usually asymptomatic.

Auditory manifestations:

The most common manifestations in this group are the external ear anomalies as described above. There have been reports of around 50% of patients with Saethre-Chotzen syndrome presenting with mild hearing loss secondary to Eustachian tube dysfunction. The majority of the ear symptoms improve spontaneously without any intervention[37].

MANAGEMENT OF SYNDROMIC CRANIOSYNOSTOSIS PATIENTS

Patients with syndromic craniosynostosis present with complex anomalies that require ongoing vigilant multidisciplinary care to enable management of their manifestations effectively and in a timely manner[7]. Management is focussed on improvement of functional outcomes related to the following issues that require intervention.

- Feeding and airway difficulties
- Obstructive sleep apnoea
- Orbital proptosis and prevention of exposure keratitis
- Dental problems
- Hearing loss
- Raised intracranial pressure.

The timing of management of these patients can be prioritised based on the urgency of intervention into:

- Crisis management
- Emergency treatment
- Elective intervention

A brief outline of the management is summarised in figure 7.

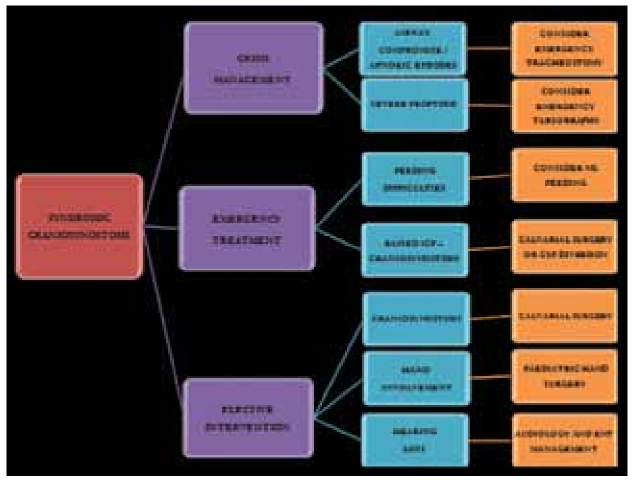

Figure 7:

SPECIFIC MANAGEMENT OF ENT MANIFESTATIONS

AIRWAY MANAGEMENT:

Emergency management:

Syndromic craniosynostosis patients are commonly linked with midface hypoplasia of varying degrees. This may result in nasopharyngeal crowding combined with varying degrees of anomalies such as choanal atresia/stenosis, nasal narrowing or an anteriorly placed larynx. These combined with adenotonsillar hypertrophy results in severe upper airway obstruction that is generally refractory to medical therapy and less invasive adjuncts such as a nasopharyngeal airway. These children may require an emergency tracheostomy in early childhood[38]. Another documented anomaly noted in many patients with syndromic craniosynostosis is the presence of a tracheal sleeve. This affects the distensibility of the normal trachea[39] as a result of lack of pars membranacea[39]. This could result in failure of growth of the trachea to support the oxygenation needs of the growing child[26].

Obstructive sleep apnoea:

Up to 50% of patients with syndromic craniosynostosis present with undiagnosed obstructive sleep apnoea[40]. This is secondary to the midface hypoplasia combined with enlarged tongue, enlarged tonsils and adenoids. Decreased muscular tone of the pharyngeal dilators during sleep results in sleep fragmentation, hypoxia and hypercapnia resulting in raised intracranial pressure. The treatment of patients with less severe obstructive sleep apnoea involves the following.

Medical management – includes pharmacological treatment with nasal/inhaled corticosteroids and antibiotics.

Non-surgical management – includes nocturnal CPAP or BiPAP and use of a nasopharyngeal airway.

Surgical management – includes either addressing the aggravating factors such as adenotonsillar hypertrophy or managing the midface hypoplasia directly[41].

Management of midface hypoplasia

Syndromic craniosynostosis patients may require intervention for their midface hypoplasia depending on the severity of the deformity and their presenting concerns. The main indications for surgery are as follows:

- To aid decannulation of tracheostomy secondary to previous upper airway obstruction (this may not always be possible following midface advancement)
- Shallow orbits requiring multiple failed eyelid procedures
- Severe obstructive sleep apnoea
- Class III malocclusion with functional issues.

The timing of surgery is variable. This is usually expectant depending on the severity of presentation. In general – this is performed preferably beyond 10 years of age to reduce the risk to the dentition and to allow skeletal development[44,45]. In our unit, we prefer to wait until skeletal maturity has completed if possible.

Cohen *et al*[42], first described a reliable method of addressing all these issues by midface distraction osteogenesis.

Several different types of distractor devices have been used to achieve midface distraction. These include –

Internal distractors: Here a linear distractor is fixed subcutaneously to the temporal bone and the midface is 'pushed' forwards.

External distractors: Here the distractor is an external frame similar to a halo frame (figure 8).

A reliable and effective device commonly used in many craniofacial centres is the Rigid External Distractor (RED) frame (KLS Martin Gmbh) (figure 8). This is a halo frame fixed rigidly to the skull by screws with additional wires attached to the mid facial skeleton to provide the necessary distraction. This process has the advantage of gradual and reliable advancement along with soft tissue lengthening resulting in a lower rate of relapse[43]. Once completed the distracted midface requires a period of consolidation to allow maturation of the new bone to prevent significant relapse on removal of the distractor device.

MANAGEMENT OF HEARING LOSS:

Up to two thirds of patients with syndromic craniosynostosis present with conductive or sensorineural hearing loss[46]. Early diagnosis of hearing loss and its treatment is paramount for appropriate speech and language

Figure 7: *Showing the pre and post operative pictures of a patient who underwent mid face advancement using Rigid External Distractor (RED) distraction osteogenesis.*

development. All patients with syndromic craniosynostosis should be screened for sensorineural hearing loss during early childhood and have regular check ups for middle ear function and hearing with specialist otolaryngologist at least until they are 18 years of age. When diagnosed, they should be treated appropriately with grommets, bone-conduction and air-conduction hearing aids and where indicated, hearing implants to ensure appropriate speech and language development[46].

CONCLUSION:

An individual patient with syndromic craniosynostosis present with multisystem manifestations that require intervention by different specialities within a MDT setting at different stages of life. A clear understanding of the aetiology and timing of manifestations is crucial. Their management should be tailored to the individual patient as their manifestations and needs are different. Their effective management should include early diagnosis, regular assessment and timely management by an experienced surgeon.

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Diagnosis of facial swellings in children

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Abstract
Facial swellings in children can present as puffiness, bloating, diffuse or localised swelling. Their clinical manifestations may be an acute swelling with inflammation, a non-progressive swelling, a slowly progressive swelling or a rapidly progressive swelling. If we take into account that the causes of swelling are varied, knowing the most common clinical manifestations and their sites of occurrence will prepare the ENT surgeon for an informed clinical differential diagnostic approach. We are presenting a practical approach to clinical diagnosis to aid interpretation of data obtained from clinical examination.

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Key words
Swelling, Facial, Paediatric

Introduction
Differential diagnosis in the clinical presentation of a child with a facial swelling should be based on three main principles: timing of presentation, clinical symptoms and examination (the nine Ss and one T criteria[1]). Above all, the ENT surgeon should be able to exclude potential diagnosis of malignancy as early as possible to start treatment, relieve symptoms and help alleviate the parent's fears.

Clinical History
Detailed history from parents or carers and the child on the first consultation is of paramount importance[2]. Presence of tooth ache, allergies or swellings somewhere else on the child's body along with age, onset, site and nature of the swelling can help with reaching a diagnosis[3]. Examination should include, head morphology, ears, oropharynx, post-nasal space, neck, chest, abdomen and general skin condition. Nerve deficit can be a sign of malignancy.

What age is the child?
Dental abscesses are rare in infants and congenital lesions are more likely to cause the swelling

When did the swelling start?
Short term is likely to be related to infection

Was there any initiating factors?
Upper respiratory infections may develop into acute sinusitis or cause dehydration leading to of acute parotid sialadenitis.

Recent or regular medications, is there a history of allergy (the child or in the family)?
Presence of allergy has familial tendency in some cases.

Allergies would be associated with eating certain food, or taking new medications.

Trauma or surgery
Localised oedema would likely be associated with a history of trauma. Scar tissue and infections might be related to previous surgery.

Has the swelling changed in size?
Infections and malignant neoplasm are likely to change in size, but usually infections cause a rapidly progressive swelling. Benign congenital anomalies increase in size slowly. Intermittent variations in size are more indicative of arterio-venous anomalies and heamangiomas.

Where is the swelling and is there any other swellings?
Swellings around the orbit are likely to be traumatic or neoplastic, while around the oral cavity are likely to be caused by infection. Unilateral swelling are a feature of localised lesions, multiple lesions can be due to a systemic process.

Fever or change in temperature
Infections and occasionally blood dyscrasias would be associated with pyrexia; infections are likely to cause higher rises in temperature.

Facial nerve deficit
Malignancy should always be suspected in case of facial nerve deficit

Last time the child ate or drank
This is useful in case of planning surgery and to establish relationship to food.

Examination:
Examination should begin with the swelling itself and should follow the principles of nine Ss and one T[4].

Site – Midline lesions tend to be developmental, while lateral lesions tend to be caused by infection. Localised oedema would likely be associated with a history of trauma. A systemic process tends to cause multiple swellings.

Size – Infections usually cause rapidly progressive swellings. Benign congenital anomalies increase in size slowly. Intermittent variations in size are indicative of vascular anomalies.

Shape – Abscesses and benign lesions tend to be spherical. Lymph nodes are ovoid. Malignant conditions often have a disorganised shape.

Smoothness – Smooth lesions tend to be benign; rough and irregular lesions tend to be malignant.

Surroundings – Benign lesions are usually well defined with obvious boundaries from the surrounding tissues. Malignant lesions don't have this demarcation due to local invasion. This observation is not always true e.g. lipomas are poorly defined and are benign.

Structure – Firm lesions are generally incompressible, lesions containing liquid usually feels firm but compressible, while gas contents are easily compressible.

Stability – Neural or vascular lesions are moveable but only in specific axis due to the inherent structure. Benign lesions tend to be moveable. Malignant lesions can be fixed.

Sound – Auscultation is mainly used in case of vascular structures for venous hum of venous malformations and bruits of vascular abnormalities.

Secretion – Discharges should be noted and sent for testing. Sebum would be consistent with a sebaceous cyst.

Sensation – High temperature is consistent with infection. Pulsatility is a sign of a vascular abnormality.

Figure 1 : *Large right facial swelling due to upper 5th tooth infection.*

Transillumination – Passage of light through a mass is suggestive of a cyst. Only cysts with thin fluid content exhibit this phenomenon.

DIFFERENTIAL DIAGNOSIS
Facial swelling can be classified, based on onset, into acute swelling with inflammation, sub-acute non-tender swelling with progressive inflammation, slowly progressive non-inflammatory swelling and rapidly progressive swelling[5]. This should be considered in association with the zone of the face affected (see "facial zones and DD").

Acute swelling with inflammation
Odontogenic infection should be suspected if swelling is around a tooth (Figure 1). Acute bacterial sinusitis present as sudden onset of unilateral periorbital swelling with background of a recent upper respiratory tract infection[6]. Swelling would be localised around the affected sinus and complications might be as severe as intracranial abscesses and subdural empyema[7].

Sub-acute non-tender swelling with progressive inflammation
Nasal dermal sinus cysts, encephalocoeles, and gliomas are the most common *non-progressive swellings* with or without associated central nervous system connections.

Facial zones and Differential Diagnosis (DD).

Nose and forehead		**The jaw line**		**Around the eye**	
Hot and fast:	Abscess	Hot and fast:	Dentoalveolar infection	Hot and fast:	Periorbital cellulitis
			Ludwig's angina		Meibomian cyst (Chalazion)[1]
Cold and slow:	Nasal dermoids				Stye[2]
	Epidermoid	Cold and slow:	Dental cysts		Lacrimal gland cellulitis
	Glioma		Neoplasia		
	Encephalocele			Cold and slow:	Entropion/extropion
	Keratoacanthoma				Viral papilloma
	Haemangioma				Lacrimal gland cyst
	Haematoma				
Around the mouth				**The Cheek**	
Hot and fast:	Herpes zoster			Hot and fast:	Lymphadenopathy
	Cheilitis				Obstructed parotid duct/parotitis
Cold and slow:	Mucous retention cyst[3]			Cold and slow:	Neoplasia
	Neoplastic				Cleft cyst
					Lymphangioma
					Haemangioma
					Vascular malformation

[1] is a cyst in the eyelid and usually treated using topical antibiotic.
[2] Inflammation of the hair follicle of the eyelid generally caused by staphylococcus aureus.
[3] Figure 5

Nasal skin dimple (pit) may be located anywhere between the glabella and columella of the nose, and continues as a dermal sinus into the cranium through a bone defect. Dermoid cysts are more common than epidermoid cysts, and are usually in midline with a tendency to occur at the glabella. Epidermoid cysts are usually paramidline (Figure 2), and tend to occur near the columella. Nasal gliomas have no neoplastic features and are either multifocal or multicentric presenting as a smooth, firm, non-compressible mass near the root of the nose. Obstruction of the lacrimal duct can cause dacryocystocoeles in infants, which is a bluish para-nasal unilateral swelling (Figure 3). Cephalocoeles are more common in oriental populations and frequently associated with midline anomalies[8]. Common features include modifications in position and shape of medial orbital walls and elongation of the nose[9]. Non-tuberculous mycobacterial (NTM) infection should be suspected if swelling is affecting a unilateral submandibular region or pre-auricular region in a systemically well child[10].

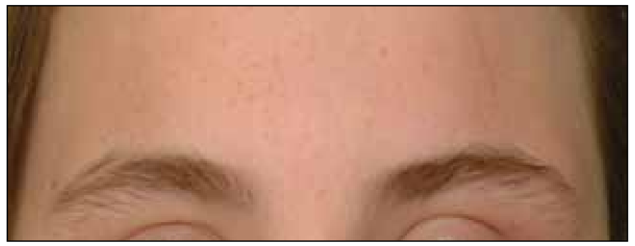


Figure 2 : *Epidermoid cyst on around left eye brow.*

Figure 3: *Congenital lacrimal cyst.*

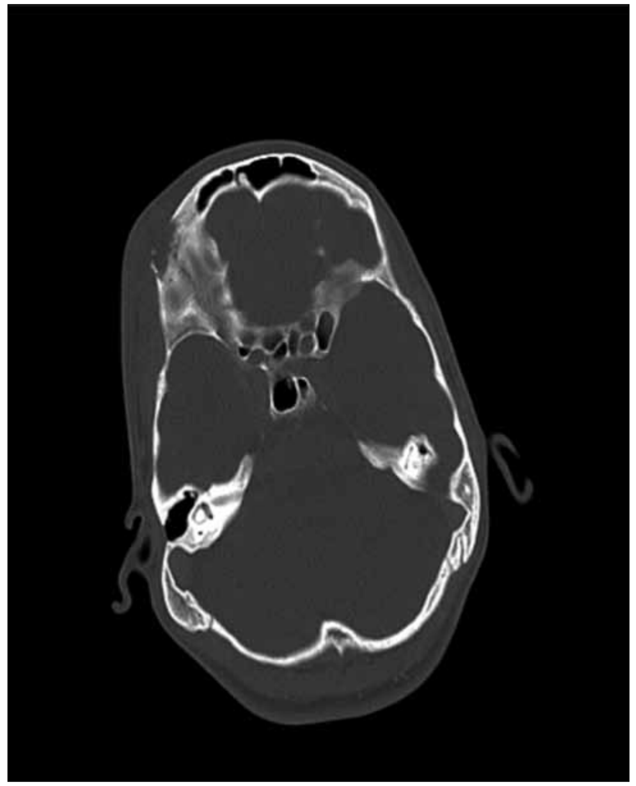
Slowly progressive non-inflammatory swelling

These can present as cystic mass, a resolved cutaneous sinus, fistulae or a congenital cervical anomaly such as neurofibroma, haemangioma, lymphangioma, vascular malformation, or associated with branchio-oto-renal syndrome[11]. Haemangiomas and lymphangiomas demonstrate a trans-spatial growth pattern due to the intrinsic nature of blood vessels and lymphatics. Capillary haemangiomas of infancy are compressible bright red lesions. Vascular malformations are developmental anomalies with no neoplastic endothelial proliferation[12].

Neurofibromatosis of the orbitopalpebral complex can involve all the orbital structures[11] and can cause macroglossia[14]. Fibrous dysplasia is another rare slowly progressive swelling condition that can cause atypical facial pain and headache, diplopia, hearing loss, and facial numbness[15]. It could be a solitary lesion or part of Albright's syndrome.

A rapidly progressive swelling

Malignancy should be suspected in these cases[16]. Lymphomas are the most common cause for head and neck tumours in children followed by soft tissue sarcomas, specifically rhabdomyosarcoma. Osteogenic sarcoma of the jaw is rare[17] but the ramus of mandible is the most common site for Ewing sarcoma in the head and neck region. Langerhans cell histiocytosis presentation can vary from benign single-system disease (eosinophilic granuloma) to the potentially fatal disseminated multisystem Letterer-Siwe disease[18]. The multifocal and systemic form of the disease is usually seen in infants and children[19]. CT examination reveals a sharply circumscribed osteolytic lesion with differential involvement of the inner and outer tables of the skull[20] (CT Figure 4). Neuroblastoma is the second most frequent malignancy in childhood and visual loss can occur in metastatic cases[21]. Both Langerhans cell histiocytosis and metastatic neuroblastoma characteristically involve the posterolateral part of the orbit[22]. Non-accidental injury usually presents as a rapidly progressive haematoma, suspicion should be raised as facial bruising is rare in infancy[23]. Cases with periorbital oedema or ecchymosis should be investigated for possible non-accidental trauma. Head injury is the primary cause for mortality in such cases and pattern of injury is important in diagnosis[24].



CT Figure 4: *Histiocytosis affecting right supraorbital rim.*

Conclusion and practical points

A swelling in a child's face has many causes. Reaching a provisional diagnosis by the clinician, although challenging, is an important step in the immediate management of that child.

There are three main considerations to aid in the clinician's differential diagnosis of these cases:

- Onset is a good clue for diagnosis of facial swelling causes.
- Congenital causes are the most likely finding in case of non-progressive swelling.
- Malignancy and non-accidental injuries should always be suspected in case of rapidly progressive swelling.

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Diagnosis and management of low flow vascular malformations in paediatric head and neck

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Abstract
Vascular malformations present a complex group of congenital abnormalities that are present at birth but may not be clinically evident; but which may only become symptomatic later in life. They have varied presentation from being asymptomatic to life threatening cardiac failure or airway compromise. They are not proliferative but grow commensurately with the patient. An accurate history and clinical examination allows the clinician to distinguish the pathology from vascular tumours. Imaging is required to aid diagnosis. A proper understanding of the natural course of these malformations with a multidisciplinary approach is required to manage these complex anomalies. It is not always possible to cure these and the aim in such cases is to control their associated symptoms and complications.

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Key words
Vascular malformation, venous malformation, lymphatic malformation

Introduction
Vascular malformations present a complex group of congenital abnormalities that are present at birth but may not be clinically evident and may become symptomatic later in life. They have varied presentation from being asymptomatic to life threatening cardiac failure or airway compromise. There is an incidence of about 1:10000 with a prevalence of 1.2%. Management can present a significant challenge and needs a multidisciplinary approach.

Vascular malformations occur as a result of localised or diffuse errors in vascular morphogenesis with normal endothelial proliferation. In contrast, endothelial proliferation forms the basis of vascular tumours[1]. They have no gender predilection and occur in equal frequencies across all ethnic groups and persist throughout life with symptoms that fluctuate. They grow slowly showing proportionate growth in relation to body volume, show no signs of spontaneous involution and may expand secondary to trauma, infection, hormonal changes, pregnancy or surgical intervention. It is essential not to confuse these non-proliferative lesions with haemangioma (vascular tumour) during this expansive period[1-5].

This article aims to address the decision-making in the current management of low flow vascular malformations, within the multidisciplinary team given the various options available for the treatment.

Classification
Vascular malformations were initially classified by Glowacki and Mulliken in 1982 based on their "biological" characteristics such as cellular kinetics, histology, histochemistry, their presenting history and clinical behaviour[1]. This classification was accepted and updated in 1996 by the International Society for the Study of Vascular Anomalies into Vascular tumours and vascular malformations as illustrated in Table 1[2]. This classification is widely used and aids clarification of the terminology used in vascular anomalies.

Table 1: Classification of vascular anomalies

Vascular Anomalies	
Vascular Tumours	Vascular Malformations
Haemangioma	Low Flow: Capillary, Lymphatic, Venous
Haemangio-endothelioma	Fast Flow: Arterial, Areriovenous fistulae, Arteriovenous
Angiosarcoma	

Table 2: Histological characteristics of vascular malformations

Vascular Malformation	Histological characteristics	Typical characteristics
Capillary	Ectatic thin walled capillaries or venule-sized vessels	Papillary and reticular dermis
Lymphatic	Multiple dilated lymphatic channels with walls of variable thickness consisting of smooth and striated muscle	Pale acidophilic fluid and clusters of lymphocytes in the cystic structure and stroma
Venous	Thin walled ecstatic vascular channelswith sparse irregular islands of smooth muscle	Blood, thrombi and phleboliths (dystrophic calcification)
Combined AVM	Thick walled, irregular calibre with hyperplastic smooth muscle within the media	Dysplastic, veins appear arterialised.

These malformations are divided according to their anatomical site of occurrence into extratruncal and truncal lesions. The former maintains its unique embryological characteristics and may proliferate when stimulated by trauma, infection, surgery and hormonal changes such as puberty and pregnancy. Truncal lesions lack these embryological characteristics and are unable to proliferate. Low flow vascular malformations (LFVM) are categorised into Venous Malformations (VM), Lymphatic Malformations (LM) Capillary Malformations (CM) and combined lesions[6].

Histology:

This is characterised by abnormal structure of blood vessels showing progressive dilatation. A flat quiescent endothelium overlying a thin single layered basement membrane lines the vascular malformations. Table 2 illustrates and summarises the differences between the different types of vascular malformations.

Clinical Presentation

The clinical presentation of low flow vascular malformations is dependent on the anatomical site involved and whether the lesions are focal or diffuse. This varied presentation and rarity of symptomatic cases has often led to multiple speciality visits before a correct diagnosis is made. Venous malformations constitute 40%, followed by lymphatic malformations 28%, capillary malformations 11% and the rest are combined malformations[7].

Most diagnoses are made on the basis of a detailed history and examination, which also aids differential diagnoses of other sinister pathologies. Common presentations include a focal mass or swelling with pain, which is not infrequently intermittent. Other reasons for presentation are aesthetic concerns.

1) Capillary malformation:

The most commonly visualised are the capillary malformations that are abnormalities of the capillary network with the skin and mucosa. This can either be isolated or in the presence of extracutaneous involvement. The superficial dermal location creates a permanent dermal stain called the port-wine stain. These slowly grow and change to a deep purple colour in adulthood. On MRI, capillary malformations are represented usually only as a cutaneous thickening. When the ophthalmic (V^1) region of the trigeminal nerve is involved, patients are at a high risk of choroidal and intracranial vascular anomalies (Sturge-Weber Syndrome). This clinical syndrome manifests with hypertrophy of the soft tissue of the face with bony overgrowth of the maxilla and CT and MRI may show cerebral atrophy, cortical calcification, leptomeningeal enhancement of affected areas and enlargement of the choroid plexus[8].

Management of port-wine stains can be conservative using camouflaging make-up or flash lamp pulsed dye laser. The latter leads to lightening of the lesion and is best achieved in younger children. Surgery has a role in selective cases where it may be possible to excise the lesion with closure using skin grafting or advancement flaps. However, this can be associated with problems arising from scarring with hypertrophy and unpredictable pigmentation of the skin graft.

2) Venous Malformation (VM):

These malformations were previously erroneously termed as cavernous haemangiomas. VM can be solely venous or combined as capillary or lymphovenous malformations. These can occur anywhere in the body but most involve the head and neck (40%), extremities (20%) and trunk (20%). They are not confined to an anatomical plane, commonly involve skin and subcutaneous tissue of the tissue or organ and may also involve multiple tissue types.

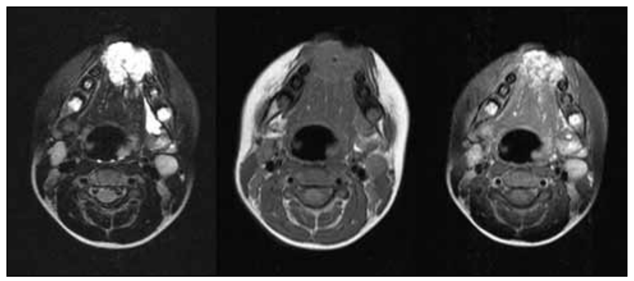

Figure 1a: *Axial MRI images of a tongue VM acquired using STIR, T1 and T1 post-contrast sequences. These demonstrate a lesion of the anterior one third of the tongue.*

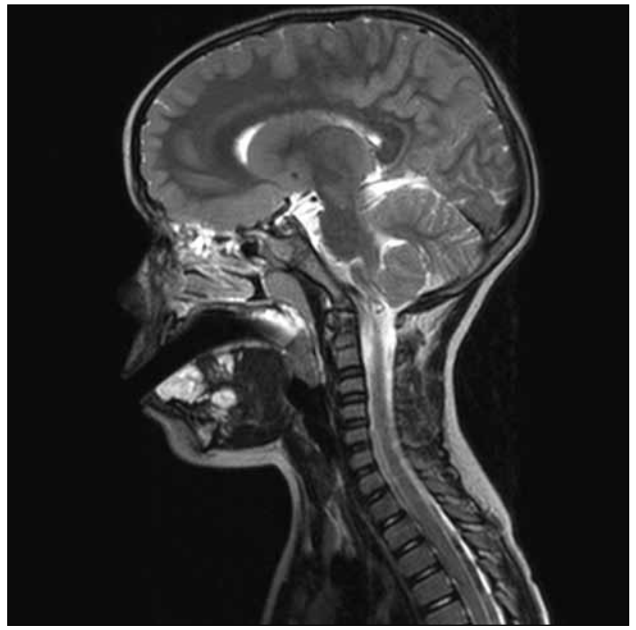

Figure 1b: *Sagittal T2 weighted images) of tongue VM illustrated in figure 1a.*

They present as a soft compressible non-pulsatile mass with a rapid refill. Phleboliths can often be palpated in larger VMs. Although they grow with the child, they have been seen to show growth with expansion during puberty, pregnancy, trauma and subtotal excision[9]. They are more likely to grow in adolescence (75%) although 25% may progress in childhood. Most commonly the lesion causes dull ache increased by activity, extremes of temperature, Valsalva's manoeuvre or dependent positioning. A history of intermittent bouts of severe pain is not uncommon and is caused by thrombosis and thrombophlebitis. VMs are often associated with coagulopathy with low fibrinogen and increased fibrin degradation products which leads to the thrombosis and intermittent pain[10]. VMs give high signal intensity on T2-weighted images and appears brighter than fatty tissue[11]. Severity of symptoms is dependent on the anatomical site, size and its proximity to adjacent vital structures. Figures 1a, 1b and 1c illustrate VM on MRI at different anatomical sites that would cause significant symptoms despite size.

Figure 2: *Left orbital VM causing proptosis and inferolateral displacement of the globe.*

Treatment of most VMs is in the form of reassurance. Sclerotherapy with multiple injections over several months using sodium tetradecyl sulphate (3% STS), bleomycin or 95% ethanol into the epicentre of the anomaly is used in some soft tissue malformations[9,12-14]. Surgical excision is indicated for the large and symptomatic malformations. This is usually not straightforward and profuse bleeding is often noted[13].

3) Lymphatic malformation (LM)

LMs are localised developmental abnormalities of the lymphatic system resulting in numerous cysts containing lymph. The head and neck (48%) is the most common site but they may occur throughout the body. Ninety percent of these malformations are evident as cystic masses at birth or detected before the age of two years. LMs are categorised according to the size of the cysts into either microcystic (cysts less than 1cm) or macrocystic (cysts greater than 1cm) variants. Macrocystic variants appear as soft, non-compressible, non-pulsatile and do not exhibit dependency with normal overlying skin. Microcystic variants infiltrate tissues affect more commonly the skin and mucosa but bone and organ can also be affected and associated bony hypertrophy may present with prognathism. Sudden swelling may occur following an upper respiratory tract infection as a result of increase in the cystic fluid. This demands prompt action, often with intravenous antibiotics. Minor trauma can cause intra-lesional haemorrhage leading to a sudden increase in size.

Tongue involvement may cause macroglossia and the tongue may be covered with vesicles, which often bleed and leak small amounts of lymph. These can commonly present with episodic bleeding and infection that can lead to acute expansion. Airway compromise can occur as a result of sudden growth secondary to haemorrhage into the cystic LVM or infection and cellulitis of involved tongue or floor of mouth. Airway compromise can also progressively occur with involvement of the tongue, tongue base, floor of the mouth and supraglottic larynx.

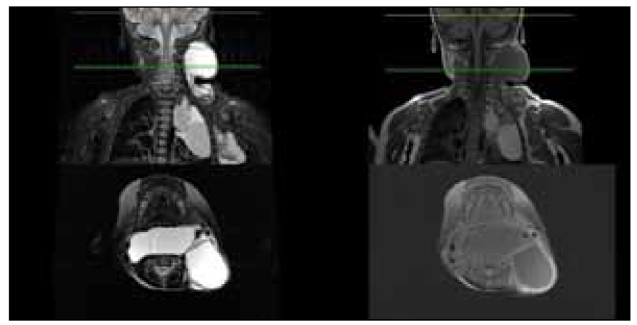

Figure 3a: *Extensive multicystic LM involving neck and chest.*

This usually occurs within the first 12 months of life and should be managed under general anaesthetic with a tracheostomy indicated as appropriate. Figure 3a illustrates an extensive LM involving the neck and chest. In the event of prenatal diagnosis of a large LM with possible airway compromise, planning is needed for controlled delivery in a tertiary centre with the expertise for immediate airway intervention. An EXIT (Ex-utero intrapartum treatment) procedure may be required in these patients.

LMs are classified into type 1 and type 2 depending on their location in relation to the mylohyoid muscle and histological findings. Type 1 lesions lie below the mylohyoid in the anterior and posterior triangle. They are often microcystic (cysts of less than 1 cm in diameter). Macrocystic LMs reveal a ring enhancement on contrast MRI and appear to be discrete and well circumscribed with no infiltration of surrounding tissue. These were previously called cystic hygromas and carry a more favourable prognosis. Type 2 lesions lie above the mylohyoid and are often microcystic (vessels of less than 1cm in diameter). Type 2 lesions commonly involve the cheek, oral cavity, tongue and parotid. They are not well circumscribed, show infiltration into surrounding tissue and may be impossible to fully excise. They also respond less well to sclerotherapy.

Combined venous and lymphatic malformations may be associated with a syndrome called Klippel-Trenaunay Syndrome (Port-wine stain, venous and lymphatic malformations, and soft-tissue hypertrophy of the affected limb)[14].

Multimodality treatment is required in the management of LMs and this depends very much on the variant of cysts, extent and nature of symptoms.

The CO2 and Nd:YAG laser have been successfully used in controlling the microcystic vesicular lesions of the tongue[16]. Radiofrequency coblation is useful in management of ulcerated microcystic lesions of the oral cavity troubled by bleeding and result in improved wound healing and diminished re-growth[17].

Imaging

Diagnosis of vascular malformation is usually based on clinical history and examination[16]. The role of imaging in the diagnosis of vascular malformations is to confirm the clinical diagnosis, determine extent of the lesion, its relationship to surrounding tissue planes and to plan treatment options.

Numerous imaging modalities are used in the imaging of LFVMs. The most useful imaging modality for diagnosis and planning of treatment include ultrasound and magnetic resonance imaging (MRI). Postnatal imaging includes ultrasound, computed tomography (CT), MRI and infrequently angiography[17].

Ultrasound (US)

An ultrasound is essential in the management of LFVMs used to differentiate it from tumours and confirm the clinical diagnosis. The lesions appear as a low reflective or heterogenous defined mass, which is either unilocular or multilocular. The VMs are compressible (except in thrombosis) and LMs are not. Phleboliths are pathognomonic for VMs and can be noted in 20%[2]. Limitations of the ultrasound include depth of penetration, extent of lesions especially in the head and neck and assessment of associated structures such nerves. Its critical and expanding role is in the assessment of lesions for suitability to treat with percutaneous sclerotherapy. Figure 3 illustrates a large LM.

Magnetic Resonance Imaging (MRI)

MRI is the imaging modality of choice due to its superior resolution particularly for soft tissue. When compared to CT, it has the advantage of not using ionizing radiation. This is particularly important in paediatric practice[19,20]. MR imaging can help characterization and diagnosis of the lesion, but its most important role is in the display of the extent and relationship of the lesion to surrounding structures[11,21]. It is this capability of MRI that helps therapeutic planning. Prenatal ultrasound combined with foetal magnetic resonance imaging (MRI) can diagnose vascular malformations as early as 16 weeks of gestation. MRI is the modality of choice and should include contrast and gradient studies. The MRI provides prognostic information, which is useful in the decision making for treatment purposes.

Spin-echo T1 weighted images define anatomy and presence of haemorrhage and haemosiderin and fat suppression techniques to increase lesion detection by suppressing fat. These sequences diagnose and assess LFVMs and also differentiate LMs from VMs and also allow differentiation from other possible diagnoses.

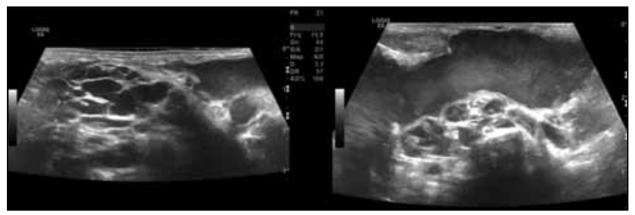

Figure 3b: *Multicystic LM in neck (of same patient as MRI in Figure 2).*

Table 3: Sclerosant agents and their therapeutic profile

Agent	Mode of action	Anaesthetic	Indications	Complications
Sodium tetradecyl sulphate	Endothelial damage resulting in thrombosis and fibrosis	GA	VM and macrocystic LMs	Pain Skin staining Nephrotoxic Rare: Stroke
Ethanol 100%	Instant precipitation of endothelial proteins, rapid thrombosis and vessel occlusion.	GA	VM and macrocystic LMs	Pain Swelling Tissue necrosis Nerve injury Hypoglycaemia, hypertension, arrhythmia and death. Has highest complication rates
Bleomycin	Cytotoxic agent causing apoptosis in growing cells	Image guided injections Sedation in older children	VM (matrix rich or 2nd line agent) microcystic LMs macrocystic LMs	Pain Swelling Ulceration Flu-like illness Pulmonary fibrosis
Doxycycline	Cellular reaction with fibrin deposition	Image guided injections Sedation in older children	Macrocystic LMs	Swelling and blistering Haemolytic anaemia and
Picibanil	Inactive strain of group A streptococcus pyogenes that stops proliferation	Image guided after drainage of cystic component	Macrocystic LMs	

Use of contrast is useful in atypical anatomical sites to aid diagnosis particularly when clinical history and diagnosis are not helpful but come at a cost and may not be required in the investigation of all cases.

Management

This is a lifelong process and treatment is indicated when patients experience symptoms or potential complications such as pain, compression or invasion of adjacent structures, decreased range of motion, bleeding, consumptive coagulopathy, and cosmetic deformity[12,13].

The management of low-flow vascular malformations is difficult and is done with a multidisciplinary team. Not all LFVMs need treatment and indications include distressing symptoms of bleeding, aesthetics, pain, infection and coagulation problems.

Observation / conservative management

Most LFVMs require reassurance with clinic follow-up and advice regarding thrombotic events and infection given.

Surgical management

Traditionally, surgery has been the modality of choice for control but is not always feasible due to the size and involved anatomical sites. It is associated with a high risk of complications and often a staged approach is used. Surgical resection may be hazardous due to major blood loss and incomplete resection. One commonly noted complication is incomplete resection of tongue lymphovascular malformation, which can be seen as persistence or worsening with blistering of the tongue that eventually could lead to bleeding. Recurrence rates are about 22% for LFVMs[22]. Roh et al reported a 75% improvement in symptoms for debulking procedures where sclerotherapy failed or was considered unsafe[23]. Complete removal of microcystic lesions is impossible but macrocystic lesions can safely be resected and therefore the extent of resection should be pre-planned. Surgery can also be performed following sclerotherapy where treatment is incomplete or when aesthetic prejudice requires correction.

Sclerotherapy

Sclerotherapy with US and fluoroscopic guidance is now a universally accepted treatment option for both LMs and VMs and is the only option available to a poor surgical candidate with extensive multicompartment disease[24]. Using sclerosant agents, it induces fibrosis to cause occlusion and significant reduction in the anomaly. It carries the risks of oedema, full thickness necrosis and nephrotoxicity secondary to haemoglobinuria. It should therefore be performed under a general anaesthetic by an

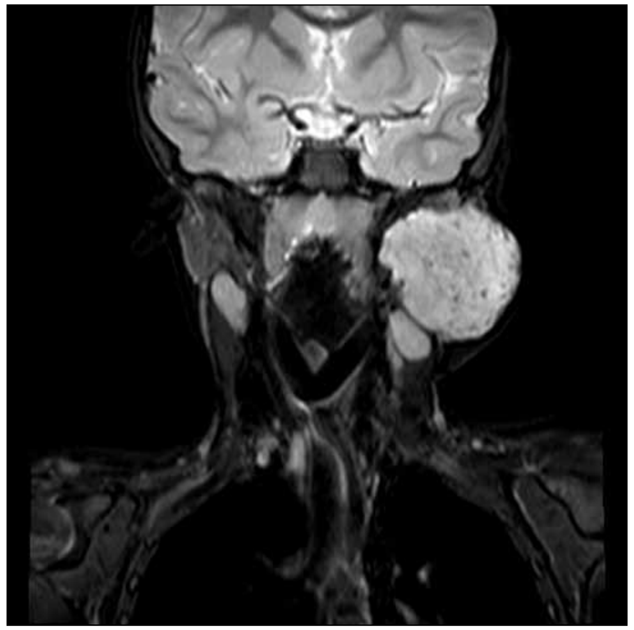

Figure 4a: *Coronal T2-weighted image demonstrating large left parotid VM.*

experienced interventional radiologist. Often it requires between 3-5 sessions with repeat treatments spaced 6-8 weeks apart[25,26,27]. Post-procedure review includes US evaluation and if little symptomatic improvement is noted, trial of a different sclerosant agent is suggested.

Numerous sclerosant agents are described for treating LFVMs, some are specific to VM or LM whilst some can be used for both. These include sodiume tetradecyl sulphate, bleomycin, doxycycline, OK-432 (Picibanil) or 95% ethanol[12,28,29]. There is no consensus on which agent is best and Table 3 illustrates each with its complication profile.

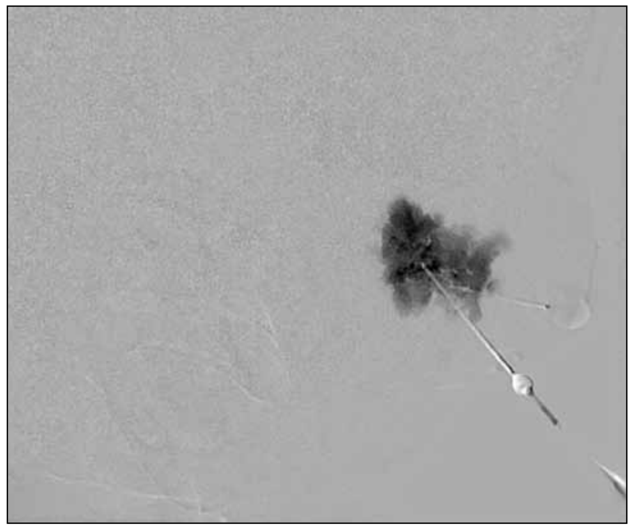

Figure 4b: *Image-guided sclerotherapy of left parotid lesion in figure 4a.*

Sclerotherapy is more effective in macrocystic lesions and treatment rates range from 88-100% with a 2-22% complication rate, most of which are local and affect skin through blistering and scarring. Sclerotherapy has been shown to be effective in management of high-risk areas such as the orbit, trachea and pharyngeal lesions. Due to post sclerotherapy swelling, prophylactic tracheostomy should be considered during their management. Figure 4a shows fluoroscopy-guided sclerotherapy of large left parotid VM. Figure 4b shows image-guided sclerotherapy of the parotid VM.

Conclusion:

Vascular malformation is a complex entity of congenital vascular anomalies and presents differently depending on its predominant histological characteristic. It is not proliferative but grows commensurately with the patient. Obtaining an accurate history and clinical examination allows the clinician to distinguish the pathology from vascular tumours. Imaging is required to aid diagnoses. A proper understanding of the natural course of these malformations with a multidisciplinary approach is requires to manage these complex anomalies. Combined malformations require careful interdisciplinary treatment planning. It is not always possible to cure these and the aim in such cases is to control their associated symptoms and complications.

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The paediatric nasolacrimal system: challenges and pitfalls

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Abstract:

Congenital nasolacrimal duct obstruction (NLDO) is estimated to occur in 5% of infants affecting one or both tear ducts. 90% of these spontaneously resolve during the first year of life. The most common cause of obstruction is failure of the membrane (Valve of Hasner) at the distal end of the nasolacrimal duct to open at birth. Typically both sexes are equally affected. Congenital NLDO is more commonly encountered in children with Down syndrome and those with craniofacial abnormalities or a midline facial anomaly. Acquired NLDO is more commonly seen in children following trauma and infection.

We discuss our approach to the management of nasolacrimal system abnormalities in children and discuss challenges and tips for achieving a successful outcome.

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Keywords

Paediatric, Surgery, Nasolacrimal Duct Obstruction, Nose.

Introduction:

Congenital obstruction of the nasolacrimal system (NLDO) is a well-recognised problem and it is estimated to affect 5% of infants in the first year of life.[1,2] Fortunately 90% will resolve spontaneously. The most common cause is failure of the valve of Hasner, the membrane at the distal end of the nasolacrimal duct (NLD), to open normally at the time of birth.

Other congenital anomalies of the nasolacrimal system including punctal aplasia and accessory puncta are surprisingly common, but rarely symptomatic[3] Table 1. Acquired NLD obstruction can occur at any age, and typically follows trauma or infection as seen in Table 2. NLD obstruction affects both sexes equally but is more commonly associated with craniofacial abnormalities and Down syndrome. The incidence of nasolacrimal obstruction in children with Down syndrome has been reported as high as 22-36%[3,4].

Anatomy of the Nasolacrimal System.

The ocular surface is maintained moist and clear of debris and bacteria by the constant flow of tears across the surface (Figure 1). The lacrimal and accessory lacrimal glands produce tears. Tears flow across the surface of the eye and drain through the lacrimal system, via the punctum, a small opening on the medial surface of each eyelid and then via the upper and lower canaliculi, which drains into the common canaliculus and into the lacrimal sac.

Table 1: Common causes of Congenital nasolacrimal duct obstruction
Failure of Valve of Hasner to open
Dacryostenosis: 2-4% newborns.
Proximal outflow dysgenesis: Absent punctum (upper, lower or both)
Abnormalities of the canaliculi
Narrow ducts
Nasolacrimal sac mucocoele, dacryocystocoele

Table 2: Acquired Nasolacrimal duct obstruction
Trauma
Infection (viral/bacterial conjunctivitis)
Acute dacryocystitis
Iatrogenic (topical antiviral medications)

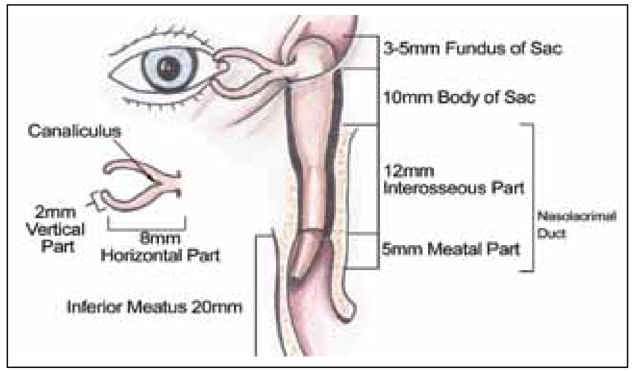

Figure 1: *Schematic diagram of the anatomy of the nasolacrimal system.*

The lacrimal sac acts as a reservoir for tears, which then drain through the nasolacrimal duct into the inferior meatus. A membrane at the distal end of the nasolacrimal duct, 'Valve of Hasner' prevents air from entering the lacrimal sac when the nose is blown.

Drainage of tears may be both active and passive, where passive drainage is facilitated by gravity. Blinking facilitates active drainage by creating a negative pressure within the canaliculi and lacrimal sac, which draws the tears into the nasolacrimal system. The orbicularis oculi muscle which lies in close relation to the tear sac and lids plays an important part in blinking and active tear drainage, both drawing tears into the sac, and pumping them on down the tear duct, thus constituting the lacrimal pump.

Signs and symptoms:

Children most commonly present with epiphora of one or both eyes. Sticky mucous discharge is common and is typically associated with periocular excoriation of the skin. Regurgitation of purulent discharge from the lacrimal sac may cause a secondary conjunctivitis and this is more common when the child has an upper respiratory tract obstruction with nasal obstruction. Gentle pressure over the lacrimal sac can often demonstrate reflux of mucous from the lower punctum.

Congenital lacrimal sac pathology may presents with an obvious swelling (dacryocystocele) of the lacrimal sac. Figure 2. This clinical picture is very typical of lacrimal sac pathology and the "bluish" appearance is supportive of 'mucocele' formation.

Secondary infection (dacryocystitis) may result, and may lead to pre-septal cellulitis, or formation of a lacrimal abscess.

Figure 2: *Clinical photograph of a young child with a classical presentation of a left sided dacryocystocele. (original images)*

Congenital dacryocystocoeles may present with respiratory distress in the newborn especially when bilateral and should be considered in the differential diagnosis of nasal obstruction in a neonate along with the more common congenital choanal atresia.

Neonates are obligate nasal breathers so respiratory distress during feeding and sleeping are the typical presentation. Despite the large size of the dacryocystocele, there is rarely any external nasal swelling to be seen. Nasal endoscopic examination will support the diagnosis but can be challenging in neonates. Figure 3. Imaging such as Computerised Tomography (CT)/ Magnetic Resonance Imaging (MRI) or even an ultrasound scan are very helpful and allow an exact diagnosis to be made. Figure 4. Probing

Figure 3: *Clinical photograph revealing a cystic swelling beneath the right inferior turbinate causing complete nasal obstruction. (original images)*

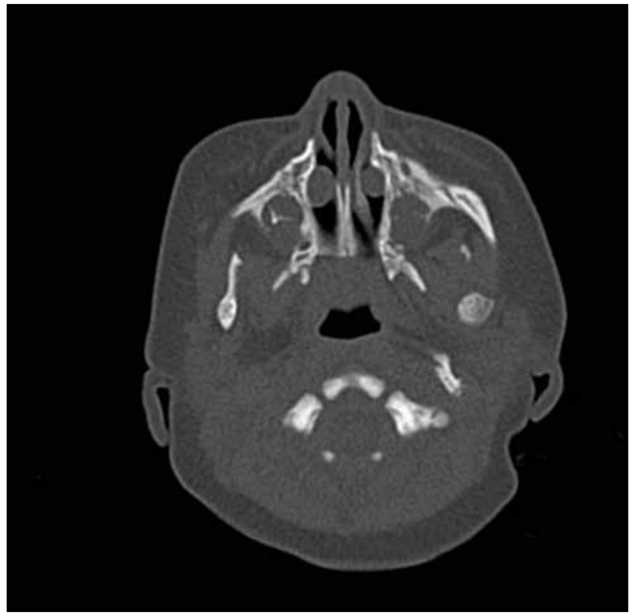

Figure 4: *Axial CT scan demonstrating bilateral cystic swellings (dacryocystocoeles) in the inferior meatus. The child presented with acute respiratory distress immediately after birth.*

of the nasolacrimal duct in conjunction with extensive marsupialisation of the cyst is the treatment of choice.

The differential diagnosis of a child presenting with nasolacrimal duct obstruction can be seen in Table 3.

Investigations for nasolacrimal duct obstruction

- The fluorescein dye disappearance test is most useful in making a diagnosis of lacrimal outflow obstruction, and can be performed at any age, in the outpatient setting.
- Dacryocystograms are very rarely indicated in children. CT scan and MRI scan are indicated if the diagnosis is in doubt, or other concomitant pathology is suspected.

Management

Expectant management is the current standard of care for congenital NLD obstruction (NLDO) in the first year of life. This is because over 90% cases will resolve spontaneously. Recurrent episodes of dacryocystitis, recurrent conjunctivitis, periocular eczema and excoriation can be indications for early intervention.

Table 3: Nasolacrimal duct obstruction: Differential diagnosis of the watery eye
Infection: acute conjunctivitis
Punctual and canalicular agenesis/ atresia
Ectropian
Triachiasis

1. Primary procedure for congenital NLDO

Primary management of congenital NLDO involves syringing and probing of the lacrimal system, and the success rate in various series ranges from 70-90%[5,6]. Although this is a relatively low risk procedure, it can be challenging to learn and to teach. As the nasolacrimal system cannot be visualised, the procedure is performed by feel, and is therefore dependent on the skill and experience of the surgeon. The authors recommend syringing of the lacrimal system through both upper and lower canaliculi after dilatation of the puncta. This is followed by probing with a 00 probe. There is some merit in probing through the upper punctum, to avoid injury to the lower.

Fluorescein dye recovery by suction from the nostrils is evidence of a patent system. However, patency does not necessarily imply sufficient drainage; a patent but narrow lacrimal outflow system can result in epiphora.

The additional procedure of an out fracture of the inferior turbinate can provide relief in some of these cases where the inferior meatus is very compressed. Figures 5a,b.

The Approach to failed probing.

In our experience, this accounts for more than 90% of referrals. For these cases a repeat syringe and probe of the nasolacrimal system is performed. In the authors experience, these cases are best performed jointly with the Ophthalmologist examining patency of the NLD whilst the Otolaryngologist performs an endoscopic examination of the nose and 'out fractures' the inferior turbinate to increase the space within the inferior meatus and to ensure the probing does not create a false passage. Figure 5. In the authors' experience, this joint technique has improved the success rate to more than 87% in our institution. Common causes for failed probing are seen in Table 4.

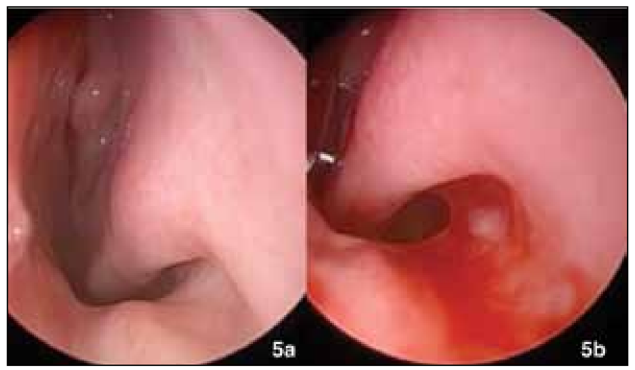

Figure 5: *Endonasal clinical images demonstrating the position of the inferior turbinate before (a) and after (b) out fracture (original images).*

Table 4 : Common causes of failed probing
Distal membrane nor perforated (submucosal)
Distal membrane reforms
False passage created at the time of probing
Tight inferior meatus
Nasolacrimal pump failure
Functional block

Nasolacrimal duct intubation is another alternative management strategy for a failed probing. Following passage of a nasolacrimal duct probe, stents either bicanalicular or monocanalicular are inserted. There are several systems available such as Ritleng tubes, Crawford tubes, O'Donohue tubes.

- Bicanalicular stents: These are placed through the upper punctum and lower punctum and the free ends of the stent are secured within the nose with a silicone (Watzke) sleeve, and occasionally secured with a resorbable suture.
- Monocanalicular stents: have a plug seated at the upper or lower punctum while the stent hangs free within the nose. Figure 6

The success of nasolacrimal duct stent as a primary procedure is estimated to be between 79 to 96%[7,8] and there is no reported difference in success rate for primary stent insertions between monocanalicular and bicanalicular stents.[8,9] A success rate of 84% was reported in a prospective study of stents following failed probing[10] however controversy remains regarding the optimal duration of these stents. Success has been reported with stents left for short periods of up to 6 weeks[7,8]. However other authors recorded reduced success rates for stents in situ for less than 8 weeks[5,6]. Similarly retained stents for more than 3 months have a reduced success rate[7]. Premature dislodgement of the nasolacrimal stent is a common problem in paediatric practice, and in our experience, this usually occurs when the punctum has been dilated for probing, and the plug at the upper end of the monocanalicular stent falls out before the punctum has regained its tone. This premature loss can be minimized by suturing the lower end of the tube to the internal lateral nasal wall using a 4/0 monofilament polyglycolic acid suture, which dissolves within a week, allowing the punctum to seal around the plug. In the event of premature loss, the authors do not recommend replacement unless symptoms of NLDO persist.

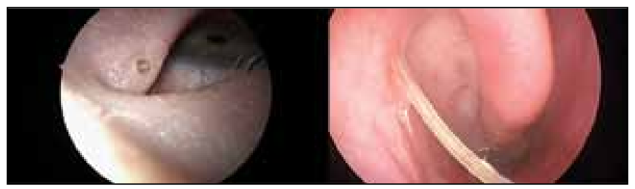

Figure 6: *Monocanalicular tube placed in the lower punctum of the right nasolacrimal system. Intranasal view of the distal end of the stent in the inferior meatus. (original images)*

Balloon dacryoplasty: Although balloon dilatation of the lacrimal duct was proposed over 3 decades ago, it has failed to gain acceptance among lacrimal surgeons. Many surgeons believe that dilating a soft tissue duct against a rigid bony canal does not provide lasting benefit, and this procedure has limited indications in current practice[8].

Dacryocystorhinostomy (DCR)

This procedure is traditionally reserved for children who have failed the above procedures. This procedure is designed to open the nasolacrimal sac directly into the nasal cavity. The endonasal technique is the preferred approach in our institution with success rates of 94%. This is in keeping with other published series[11,12,13]. Although this success rate is slightly lower than the external approach, it does have has the obvious advantages of leaving no external scar and it does not involve disruption of the medial canthus. Furthermore intranasal pathology can be identified and dealt with appropriately[14,15,16].

- **Endonasal dacryocystorhinostomy**

Pitfalls with endonasal surgery in very young children especially when Down syndrome or craniofacial anomalies are present, include a limited awareness of developmental anatomy of the nose and paranasal sinuses. The skull base is low above the lacrimal sac and care must be taken when removing bone from over the lacrimal sac. Anterior ethmoidal air cells are underdeveloped and damage to the orbit is a significant risk.

The pyriform aperture is wide and bony nasal projection is very limited in very young children and does not provide good support for the endoscope. The authors recommend the use of the 4mm 0 degree rigid endoscope in all cases, irrespective of the nasal aperture. The alar soft tissues slowly stretch and visibility improves with patience.

The surgical techniques are different and the authors regularly excise the mucosal flap as this limits the operative space. The medial lacrimal sac flaps are also removed so the lacrimal sac is fully marsupialised into the nasal cavity. Bicanalicular stents are routinely used and left in situ for 6-12 weeks and removed under general anaesthetic where removal of any granulations from around the DCR site can be dealt with. The use of the nasolacrimal 'light pipe' is an extremely useful when performing endonasal DCR in very young children with craniofacial abnormalities as the anatomy may be very challenging.

- **External dacryocystorhinostomy**

This procedure is reserved for cases with canalicular obstruction, where an endonasal DCR is not suitable. It is also a useful technique in cases of acquired epiphora following trauma, foreign bodies, and destructive bony or nasal mucosal disease particularly granulomatosis with polyangitis (a.k.a Wegener's granulomatosis) or failed endonasal DCRs. Success rates are reported from 80-99%[17]. The scar on the lateral aspect of the nose is an obvious drawback of the external approach and care must be taken to minimise damage to the medial canthal ligament. Awareness of nasal anatomy is crucial as opening into the ethmoidal sinuses as opposed to the nasal cavity is a common reason highlighted as a cause of failure[18].

Summary:

Anomalies and pathology of the nasolacrimal system in children are common. Resolution of symptoms with simple probing is still the first line management with good reported success rates. Those children who fail to respond and those with conditions predisposing them to more complex nasolacrimal pathology still achieve good outcomes with more advanced surgical techniques. Ophthalmology and Otolaryngology have a joint role in the management of the more complex and refractory cases in order to achieve the best outcomes.

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Paediatric anterior skull base surgery

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Abstract

Paediatric endoscopic anterior skull base surgery (PEASBS) is a relatively new approach to managing a wide range of diseases that were previously within the domain of the neurosurgical and cranio-facial teams. Transferring the skills developed in adult endoscopic skull base surgery to a paediatric setting requires modifications related to anatomy, physiology and disease-specific pathology. In addition, the long-term sequelae of this surgery are not fully understood. This review summarises the key points of anatomy and physiology that must be addressed by the surgeon performing PEASBS, as well as examples of the types of pathology encountered and the potential complications, based on current literature and review of our own practice.

J ENT Masterclass 2015; 8 (1): 39 - 45.

Keywords

Paediatric, skull base, surgery, endoscopic, sinus and nose.

Introduction

Endoscopic anterior skull base surgery is a well-established practice in the adult world, with a multidisciplinary approach and both otolaryngologists and neurosurgeons performing cases. In paediatric practice however, concerns regarding potential complications and operative difficulties have led to a slow take up of the surgical techniques. Over the last decade, advances in instrumentation and increasing good quality results in adult practice have resulted in an increase in endoscopic anterior skull base surgery in children.

This review will set out the challenges associated with this emerging field, and discuss the literature that supports it.

Anatomical considerations

The paranasal sinuses develop at different rates throughout childhood (Figure 1), which means that a "one size fits all" approach is not appropriate and will result in avoidable complications. A thorough knowledge of sinus and facial development is essential, and close co-operation with a head and neck radiologist invaluable.

Nasal cavity

The first major restriction encountered by the surgeon is the pyriform aperture. The aperture is significantly narrower in children under 6-7 years compared to adults, and rises steadily from a mean of 17.2 mm in children under 24 months, to 22.2 mm in adults[2]. This has significant implications for the size, choice and number of instruments that may be used as well as optimal positioning for the endoscope.

Maxillary sinuses

This is the first sinus to develop and is fluid-filled at birth. Initial outgrowth is postero-laterally as opposed to inferiorly towards the maxillary teeth. In small children, an external Caldwell-Luc approach is not possible without significant morbidity to both sets of teeth. Developing teeth buds are present for both deciduous and early permanent dentition and these may need to be removed as part of any tumour resection. The nasolacrimal system lies more posteriorly in the very young nose and is easily damaged when performing middle meatal surgery.

Ethmoid sinuses

These are present, although very small and fluids filled, at birth and grow to pneumatise up to the age of 12 years. The anterior and posterior ethmoidal arteries have a variable course in the developing nose and caution is essential to avoid damage and haemorrhage.

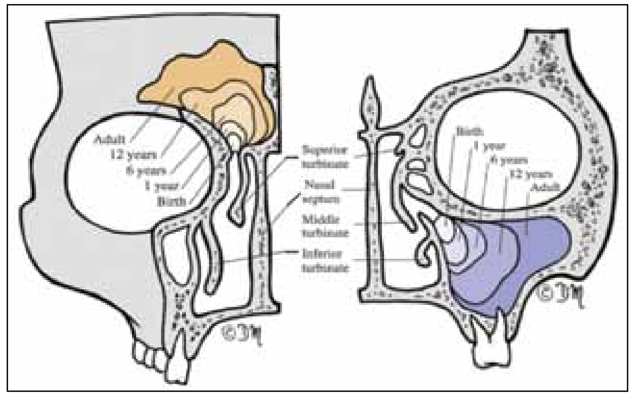

Figure 1: *Rate of growth of the maxillary and frontal sinuses 1.*

Frontal sinus

The frontal sinus is absent at birth; it is first noticeable on x-ray at around 2 years of age and eventually reaches adult size in late adolescence. For the anterior skull base surgeon, the techniques of craniofacial resection and repair are challenging since procedures such as a Draf III are difficult and may not be possible, and the long-term effects on frontal sinus and facial growth are still unclear.

Sphenoid sinus

As in adult practice, the sphenoid sinus provides a vital corridor to the anterior skull base. The sphenoid sinus does not begin to pneumatise until the age of 3 years, and proceeds posteriorly. By 7 years, the sphenoid face is fully pneumatised and "adult" pattern pneumatisation is seen by around 13 years[2] (figure 2). This age-dependent progression results in the absence of many of the landmarks used in adult surgery to navigate the region. The safest point of entry is at the medial antero-inferior margin, as this is the area of earliest pneumatisation. As would be expected, inter-carotid distance is reduced in young children and below the age of 3 years, may be prohibitively narrow. However, after this age an average of 10mm cavernous inter-carotid distance is observed, making this route accessible to experienced surgeons. At the level of the superior clivus, inter-carotid distance is relatively stable from 3-4 years to adulthood. For landmarks, pneumatisation up to the level of the ICAs increases from the age of 6-7 years to a maximal level at 16 years, therefore for most young children there may be no protrusion of the vertical segment of the ICA into the sinus to aid identification[2] (figure 3). The neurosurgical Microvascular Doppler System (Vascular Technology, Inc., USA) is a very useful adjunct to aid identification of the ICA.

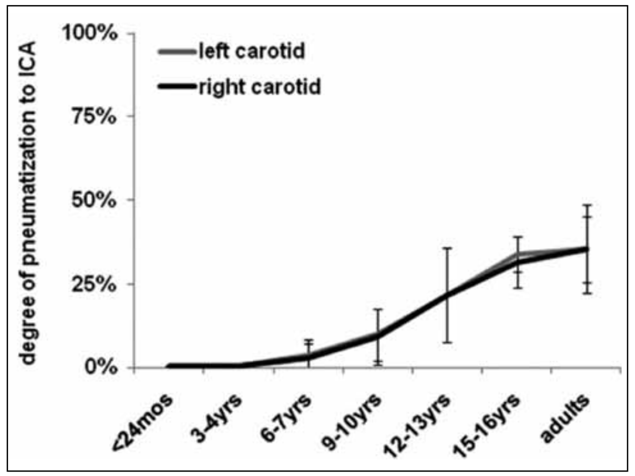

Figure 3: *Degree of pneumatisation of the sphenoid sinus to ICA by age 2.*

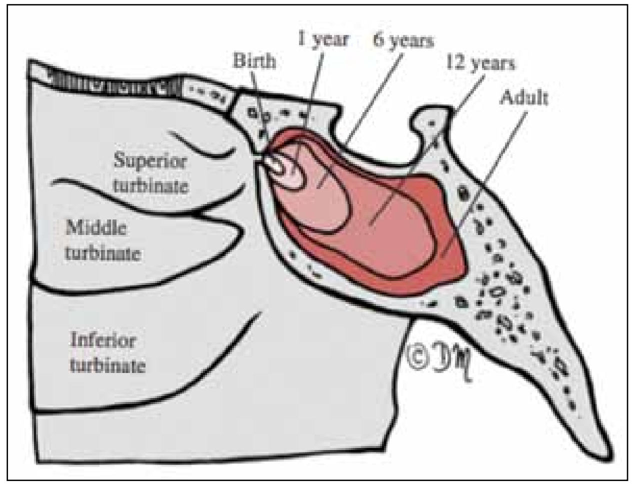

Figure 2: *Degree of pneumatisation of the sphenoid sinus at different ages 1.*

Physiology

An appreciation of child physiology is essential when managing and planning these cases. Pre-operative preparation should be tailored to the child's weight and age. Correct dosing based on the child's weight for lignocaine, adrenaline, cocaine or any other topical or injected drug is mandatory, as is close anaesthetic monitoring. The circulating volume for a child is 80 ml/kg; therefore the total volume for a 5-year-old child (estimated weight 18 kg) is only 1400 ml. A blood loss of 210 ml, which may be quite acceptable in an adult, represents a 15% loss placing them in to Class II shock, while 500 ml loss is severe (Class III)[3]. Children compensate for this for a longer period of time than adults; therefore to an inexperienced team monitoring may not suggest a problem until a precipitous deterioration and collapse.

Anaesthetic considerations

The child undergoing an endoscopic surgical approach to the anterior skull base is likely to need several general anaesthetics both in the preparatory stage (diagnosis, MRI/CT imaging) and subsequently (nasal decrusting, repeat scanning etc.). Early liaison with the anaesthetic team enables an individual plan to be made for the child and helps parents/carers support the child through the process.

The primary considerations are that surgery may be prolonged (more than 2 hours at least), access to the patient is limited, and blood loss (whether anticipated or not) may be insidious and difficult to measure. Preparation includes means of keeping the child warm, equipment to deliver warm intravenous fluids or blood rapidly if needed, and a system of monitoring blood loss. It is not necessary to obtain central venous access routinely; usually two reliable large bore peripheral cannulae will suffice. Arterial access is useful for haemodynamic and blood gas monitoring, and serial haematocrit measurement.

Once positioned and surgically prepared, there is little opportunity to revisit endotracheal fixations etc. In older children a cuffed or uncuffed reinforced (armoured) endotracheal tube (ETT) is less likely to become kinked or obstructed. In the younger child a preformed angled (RAE) tube is appropriate although the pre-determined length of this tube may lead to inadvertent endobronchial intubation in infants for whom a standard ETT is preferential. A throat pack is then placed.

Intraoperatively, it is imperative that there should be no unplanned movement of the patient that might jeopardise the navigational markers. Usually, after an initial dose of neuromuscular blocker to facilitate endotracheal intubation, analgesia and muscle relaxation are maintained by infusion of the opioid remifentanil and ventilation with

Figure 4: *Intra-operative photograph of a child with face mask navigation set up.*

isoflurane in an air/oxygen mix. Towards the end of surgery the delivery of these can be titrated to allow a controlled emergence from anaesthesia, with perhaps a small dose of morphine (0.1mg/kg) to cover the removal of remifentanil at the end. It is worthwhile planning to replace the ETT with a laryngeal mask airway (LMA) at this point, thereby allowing the patient to emerge smoothly without coughing, straining, or otherwise expressing any carefully placed topical haemostatic agents.

Postoperative analgesic requirements are usually minimal, most children receive simple oral analgesics (paracetamol, ibuprofen), and are able to eat and drink normally. The exception comes if the nose has been extensively packed, in which case nurse or patient controlled morphine infusion may be required. Anti-emetics are routinely given.

Surgical Considerations

For nasal decongestion, 0.5 or 1 inch neuro patties (depending on child size) soaked in a weight-appropriate amount of 1:10,000 adrenaline are inserted into the nasal cavity under direct vision once the child is anesthetized and prior to any further equipment set up.

Adequate planning will help to anticipate potential problems and ensure the surgeon is well equipped to handle any that arise. All patients should have fine slice cross-sectional imaging, usually CT but in many cases MRI, and these should be done using a protocol that will support navigation. Surgical navigation assistance is essential in anterior skull base cases for all the reasons mentioned above. In paediatric cases the surgical team should ensure they choose an appropriate navigation system that is accurate and useable in children of all ages. The authors use the Stryker Nav3i system (Stryker UK Ltd, UK), using a facemask for registration (figure 4).

Blood should be taken for group and save but depending on the nature of the surgery, cross-match of packed red cells may be appropriate. The decision for managing blood loss should be discussed with the anaesthetist pre operatively. Haemostasis must be well maintained throughout the surgery, both for the limited reserve of the child but also to preserve a clear surgical view.

A well-briefed theatre team is also essential, and as much as possible the same team should be used for all cases, allowing for familiarity with set up and instruments and an awareness of what will be required ahead of time.

Instruments and theatre layout

The layout of the operating theatre may be different to that of other endoscopic nasal surgery. A detailed count of

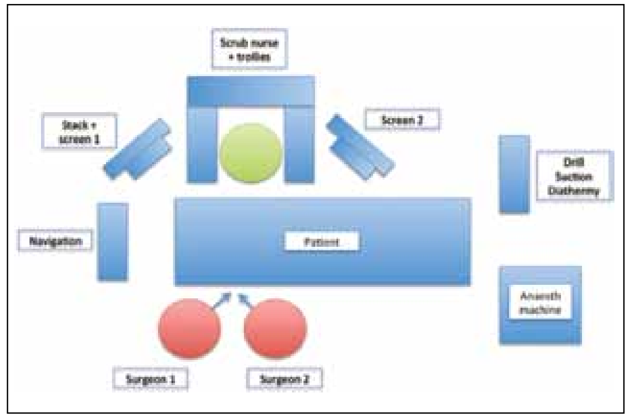

Figure 5: *Operating room set up for endoscopic anterior skull base surgery.*

fluid input and drainage must be recorded and in clear view of both the anaesthetist and the surgeon. Typically, three suction units are employed and are clearly labelled for 1. Microdebrider / coblator system, 2 . High speed drill and 3. General suction/ suction monopolar diathermy. Figure 5 shows a schematic for how the senior author prepares the operating theatre.

A 4 mm 0 degree endoscope is routinely used in all cases irrespective of age. Lens irrigation is very helpful but it can compromise the available instrument space within the nostril in the smaller child and so it is not routinely used in our practice. A significant problem is that of pressure sores and necrosis (figure 6a) around the alar rim due to stretching and pressure from multiple instruments; a Vaseline impregnated gauze splint may be used to protect the columella (figure 6b).

Since there are few endoscopic instruments designed for the very small child and the number of instruments used in such a nose may be restricted, standard mastoid and middle ear instruments are often an ideal size and length and should be made available for cases. Specific paediatric suction monopolar diathermy and the choanal atresia microdebrider are other very useful pieces of equipment.

Figure 6: *a) Pressure damage to the columella and alar rim from instrumentation. b) Vaseline impregnated gauze to protect the columella.*

The surgical techniques used in adults are well described but not always appropriate in children. The well-described Hadad nasoseptal flap[4] can be used, but can be challenging in infants. The "Reverse" or contralateral flap is not routinely used in paediatric case since this further encroaches on the operating space. Great care should be taken when resecting the posterior septum as cases of saddle deformity still arise when the entire quadrilateral cartilage is intact. This emphasises the importance of the vomer and posterior septum in nasal growth. Another alternative is to use free mucosal flaps or lateral wall pedicled flaps, typically from the inferior turbinate. Synthetic materials such as Biodesign® and Duragen® to repair defects can also be considered.

Intrathecal fluorescein can be used to help identify sites of CSF leakage, although this is an "off label" use in children. The authors use a dose of 0.05 ml of 5% sodium fluorescein (without additives) per 10 kg body weight, mixed with 5 – 10 ml of CSF and injected 30 minutes before surgery. Unlike adults, children typically require a general anaesthetic for the lumbar puncture and then remain anaesthetized providing sufficient time for the fluorescein to circulate, thus lengthening the operative time.

Resorbable nasal packs are preferable as removal may be difficult in young children. Adequate analgesia and anti-emetics must be available.

Post-operative and complications

Almost all children undergoing endoscopic sinus/skull base surgery develop problems with nasal crusting, due to poor compliance with nasal douching. Many children require frequent decrusting under general anaesthetic until old enough to douche at home; the authors recommend swimming, which has an irrigatory effect, and helps reduce the crusting and need for surgical clearance.

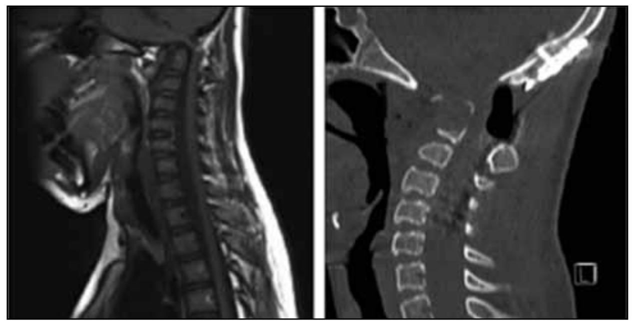

Figure 7: *A) Sagittal T1 MRI demonstrating a very significant craniocervical stenosis. B) Post operative sagittal CT scan following transnasal endoscopic resection of the odontoid peg with external cervical fixation. The defect in the nasopharynx was filled with fat from the abdomen.*

Endoscopic surgery is associated with an improved post-operative course compared to open, with a reduced length of stay (4 vs. 5.7 days), reduced pain (both early and late), reduced blood transfusion (23% vs. 71%) and reduced PICU admissions (35% vs. 100%)[5].

Other complications are as for adult surgery, although the paediatric cohort will be more susceptible to saddle nose deformity due to the fragile nature of the support mechanisms of the nasal pyramid. This highlights again that great care must be taken with the nasal septum during surgery.

Range of pathologies

Unlike adult patients, children have a much more heterogeneous mix of pathologies and most present to the ENT surgeon with ENT related symptoms. A recent review of our practice, highlighted the common pathologies being post-traumatic CSF leaks, encephalocoeles, extensive mucocoeles, juvenile nasal angiofibromas and pituitary adenomas (Table 1). There were a large number of more unusual disease entities that were diagnostically more challenging. An experienced histopathologist is an essential member of the paediatric skull base team

Table 1: The more common pathology encountered in endoscopic paediatric anterior skull base surgery at Birmingham Children's Hospital. 2009-2015
CSF leaks
Meningoencephalocoeles
Juvenile nasal angiofibromas
Extensive mucocoeles
Midline nasal dermoids
Orbital foreign body removal
Fibrous dysplasia: optic nerve decompression
Pituitary pathology
Craniopharyngiomas

Table 2: The wide variety of more unusual pathology encountered at Birmingham Children's Hospital. 2009-2015
Nodular fasciitis
Nasal chondromesenchymal harmatoma
Nasal gliomas (nasal glial heterotopia)
Ossifying fibromas
Odontogenic myxomas
Teratomas

Table 3: Other paediatric endoscopic anterior skull base surgery procedures at Birmingham Children's Hospital. 2009-2015
Odontoid peg resection for craniocervical stenosis
Biopsy of petrous apex lesions
Excision of tumours in close proximity to the brain stem prior to proton therapy

(Table 2). Anterior skull base surgery in children has also proven to be a very valuable adjunct to other treatment (Table 3). Transnasal resection of the odontoid peg is now an accepted and successful management for craniocervical stenosis[6] (figure 7) and it also gives access to other parts of the skull base such as the petrous apex (figure 12A) and access for debulking of tumours from the region of the brain stem prior to proton therapy. For the most common finding of CSF leaks and encephalocoeles, endoscopic management has been shown to be as effective as open surgery[7].

Despite concerns over removing portions of the sinonasal skeleton in young children, bone regrowth occurs even following quite extensive resection (figure 8A-C). For very extensive juvenile nasal angiofibroma, staged surgery may be necessary, (figure 9A & B). Pre-operative

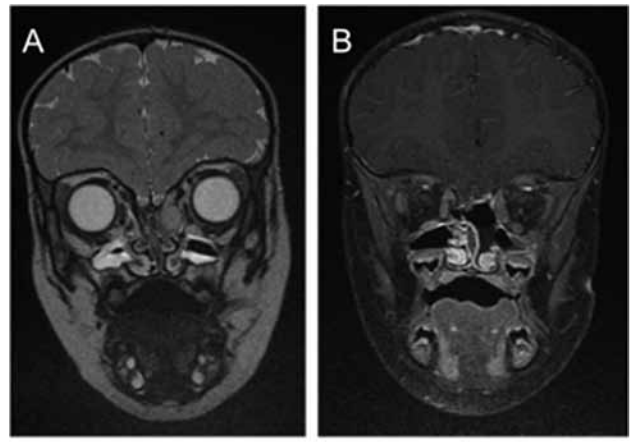

Figure 8: *Left nasal chondromesenchymal hamartoma in a 1 year old child extending into the orbit and through the left anterior skull base. A: Pre-operative coronal T2 MRI. B: Post operative coronal MRI scan 3 months following an endoscopic craniofacial resection of the nasal chondromesenchtyma hamartoma and repair with a nasoseptal flap. C: Coronal CT scan 2 years post surgery. Regrowth of the cribriform plate and lamina papyracea is clearly evident.*

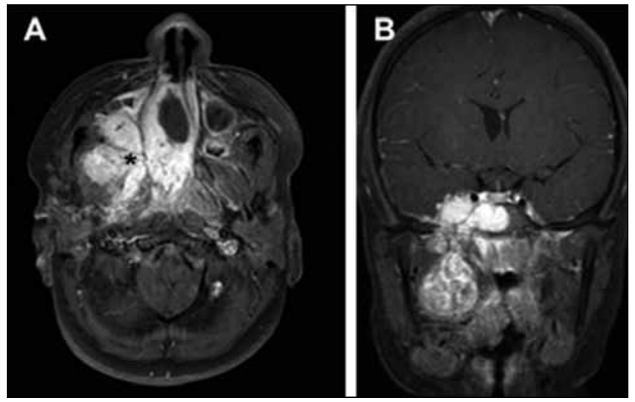

Figure 9: *A) Axial MRI and B) Coronal MRI demonstrating an extensive right angiofibroma with extension into the middle cranial fossa, involvement of the right internal carotid artery and deep extension into the parapharyngeal space with airway compromise. This was fully excised with staged surgical procedures.*

embolisation is recommended up to 48 hours prior to surgical resection.

While a large amount of disease may be resected endoscopically (e.g. figure 10), not all pathology is accessible via an endoscopic approach and a full armamentarium of surgical procedures is necessary. An open approach is still a very valuable option in combination with endoscopic clearance (figure 11).

Figure 10: *Large frontal osteoma (*), resected via a combined endoscopic and open craniofacial approach.*

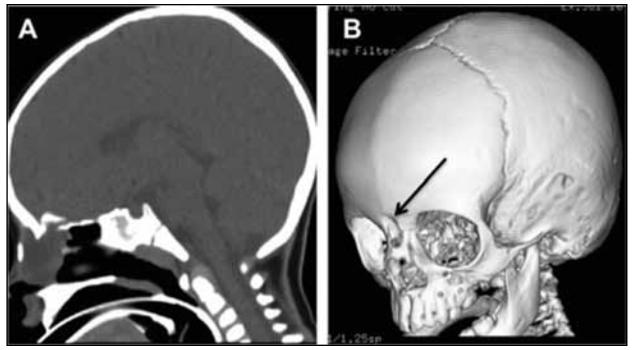

Figure 11: *A) Sagittal CT and B) 3D reconstruction showing a left anterior nasal glioma (nasal glial heterotopia) in a 10 month old child, with extension through the nasal bones (black arrow). This was resected via an entirely endoscopic transnasal approach.*

For malignant sinonasal and skull base lesions, the endoscopic approach is gaining momentum. Certainly for diagnostic purposes, biopsy is possible even for challenging regions such as the petrous apex (figure 12A) and orbital apex (figure 12B) and in selected cases radical resection with negative margins is achievable[8].

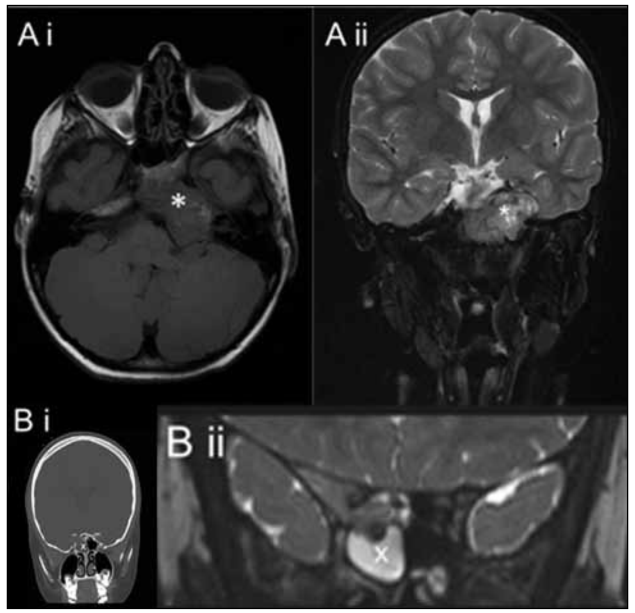

Figure 12: *A) Axial T1 (i) and coronal T2 (ii) MRI showing an extensive Ewing's sarcoma recurrence of the clivus and petrous temporal bone (*). This was successful biopsied via a transnasal endoscopic approach and the child discharged home the following day. B) Coronal CT (i) and T1 MRI (ii) demonstrating a right orbital apex lesion (x) with marked bony destruction. The MRI shows the lesion extending from lateral to medial passing inferior to the optic nerve. Biopsy was performed using an endoscopic transnasal approach to reveal Langerhan cell histiocytosis.*

Controversies

A concern with paediatric sinus/facial surgery in any form is the effect it has on facial skeleton growth. A number of studies have attempted to address this in both animal models and retrospective studies on human patients. Early studies on piglets being subjected to unilateral FESS showed a significant impact on midfacial growth, with even limited surgery having an effect[9,10]. A more recent study on patients undergoing surgery for cystic fibrosis showed that there was no difference in facial measurements in adults who underwent FESS between the 1st and 2nd growth spurts, after the 2nd growth spurt[11], and those having no surgery at all. In this study all patients were over 12 years old at the time of earliest surgery and as yet there is no corresponding data for patients, such as ours, undergoing surgery at a younger age. Similar to other retrospective reports[12], we have not observed any problems in our cohort of patients.

Conclusions

Paediatric anterior skull base endoscopic surgery continues to grow as more surgeons transfer the skills gained in the adult population to children. As technologies and abilities improve, the approach will become more routine in all but the very youngest of patients. Its applicability to malignant lesions of the region is still being explored, but it is likely that more and more tumours will be resected via this approach, with only the most extensive requiring craniotomy. A paediatric anterior skull base multidisciplinary team is essential to ensure a good quality service.

Declaration

The authors have no competing interests. Some of the data in this paper was presented at the British Skull Base Society Annual Meeting, Dublin, Ireland, January 2015.

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Objective and subjective testing of hearing in children

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Abstract
Hearing impairment is the most prevalent sensory congenital condition in the UK with 1:800 babies born with deafness[1]. Hearing impairment effects communication, especially speech and language acquisition and educational achievement[2,3] meaning there are personal implications for patients and also an overall cost to society[4].

Hearing tests for children are aimed at early identification of hearing impaired patients and subsequent early intervention. They can be categorised as objective or subjective tests. This article reviews the main objective and subjective tests available for children as it is important for an ENT surgeon to be aware of the different types of hearing screening for children at appropriate stages of development.

J ENT Masterclass 2015; 8 (1): 46 - 50.

Key words
Deafness, ABR, OAE, VRA, PTA

Introduction
Neonatal hearing screening in the UK detects hearing loss[5] in 1.06 per 1000 live births. This prevalence increases to 1.33 per 1000 aged 5 and older suggestive of progressive or late onset hearing loss which is associated with autosomal dominant genetic defects[1]. The increase in prevalence in the first 5 years could also be due to missing the newborn screening.

Testing the hearing of children poses several challenges, including the ability to distinguish children who have speech delay secondary to hearing loss or to a primary language deficit as seen in global developmental delay. Hearing tests are categorised as either objective or subjective. An objective test is a functional test of the middle or inner ear and the auditory pathway and can be performed independently of the child's age and developmental stage. Subjective hearing tests are behavioural and require a response to a sound, from a simple movement such as a head turn, to following a task such as placing figures in a boat.

Identifying hearing loss as early as possible in children allows intervention in the form of amplification or surgery and hence overall improvement or resolution of the hearing deficits which is the fundamental reason for vigilance and knowledge of this important area in ENT[6].

OBJECTIVE HEARING TESTS

Newborn Hearing Screen
The newborn hearing screening programme was initiated in the UK after the commissioning report by Davis *et al* in 1997[2]. It is based on testing for transient otoacoustic emissions (TOAE) from the outer hair cells[7]. Outer hair cells are organised into three rows along the cochlea. They are located on the basilar membrane and have a function in the fine tuning and modulation of the inner hair cells (Figure 1). A probe is inserted into the external auditory canal and cot-side testing is performed of each ear sequentially. A series of broadband clicks are presented and after an interval of up to 15ms an amplified version of the stimulus is recorded by the probe. The principle of the test is that the auditory signal stimulates the inner hair cells, activating a reflex down the efferent nerves. This causes the outer hair cells to contract, moving the tectorial membrane which subsequently generates a sound. This sound escapes via the round window, travels through the middle ear, tympanic membrane (TM) and is detected by the probe's microphone. A large number of stimuli are combined to allow averaging. This works on the principle that responses to a stimulus present after a fixed latency period, allowing the signal to be distinguished from background noise. Different frequencies are tested at different amplitudes.

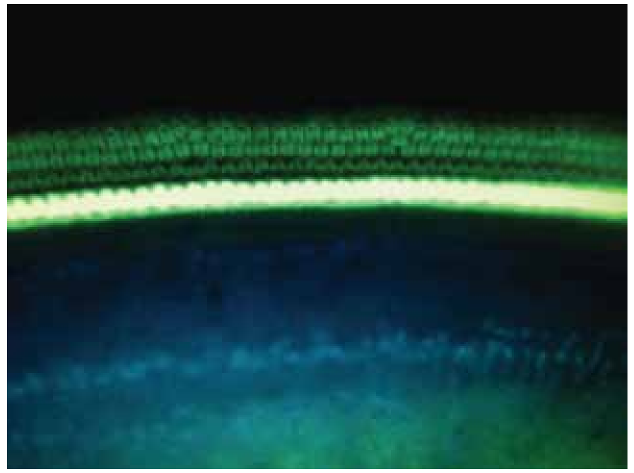

Figure 1: *Section of cochlea treated with immunofluorescence; three rows of outer hair cells and a row of inner hair cells.*

Thus TOAE demonstrates normal outer hair cell function in the cochlea. Prevalence of hearing loss >40dB in the better ear averaged over 0.5, 1, 2 and 4kHz is 1.06 per 1000 of the population[5].

Advantages of the TOAE screening include cot-side testing which is unaltered by sleeping, easy to perform by a wide variety of medical staff, affordable in terms of equipment and staffing costs, little interpretation and most importantly early identification of potentially deaf children which is associated with better outcomes[2]. It is an excellent test with up to 97% sensitivity and has revolutionised screening for deafness with up to 96% of all target babies in England being screened[8].

Disadvantages include the low specificity which can be influenced by Otitis Media with Effusion (OME)[9] and debris in the External Auditory Canal (EAC); failures can also be caused by noisy environment such as a medical ward and there is also a lack of threshold detection. The newborn hearing screening also lacks the ability to detect auditory neuropathy or processing disorders and detection of defects in the OTOF gene which, although rare cause abnormal inner hair cell synaptic transmission[10].

If the newborn screening is failed, it is repeated within four weeks and after a second failure, a referral to audiology is made. During this appointment, a different version of OAE or an Auditory Brainstem Response (ABR) test is performed whilst the infant is sleeping.

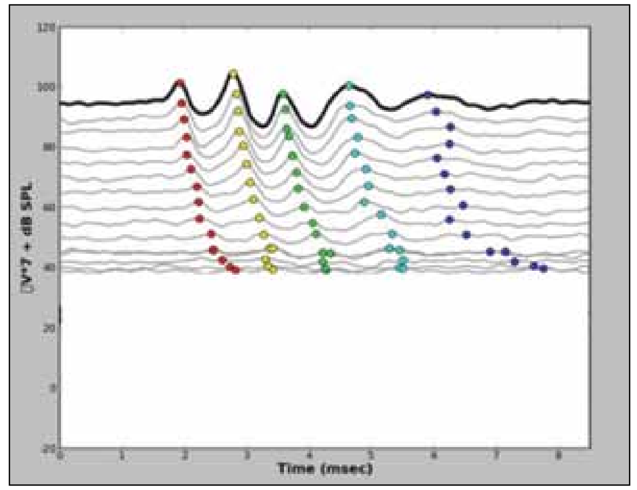

Figure 2: *ABR recording form a guinea pig from supra-threshold 95dB to threshold at 38dB. Five clear waves can be identified. Wave I (red) auditory nerve, wave II (yellow) cochlear nucleus, wave III (green) superior olivary complex, wave IV (light blue) lateral lemniscus, wave V (blue) inferior colliculus.*

Auditory Brainstem Response
The ABR was refined and described in 1971[11]. For an ABR, sound signals are presented to the ear which stimulate the inner hair cells. Their electrical signal travels up the auditory nerve (I) to the cochlear nucleus (II) then onto the superior olivary complex (III), lateral lemniscus (IV) and then onto the inferior colliculus (V) (Figure 2). The scalp electrodes map this pathway with waves I – V; an absence of signal indicates deafness.

The ABR waveform is generated after multiple repeat stimuli and averaging. The stimulus is altered typically from a high amplitude in a step wise manner to find threshold. This is repeated at different frequencies, typically between 0.5 and 4kHz. This allows accurate threshold measurement with a >90% specificity and sensitivity.

The latency range of ABR recordings are typically in the range of 0-15ms. The latency values however vary according to the child's age and hence reference values must be carefully applied which alter weekly in the neonatal preterm period, biweekly until 3 months and monthly until 24 months old[12].

ABR can be used to predict developmental outcomes in neonates who are at risk for neuro developmental delay[13] such as prematurity and admission to neonatal high dependency. Abnormalities in the ABR include a reduction in the amplitude of wave V compared to wave I. Increased latencies between I-V have been associated with perinatal hypoxia[14] and autistic spectrum disorder[15]. ABR also has the potential in monitoring treatment, for example during chemotherapy, and disease progression on medical conditions affecting the central auditory nervous system[16]. ABRs are robust and are not degraded by anaesthetic, but are sensitive to the sound level in the environment and extraneous electrical noise.

ABR testing is resource intensive, frequently requiring an anaesthetist, theatre team and audiologist. In very young infants, the ABR can be performed whilst in a post prandial sleep and swaddled. ABR recording can also be affected by electrical noise including brain or cardiac electrical activity and other electrical equipment. It is also influenced by core body temperature[17] and hypoxia[18].

Tympanometry and acoustic reflexes

Tympanometry is a measure of sound transmission through the TM and middle ear. In fact, this is the admittance of sound which is the reciprocal of impedance and is how results are usually expressed. A probe consisting of three tubes is inserted into the EAC. The first tube delivers a sound at 220Hz, usually a pure tone (1kHz under 4 months). The second measures the sound level in the EAC and the third measures the pressure in the EAC between -300 and +200daPa (mmHg). The maximum transmission of sound through the EAC, TM and the ossicular chain is when the TM is intact and is in its neutral position. A tympanogram is produced which is either type A (normal), B (flat as seen in OME), C1 (negative peak with pressure between -100 and -200daPa), C2 (pressure lower than -200daPa) and type D (abnormally high peak) according to the Jerger classification[19,20]. The probe also measures the volume of the EAC and hence helps to interpret the results, particularly in type B, which would be due to TM perforation or OME.

Acoustic reflexes

Stapedial reflexes are also recorded by the tympanometry. This reflex is facilitated by stapedial muscle contraction after exposure to a sound stimulus of 70dBHL. This protective response decreases the admittance of sound to the stapes and reduces transmission to the middle ear. It is also an indication of the reflex arc through the afferents to the cochlear nucleus to the brainstem, and the efferents via the facial nerve and to stapedius. Hence this is an objective test which provides information of the brainstem function. It has little technology involved and can be used from birth. It is also useful in detecting non organic hearing loss if the reflex threshold is lower than the behavioural auditory threshold.

Tympanometry, including the recording of stapedial reflexes, can be performed in a clinical setting and at any age. It does, however, require an EAC free from debris and discharge.

Figure 3: *McCormick Toys.*

SUBJECTIVE HEARING TESTS

Visual Reinforcement Audiometry (VRA)

The development of VRA arose from infant hearing assessments described by Ewing and Ewing in 1944[21] and refined by Dix and Hallpike in 1947[22]. This test is suitable for children with a development age of 6 months to 3 years and requires a specialised room and two testers. The child sits on a parent's knee and distracting toys are shown to the child directly in front of the child. A second tester is also facing the child with a view of the child's face but behind a one-way window. A sound is produced to the side, and on turning their head the child receives a reward in the form of a visual display such as a dancing animal. The frequency and amplitude of sounds is altered after initial conditioning. Each ear can be tested separately and bone conduction can also be performed if required. Frequency specific data is provided. The presence of a parent or carer makes VRA testing family centred and helps to establish a holistic approach to hearing loss[6].

Speech Audiometry: McCormick Toy Discrimination Test

This test was designed to provide a quick screening of hearing in children. It consists of 14 toys which have a similar sound when heard at quiet levels (Figure 3). The toys were selected as paired monosyllabic words which are familiar to children with a developmental age of 2 years and have maximal acoustic similarity in the pairings[6]. Normal hearing is deemed as an 80% accuracy in identifying a toy when shown the matching pair at sound levels of 40dB. Lip reading can also be eliminated by covering the tester's mouth. This test has been shown to have a 100% sensitivity and 94% specificity in detecting conductive hearing loss in 3 year olds[23].

Conditioned Play Audiometry (CPA)

This is play audiometry where a child is asked to perform a simple repetitive task such as placing toys in a boat when the tester says "go". After conditioning, the game starts with a sound signal such as a frequency modulated warble tone. This is binaural testing and must be in a sound proof environment. Different frequencies and amplitudes are tested. This is a reliable test with one tester required.

Table to summarise the advantages and disadvantages of Objective Subjective hearing tests

	AGE	ADVANTAGES	DISADVANTAGES
OBJECTIVE			
OAE	From birth	Cot-side non invasive, inexpensive, quick specificity 97%	Ambient noise/ OME can cause fail
ABR	Any	Robust test Monitor ototoxicity	Resource intensive Sensitive to noise
TYMPANOMETRY	Any	Clinic based test, simple technology, quick	EAC clear of debris/infection
ACOUSTIC REFLEXES	Any	Clinic based test, simple technology Information on brainstem	EAC clear of debris/infection
SUBJECTIVE			
VRA	➢ 2 years	Holistic – involves carer Non invasive	Co-operation required for conditioning, sound proof room, 2 testers
CPA	➢ 2 years	Non invasive	Co-operation, single tester
PTA	➢ 4 years reliably	Both ears separately, detect threshold, Bone conduction	Calibration

Both the VRA and CPA require a degree of co-operation from the child, manual dexterity and intelligence. This therefore may not be suitable for all children, especially those with developmental delay.

Pure Tone Audiogram (PTA)

This is a hearing test that can be reliably performed in children with a development age of over 4 years. It requires a sound proof booth and an audiologist. Each ear can be assessed individually and bone conduction studies can be performed. A pure tone with a single frequency of vibration is presented via headphones or insert earphones and the patient's detection of the sound stimulus at discrete frequencies and amplitudes is measured. The child is initially conditioned to respond to the sound by placing a simple motor skill such as toy stacking.

Abnormalities along the sound conduction pathway from middle ear to cochlea can be detected. Equipment calibration is important for PTA to be representative and can result in up to 20dB inaccuracies[24]; measurements are also affected by patient motivation, background noise and environmental factors such as temperature and ventilation of the test room[25].

Summary

Different hearing tests are available for children who have different advantages and disadvantages. The child's age, developmental status including motor skills, attention and visual abilities should be considered before selecting appropriate testing, especially in the subjective category. Minimal intervention, for example OAE, tympanometry and stapedial reflexes should be considered before subjecting a child to ABR testing. It is important that an ENT surgeon is aware of the attributes and limitations of both objective and subjective hearing tests in children to facilitate the earliest and most accurate diagnosis of hearing impairment.

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Single sided deafness (SSD): an overview

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Aim:
This article seeks to review the issues surrounding single sided deafness (SSD) and provides an overview of the management options available. We reviewed the literature particularly looking at the effectiveness of available treatments and management strategies.

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Introduction:
Single sided deafness (SSD) can be defined as a permanent severe to profound sensorineural hearing loss in one ear with normal hearing on the un-affected side. Normal audiometric function is described as hearing thresholds that are no poorer than 20dB hearing level (HL) for pure tone averages of 500Hz,1,2 and 4kHz. This is in contrast to an asymmetrical hearing loss in which both ears may be affected to varying degrees. A key factor in single sided deafness is that the affected ear will not receive benefit when traditional acoustic amplification is applied.

Incidence:
The exact prevalence is unknown however, overall, sudden sensorineural hearing loss has an estimated incidence within the adult population of between 5 and 30 cases per 100,000 per year[1].

It is thought that there are approximately 7500 adults within the UK, who experience profound unilateral sensorineural hearing loss each year.[1]

Aetiology of Single Sided Deafness:
There are many important causes of single sided deafness that must be considered and these can be seen in Table 1. Most of these will be identified during a thorough clinical assessment. In many cases no cause can be identified.

Table 1: Aetiologies of Single Sided Deafness

Adult	Paediatric
Acoustic / CPA Tumours	Inner ear malformation
Cochlear / Head Trauma	Perinatal / Intrauterine Causes including maternal infections (TORCH)
Idiopathic Sudden Loss	Bacterial Meningitis
Meniere's Disease	Viral Infections (Mumps, Measles)
Labyrinthitis	Cochlear / Head Trauma
Vascular events / CVA	Acoustic / CPA Tumours

Consequences of Single Sided Deafness (SSD)
When considering the issues associated with the loss of binaural hearing, it is important to be aware of the physical properties of sound along with the hearing mechanisms and neural processes used by the auditory system in everyday life. Some of these are discussed below:

Head-Shadow Effect:
This refers to the physical properties of sound. When a sound originates from the side of the non-functioning ear, the functioning "good" ear will actually fall in the shadow of the head. As shown in Figure 1.

In reality, the head-shadow phenomenon has a greater impact on higher frequency sounds with shorter wavelengths. These tend to be reflected and attenuated by the head which can create difficulty in audibility and

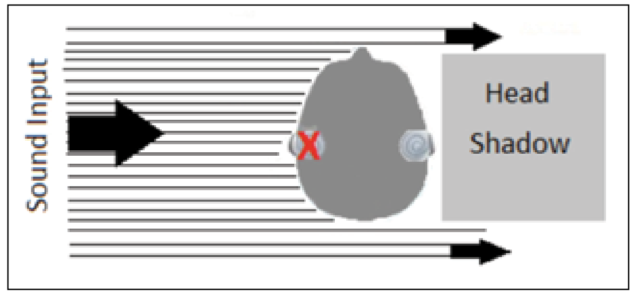

Figure 1: *Basic Demonstration of Head-Shadow Effect.*

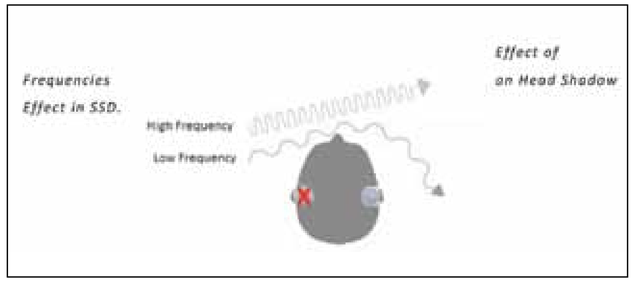

Figure 2: *Effect of Frequencies on Head Shadow Effect in SSD.*

clarity. Low frequency sounds, because of their long wavelength, tend to bend (diffract) around the head and suffer less distortion. (See Figure 2) Overall, the head may attenuate speech intensity by around 6dB but the effect increases to approximately 20dB in frequencies above 5000Hz.[2]

Binaural Loudness Summation / Redundancy:

This refers to the fact that a sound presented to both ears will be perceived to be louder than the same sound presented to one ear only. If a signal is presented to a binaural hearing individual, the auditory system has two opportunities to "look" at the signal received. This results in a reduced chance of missing information and allows the auditory system to more thoroughly assess the information it receives.

Spatial Hearing

SSD results in the loss of the ability to identify the localization of sound. The auditory system uses specific cues to allow spatial hearing, these are the interaural time difference, interaural level difference and head related transfer function (HRTF).

Interaural Time Difference:

This represents the small difference in time it takes sound to reach the ears. If a sound is directly in front or behind the head, sound will reach the ears at the same time, whereas if the sound originates to the left side of the head, then there will be a small difference in the time taken for sound to travel to the right ear. This time difference is approximately 0.6-0.7 milliseconds. This is a frequency dependent phenomenon and occurs with lower-frequency sounds.

Interaural Level Difference:

The interaural level difference refers to the sound pressure levels reaching each ear. This is a similar phenomenon to the head shadow effect, where sound is slightly louder on the side on which it is presented. This tends to be more pronounced in the high frequencies (above 1500Hz) due to less attenuation.

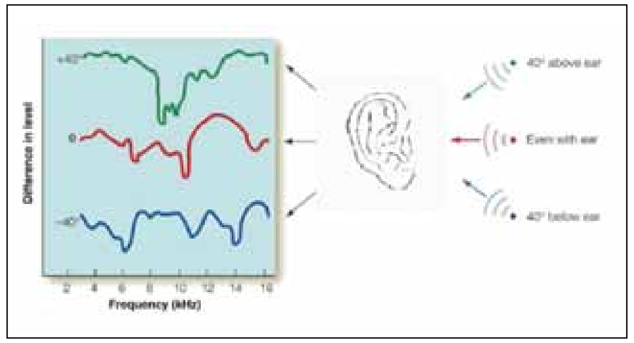

Figure 3: *Diagram of differences of sound intensities at specific frequencies due to HRTF*

Head Related Transfer Function (HRTF)

The pinna and the shape of the head introduce modifications to the impinging sound spectrum depending on the direction of the arrival of sound. Measurements have been performed by placing small microphones in the ears and comparing the intensities of frequencies with those at the sound source when presented at different angles to the head. Typically in a vertical plane. (See Figure 3) The differences can be used as a spectral cue since the information about location comes from the spectrum of frequencies.

Binaural "squelch"

This terminology refers to the neurological process in which the auditory centers within the brainstem are able to analyze, integrate and fuse information received from the two ears and give greater emphasis to the meaningful signal. The unwanted background signal / noise is not given the same neural processing and is therefore somewhat diminished.

In effect, it is a way in which the brain "teases out" the desired sound from background noise.

Overall Consequences of SSD:

As a result of the loss of binaural hearing, the mechanisms previously described are lost which results in many difficulties. Firstly, there is a reduction in overall listening ability with specific difficulties of hearing speech in noise and with regards to directional hearing. Adults suffering SSD experience problems in their daily life in social interactions and communication.[3] Some adults may also report a level of psychological distress that can appear disproportionate to their level of residual acoustic hearing[4].

Children are at risk from delays in speech and language development, cognition and behavioral problems[5]. In one study, parents and teachers reported behavioral problems and academic weaknesses or areas of concern in 25% of children with SSD[6]. Children also appear to have increased rates of grade failures and a need for educational assistance[7,8].

Treatments for Single-Sided Deafness

Contralateral Routing of Signal (CROS) Devices:

The CROS design was originally described in 1965 by Harford and Barry[9]. These devices work to re-route a signal detected at or near the affected "bad" ear to the un-affected "good" ear thereby reducing the head shadow effect. Traditionally, this involved a microphone being placed on the bad ear with placement of a receiver and amplifying system with an open-fit hearing aid on the good side.

Early devices were quite large and required wires connecting the microphone and amplifier; however, modern systems utilise wireless technology and advanced streaming of signals associated with much smaller microphones and amplifiers resulting in much more cosmetic and functional devices. Some can be built into "in-the-ear" products as well as small "behind-the-ear" devices.

Quasi-transcranial CROS

Utilising the fact that the cochlea are present within the skull / temporal bones and do not have absolute acoustic isolation, it is known that if an air conduction signal of high enough intensity is presented to the cochlear of an impaired ear then the signal will eventually overcome any isolating mechanism (interaural attenuation) and be heard in the cochlear of the better ear. This means the use of a conventional high output air conduction hearing aid, either in-the-ear or behind-the-ear, placed in the impaired ear can provide enough signal which may cross through the head and be heard by the cochlea of the normal ear by bone conduction[10-14].

Overall, CROS systems have been shown to provide some improvement in the perception of speech in noise compared to the unaided condition. This benefit is maximal when the speech is presented to the impaired side[15-17] or to the fron[18-20]. while the noise is presented to the un-impaired "good side". A reduction in self-reported difficulty with background noise, communication and reverberation has also been shown[21]. It is well known that CROS systems have some pit-falls. Firstly, speech perception in noise worsens if the noise is presented to the impaired ear, because this signal is then routed to the good ear interfering with the speech signal[15,17,20,22]. The CROS systems do not improve localisation accuracy[15-17] and patients also report some dissatisfaction with having to wear a hearing aid in the better ear[19,23].

Bone Conduction Systems

The very first reference to bone-conduction hearing enhancement devices came in 1876. A physician named Paledino in Italy developed the Fonifero, which consisted of a metal rod with a stirrup at one end. The stirrup was placed over the speaker's larynx who then vocalises. The laryngeal output is transmitted through the rod which was placed either on the patient's teeth or on the mastoid thereby creating a bone conduction pathway[24].

Worn bone conduction aids, such as hard or softband hearing aids, work in a similar manner to the Fonifero: a sound receiver and amplifier are attached to an oscillator which is pressed to the head firmly. Sound energy is then conducted through the soft tissues into bone which then travels across and through the skull to the contra-lateral "good" ear.

Newer examples which work in this manner include the TransEAR system and the soundbite. TransEAR involves a behind-the-ear receiver attached to a bone conductor which is fitted quite deeply into the ear canal. As the medial portion of the ear canal is bony, sound is conducted through the skull to the better ear.

The soundbite requires a prosthesis, which is similar to a retainer, to be fitted to the rear upper teeth. The bone conduction component is then worn inside the mouth and sound conduction travels via the teeth and maxilla to the ears.

A problem with worn bone conduction systems is that a tight seal between the device and soft tissues is often required to overcome attenuation of sound by the skin. Unfortunately this can be uncomfortable when worn for long durations and individuals sometimes dislike the tactile vibratory sensation of the device against the skin or within the ear canal.

Bone Conduction implantable Devices

Within the last few years the implantable options for SSD have significantly increased and include both percutaneous and transcutaneous technologies. Percutaneous devices require the implantation of a titanium fixture within the skull which attaches to a titanium abutment that protrudes through the skin. A sound processor is then clipped onto the abutment directly. These devices generally produce greater gain than transcutaneous devices but have the disadvantage of being skin penetrating. However recently adopted changes in surgical technique may reduce the risk of skin reactions.

Newer systems have adopted an intact skin approach such as the Sophono, Cochlear BAHA Attract and Bonebridge.

These all involve the use of implanted magnets to retain the external component of the device instead of a protruding abutment. The sound processor can then be attached using magnets. Greater gain is generally achieved where the vibratory component is implanted such as in the Bonebridge however the gain is less than the percutaneous devices, skin problems can occur from the pressure of the magnetic attachment and there will be inevitable distortion around the implanted magnet on MRI.

There is evidence to show that users of a bone conduction implants show objective and subjective improvement in audiologic metrics and have improved quality of life compared to unaided conditions[15,19,25-27].

Cochlear Implants (CI) for SSD:

Cochlear implantation is emerging as a promising treatment option for single sided deafness. Since cochlear implantation restores input on the impaired side it may overcome the limitations of CROS aids and bone conduction devices in that it can restore binaural hearing. There is some evidence that speech perception in noise and sound localisation improves in patients with SSD receiving cochlear implants[28-30] along with a reduction in tinnitus and improved quality of life[31]. A recent systematic review confirmed the important benefits of cochlear implantation regarding sound localization, quality of life and tinnitus but suggested that there were varying results for speech perception in noise[32].

Summary:

There are significant difficulties inherent to mono-aural hearing which have been shown to impact everyday life. Patients however seem to vary to what extent they are inconvienienced by this, many seem content with no rehabilitation whilst others find SSD a great disability. Treatments have developed over time which have demonstrable benefit however full reclamation of "normal" hearing remains an elusive goal.

The only treatment that has the potential to provide binaural hearing is cochlear implantation with some evidence to indicate significant benefits for selected patients with SSD. This is currently under investigation in the UK and is not as yet an accepted standard of care on the NHS.

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Benign paroxysmal positional vertigo

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ABSTRACT

Purpose of review
Benign Paroxysmal Positional Vertigo (BPPV) is the most common vestibular disorder, has a high incidence in the general working population and increases with age. This makes it an extremely important condition. This review aims to highlight recent advances in understanding and treatment.

Recent findings
The use of mastoid vibration devices confer no advantage when performing an Epley manoeuvre for traditional treatment of BPPV, and post-Epley postural restrictions only confer a slight improvement. The Semont manoeuvre is equally as effective as Epley in the short term, but less so in the long term. A highly successful treatment for the rare lateral canal BPPV is the Gufoni manoeuvre. These manoeuvres are superior to the use of exercises. Surgical canal occlusion has been shown to be very effective and safe.

Summary
The incidence of BPPV in the elderly population is rising and it has a link to the prevalence of decreased serum levels of Vitamin D, Osteopenia and Osteoporosis. Therefore, with an increasing elderly population, knowledge of effective treatments is paramount.

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Keywords
Positional, Vertigo, Canalithiasis, Cupulolithiasis, Epley.

INTRODUCTION
Dizziness is exceptionally common and is described by 20% of the working population.[1] It presents with a multitude of vague symptoms whereas vestibular aetiology presents with true vertigo defined as a hallucination of movement. Vestibular vertigo accounts for approximately 40% of diagnoses in balance clinics[2]. Benign Paroxysmal Positional Vertigo (BPPV) is the most common cause of vestibular vertigo and represents 30% of those diagnoses [3].The prevalence of BPPV is quoted as up to 64 per 100,000 population[4] with a lifetime prevalence of 2.4% and a 1 year incidence of 0.6%[5]. This review of the literature highlights recent advances in understanding and treatment of this extremely common condition.

PATHOPHYSIOLOGY
The otolith organs situated within the vestibule of the labyrinth, namely the utricle and saccule facilitate the perception of linear acceleration. They have otoconia, calcium carbonate crystals, which sit on a gelatinous otolithic membrane within the maculae of these organs and embedded in the base of this membrane are the sensory hair cells. A change in posture leads to movement of the otolithic membrane as the weight of the otoconia causes a shift of the membrane due to gravity. This stimulates the hair cells and thus is detected as a posture change. The utricle and saccule detect movement in the horizontal and vertical planes respectively.

In contrast, the semicircular canals do not normally contain otoconia. Instead, the sensory hair cells in these canals are embedded in the gelatinous cupula, which completely seals the canal in the ampulla. Change in posture in an angular or rotational plane causes movement of the endolymph fluid in the semicircular canals and so deflection of the cupula, stimulating the hair cells in the ampulla and so is detected by the brain as a rotational movement of the head.

In patients with BPPV, the otoconia become dislodged from their usual position within the utricle and migrate into one of the semicircular canals.

Cupulolithiasis
This theory, initially postulated by Shuknect, suggests that loose otoconia become attached to the cupula of the affected canal causing it to become heavy [6]. On movement of the head relative to gravity, the cupula is weighed down by the otoconia thereby inducing an immediate and sustained stimulation of the sensory hair cells. This theory explains the general disequilibrium experienced by some BPPV sufferers and the prolonged vertigo experienced in certain positions.

Canalithiasis
This theory, initially postulated by Hall, suggests that loose otoconia float freely in the endolymph of the semicircular canal.[7] Angular acceleration in the plane of the canal will cause movement of the endolymph and free otoconia will move with the endolymph but will continue, by inertia after acceleration has ceased. There is therefore a continued deflection of the cupula for a few seconds, which produces the symptoms of BPPV. This theory explains the latency of the symptoms in BPPV.

The posterior semicircular canal is the most commonly affected of the three canals, and is implicated in 60 to 90% of cases[8,9]. The lateral semicircular canal is involved in 8 to 35% of cases[8,9]. Despite its anatomical orientation some authors feel the superior semicircular canal may be responsible in a handful of cases[8,9].

AETIOLOGY
BPPV is most often idiopathic, but may be associated with head trauma or surgery, ear surgery, ear infection, vestibular neuronitis, or ischaemia in the territory of the anterior vestibular artery. Essentially, any potential mechanism by which the otoconia in the inner ear may become displaced and float into the semicircular canals, may cause BPPV.

BPPV is common in increasing age, with a ten-fold increase in incidence from the age of 20 to the age of 80 years.[5] A study of large population 75 years olds showed a prevalence of 11%.10 Deranged calcium metabolism, Low levels of Vitamin D, Osteopenia and Osteoporosis have all been linked to BPPV[11]. It is very rare in childhood and has never been reported in anyone under the age of 11 years[8].

HISTORY
Benign -BPPV is a self-limiting disorder (therefore the term benign) and tends to undergo remission spontaneously after around 40 days for Posterior canal BPPV and 16 days for Horizontal canal BPPV.[12] The condition tends to recur however, with a recurrence rate of 27%[13].

Paroxysmal – BPPV symptoms occur in paroxysms (defined as short lived attacks that tend to recur) and classically present with repeated episodes of short-lived rotatory vertigo lasting for a few seconds at a time and characteristically less than 1 minute.

Positional – BPPV is postitionally induced and occurs on a change in head position. Patients tend to report vertigo on looking upwards, bending down, turning the head suddenly, and rolling over in bed. Certain head positions when asleep are associated with recurrence of BPPV[14].

Vertigo – Defined as a hallucination of movement and classically described as the room spinning for a few seconds. Occasionally it is associated with nausea, vomiting, or oscillopsia (oscillation of the visual fields). Elderly patients can report associated falls[5,10]. Patients will often say that they feel generally dizzy or off balance for a few hours after the attacks. It is therefore important to ask about the episodes of actual vertigo. A prolonged feeling of general imbalance is seen in a number of patients and may be secondary to utricular dysfunction. It may persist even after successful treatment of the vertigo[5]. A history of loss of consciousness is not compatible with BPPV and a central neurological or cardiac cause must be sought.

EXAMINATION
All patients with vestibular presentation should undergo full neurotologic examination with special attention paid to the vestibular system. Frenzel glasses or videonystagmography are ideally required to pick up nystagmus which may otherwise be visually suppressed. The Halmagyi Head Thrust and Utricular Shift tests are also useful components of the vestibular examination. In order to rule out middle ear, or other inner ear conditions, patients should have otoscopy, tuning fork, and audiometric assessment. Cranial nerve examination is essential to pick up subtle central signs, as is coordination testing such as cerebellar tests and gait. Romberg's and Unterberger stepping test may be useful to further evaluate proprioceptive and peripheral vestibulopathy respectively.

However, the Unterberger test is a soft sign, may be related to cerebellar pathology, and with osteoarthritis so prevalent in the affected population, may not be adequately performed. With isolated BPPV all these examination findings should be normal, however other vestibular disorders may co-exist[8]. The primary diagnostic test for BPPV is the Dix-Hallpike test (DHP) or manoeuvre, also known as the Nylen-Barany test.

Dix-Hallpike Test
As originally described by Dix and Hallpike in 1952[15]. As BPPV is such a common entity, all patients who present with dizziness should undergo this test. It has a sensitivity of around 80% and a specificity of 75%[16].

The patient sits upright with legs extended on a couch. The head is then rotated 45 degrees towards the side of the suspected pathology. The patient is then dropped backwards into a lying position. It is not necessary to hang the head over the edge of the couch. Ideally if overextension is required, the head of the couch should be lowered separately, to remain supportive. For most patients, age has produced an exaggerated thoracic kyphosis, which will give the necessary 30 degrees angulation, simply by laying them flat without a pillow. The eyes are then observed for 30 seconds due to a characteristic 5-6 second latency prior to nystagmus.

A geotropic (towards the floor) torsional nystagmus is considered positive for posterior canal BPPV, the most common form, accounting for 60-90% of patients[8,9]. The fast phase of the nystagmus is toward the underlying ear, i.e. towards the ground and is termed geotropic. When sitting the patient back up the eyes should be observed again as further nystagmus may occur in the opposite direction. If the test is then repeated, it classically habituates, i.e. produces weaker responses on each re-test.

The Dix Hallpike test is more likely to be positive when performed in the morning, before vertigo habituates, secondary to daily tasks. This increased habituation and performing a test late in the day may find it to be weak or negative. If a positive test result is found, an otolith repositioning technique should be performed before moving on to test the other ear. The test can then be repeated for the opposite ear as BPPV can be bilateral. Frenzel glasses may assist in observing the nystagmus.

Rarely, a patient with a classic history of BPPV may have a negative Dix-Hallpike test. However, many of these patients may experience vertigo on sitting up and also a trunkal retropulsion (sensation of falling backwards). This is often seen in patients with a pushing backwards of their truck on sitting up. This has been shown to be associated with a positive diagnosis of BPPV despite a negative Dix-Hallpike[17].

Lateral Canal BPPV

This is much rarer than posterior canal BPPV, accounting for up to 35% of cases and may present with more severe and prolonged episodes of vertigo[18,9]. It may occur as a complication of treatment for posterior canal BPPV with an Epley manoeuvre as otoconia fall out of the posterior canal and into the lateral canal[19]. Nystagmus seen in lateral canal BPPV is not rotatory, but horizontal in orientation. It may be geotropic (towards the ground), or ageotropic (apogeotropic) (towards the ceiling)[18]. It is best seen with the patient supine with head rolled to the side. This is known as the supine roll test[20]. Horizontal geotropic nystagmus is seen in 75% of cases, whereas ageotropic nystagmus is seen in only 25% of cases and is thought to be caused by debris that is anteriorly placed and closer to the ampulla[18]. Lateral canal BPPV should be treated with a Barbeque manoeuvre or Gufoni manoeuvre (see below).

Superior canal BPPV

This is extremely rare, accounting for up to 2% of patients with BPPV.[9] This is thought to be due to the anatomical position of the canal, at the highest point of the labyrinth. Classically superior canal BPPV exhibits downbeating nystagmus on Dix-Hallpike testing without torsional element.[21] This nystagmus can occur more commonly than the actual diagnosis of superior canal BPPV[22]. However, this is also present in a number of serious central conditions such as, Chiari malformation, Cerebellar disorders and tumours, demyelinating diseases and centrally acting drugs[8]. Excluding central causes should be considered a priority in all patients displaying downbeat nystagmus. Due to its rarity, superior canal BPPV will not be discussed further.

MEDICAL TREATMENT; PARTICLE REPOSITIONING MANEOUVRES

Following a positive Dix-Hallpike test, simple medical treatment will often be successful. However, studies show that spontaneous resolution of symptoms will occur without any treatment in as many as 84% of cases[23,12]. Despite this it is still advised that patients suffering symptoms, with a positive Dix-Hallpike test receive primary treatment, which is a particle repositioning manoeuvre.

The most common of these is the Epley manoeuvre first described in 1992[27]. Studies have shown a success rate of around 80% after a single treatment[24,25]. A recent Cochrane Review into the Epley showed that Post-Epley postural restrictions, that have been used over the years, only confer a slight improvement of an already excellent success rate and use of mastoid vibration devices confer no advantage[25]. Subjective vertigo during position two of the manoeuvre (point 7, below) has high correlation with a successful cure[26]. The following are procedures for the Epley and Semont manoeuvres.

Epley[27]

1. Firstly perform Dix-Hallpike test.
2. If positive, wait for the nystagmus to settle.
3. Support the head for 1 minute.
4. Turn head 90 degrees to other side.
5. Support for 1 minute in this position.
6. Roll patient onto their side in direction they are facing.
7. Turn head a further 90 degrees to look down at the floor.
8. Support for 1 minute in this position.
9. Return to sitting position and remain supporting for 1 minute in this position; they may feel they are falling backwards. If dizziness in the first position of testing is longer than 1 minute the duration of other positions should be extended accordingly.
10. It should be remembered that when otoconia return to the vestibule from the posterior canal some may fall into the entrance of the lateral canal[19]. Although rare, it is important to repeat Dix Hallpike test after an Epley manoeuvre has been performed to check. If nystagmus is horizontal, the Barbeque Manoeuvre or 360 degree roll should be used to reposition the errant crystals (see below).

Semont[28]

Also known as the Liberatory manoeuvre, this is an alternative particle repositioning manoeuvre and is often used when Epley has failed. It is highly effective in the short term, but less so in the longer term[29,30]. It is often preferred as the manoeuvre of choice in cupulolithiasis[31].

1. Patient asked which side causes the dizziness. (Right in this example.) Patient sat upright in the centre of couch with the legs over edge.
2. Head is turned 45 degrees to the left.
3. Patient is rapidly moved down to lie on right side with head still looking 45 degrees upwards towards left.
4. Support head for 1 minute or until nystagmus ceases.
5. Patient then rapidly moved through 180 degrees to lie on left side without changing head position.
6. Support head for 1 minute in this position – nose should be facing into couch.
7. Very slowly return patient to seated position.
8. Instruct patient to keep head in neutral position for the next 48 hours i.e. no looking up or down.

Barbeque Manoeuvre or 360 degree roll[32]

This is treatment of choice for lateral canal BPPV[32]. A very effective treatment with 74% cure rate after single manoeuvre and 85% cure rate after three[32].

1. Firstly perform Dix-Hallpike test or Supine Roll Test.
2. If positive (with horizontal nystagmus), wait for nystagmus to settle.
3. Roll 90 degrees towards the unaffected side.
4. Support head in this position for 30 seconds
5. Turn a further 90 degrees to look down at floor.
6. Support head for 30 seconds in this position.
7. Turn a further 90 degrees.
8. Support head for 30 seconds in this position.
9. Return to supine position and remain supporting for up to 1 minute.

Gufoni Manoeuvre

This is highly effective for Lateral-canal BPPV with a success rate of up to 83%[33]. It is equally efficacious for Geotropic and Ageotropic forms of Lateral-canal BPPV and is extremely simple.

1. From seated position, patient is rapidly moved down on unaffected lateral side with head still facing forwards.
2. Maintain position for 1 minute or until nystagmus resolves.
3. Head is then briskly rotated 45 degrees towards the floor.
4. Maintain position until vertigo resolves.
5. Slowly sit up.

MEDICAL TREATMENT; EXERCISES

Vestibular rehabilitation exercises are commonly used for many peripheral vestibular disorders. They speed up natural neural compensation mechanisms, habituate, adapt and rehabilitate a patient's balance. There are various forms of these exercises tailored for the diagnosis. With respect to BPPV, Brandt and Daroff devised a set of specific exercises for the rehabilitation in 1980[34]. These exercises are similar to the Semont manoeuvre, with one important variation, see point 5 below.

Brandt-Daroff

1. Patient sat upright in centre of couch with the legs over edge.
2. Head turned 45 degrees to left.
3. Patient lies down on right side with head still looking upwards towards their left.
4. Remain in position for 1 minute after vertigo settles.
5. Patient then rapidly moves through 180 degrees to lie on left side whilst rotating head 90 degrees to right, so end looking upwards towards their right. (The mirror image of position in point 3).
6. Remain in position for 1 minute after vertigo settles.
7. Gradually return to seated position.

Recent studies show Particle Repositioning Manoeuvres are more effective than exercises for treatment of BPPV[31,35,36]. A trial in 2001 looked at 147 BPPV patients who were randomised to treatment with Epley, Semont, or Brandt-Daroff exercises. Symptom resolution among those treated with either Epley or Semont manoeuvres at 1 week was the same (74% vs 71%) but only 24% for Brandt-Daroff exercises. At 3-month follow-up, however, patients treated with Epley demonstrated superior outcomes compared with those treated with the Semont manoeuvre (P=0.027)[29].

SURGICAL TREATMENT

After remission there is approximately a 27% recurrence rate of BPPV[13]. Repeating Epley or Semont manoeuvres in these patients will be effective in up to 98%[25,37]. Rarely with intractable recurrences or cases with intractable disabling vertigo, a surgical option may be required. There are three surgical approaches to BPPV; Singular nerve section, Vestibular nerve section and Semicircular canal occlusion[38].

Singular Nerve Section

Also termed Posterior Ampullary nerve section, this seldom used surgery is aimed at the singular nerve which carries the afferent fibres from the ampulla of the posterior semicircular canal. It was originally described by Gacek in 1974 and performed under local anaesthetic[39]. The nerve is approached transmastoid and found in a small canal inferior to the round window. Due to close proximity to the cochlea, there is a high risk of sensori-neural hearing loss associated with this procedure and thus it has lost favour. However, Gacek published his own results in 2002 showing a success rate of 97% with a 4% incidence of sensorineural hearing loss[40].

Vestibular Nerve Section

This procedure ablates the ipsilateral vestibular nerve in order to cure symptoms. It is rarely performed for BPPV and more commonly for severe Menieres disease[41]. The surgery is via a retrosigmoid approach to the internal acoustic meatus. It is usually performed in conjunction with neurosurgeons and has a success rate of 94%. There is a risk to sensorineural hearing of 9%[41].

Posterior Semicircular Canal Occlusion

This is the most commonly performed surgical procedure for BPPV and involves preventing movement of free otoconia by physically plugging the posterior semicircular canal. The procedure is performed transmastoid where the posterior semicircular canal is identified as it lies within a 10mm arc of the incudal recess. The canal is drilled down so that the membranous canal is just visible but not opened. This is termed "blue lining the canal". A bone pick is then used to carefully remove the remaining overlying bone without disturbing the membranous labyrinth. The occlusion is performed using a plug of muscle, bone pate, bone wax or a combination of materials which is pushed into the opening to compress the canal. The area is then sealed with a fascial graft to prevent CSF leak. The procedure is safe and results are very encouraging with an almost 100% success rate and a low risk of severe sensorineural hearing loss[42,43].

CONCLUSION

BPPV is the most common vestibular disorder and has high incidence in the general working population, which increases with age. It is caused by loose otoconia in the semicircular canals, either freely floating or abnormally attached to the cupula of the canal. Although the natural history is for spontaneous resolution, it typically has a recurring pattern. Simple particle repositioning manoeuvres are extremely successful and rehabilitation exercises are useful. There are surgical options for treatment in intractable and severe cases and these are highly effective and safe. With an increasing elderly population, it is envisaged that the overall prevalence of BPPV will rise and thus further analysis of its effective treatment in this age group will be required.

KEY POINTS

- The prevalence of BPPV is 64 per 100,000 in the general population with a lifetime prevalence of 2.4%, although the prevalence in those over 75 years of age however, is 11%. It is envisaged that with an increasing elderly population, the prevalence of BPPV will rise.
- The primary diagnostic test is the Dix-Hallpike test, in which the type of nystagmus seen can distinguish which semicircular canal is affected.
- Spontaneous resolution of BPPV will occur in up to 84%, with recurrence in 27%.
- Manoeuvres, such as the Epley have a success rate of 80%, but the use of mastoid vibration devices confer no advantage, and post-Epley postural restrictions only confer a slight improvement.
- For rare lateral canal BPPV with horizontal nystagmus on Dix-Hallpike test, a barbeque roll manoeuvre or Gufoni procedure have a success rate of up to 85%.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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Assessing canal and otolith function

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Abstract

The formal assessment of a dizzy patient requires taking a thorough history and performing a clinical assessment supplemented, where necessary, by special investigations that may include imaging. This review aims to describe the clinical and special investigations that may be performed to identify abnormalities of the individual semicircular canals and otoliths of the peripheral vestibular system.

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Introduction

The inner ear is contained within the bony *labyrinth*, a dense portion of bone within the petromastoid part of the temporal bone. Contained within this confluent and structurally complex cavity and supported by connective tissue, lies the membranous labyrinth (note figure 1). This structure is divided into two functionally different parts, the cochlea that is responsible for hearing, and the peripheral vestibular system that detects linear and angular head tilt and acceleration.

The membranous labyrinth is filled with endolymph and consists of five confluent but functionally different membranous segments involved in the detection of movement. The saccule and utricle are responsible for detecting static head tilt and linear acceleration, the utricle in the vertical plane and the saccule in the horizontal plane. The semicircular canals are orthogonally orientated and organised into functional pairs: the horizontal semicircular canals, and the posterior and superior contralateral canals[1].

Functions of normal human balance include providing spatial awareness, and maintaining posture and gaze stabilization. As the peripheral vestibular apparatus is essentially inaccessible, its function is assessed indirectly by assessing the vestibulo-spinal and vestibulo-ocular reflexes (VOR)[2].

The vestibulospinal reflex allows rapid correction of posture in response to head acceleration (contraction of the contralateral limbs and extension of the ipsilateral limbs). This pathway is mediated through the superior semicircular canals and otolithic organs via the lateral vestibulospinal tract. In contrast, the medial vestibulospinal tract maintains head position in the horizontal plane irrespective of trunk position, the *righting reflex*.

The vestibulo-ocular reflex provides image stabilization during head tilt and rotation. This reflex forms the basis for a number of important clinical investigations of peripheral vestibular function and is depicted in Figure 2.

Assessment of the peripheral vestibular system

A formal assessment of the peripheral vestibular system requires a thorough history and clinical assessment, supported by special investigations that on occasion may include imaging. The reader should be aware that no single investigation in isolation is likely to provide a diagnosis and cause for a peripheral vestibular disorder and any abnormalities must be taken in context.

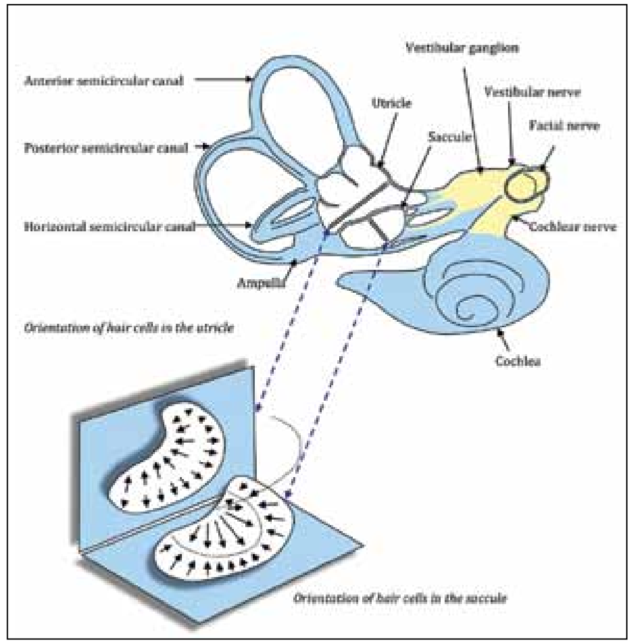

Figure 1: *The membranous labyrinth. The maculae of the saccule and utricle are orientated at 90 degrees to each other in order to detect vertical and horizontal movement. The semicrcular canals are similarly orthogonally arranged to detect pitch, roll and yaw.*

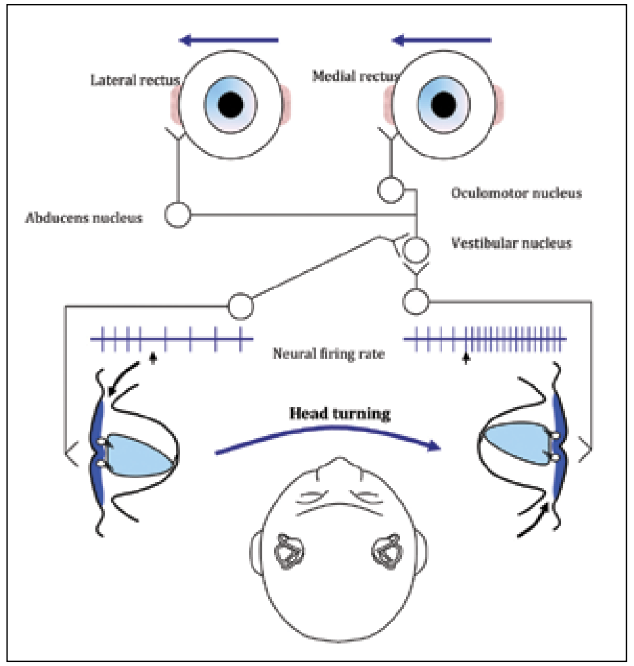

Figure 2: *TThe excitatory pathways of the vestibulo-ocular reflex. As a result of head rotation, endolymph flow results in cupula deflection and stimulation/inhibition of ampullary nerve fibres. Neural connections to the IIIrd and VIth cranial nuclei result in contraction of the left lateral rectus and right medial rectus stabilizing gaze [ñ - start of head rotation].*

This summary aims to provide a framework for clinical assessment and interpretation of abnormalities demonstrated during testing of the peripheral vestibular system.

Assessment of ocular movement

Spontaneous nystagmus and gaze-evoked nystagmus may be elicited by asking a subject to follow a target (e.g. an examiner's finger). This should be performed in both the horizontal and vertical planes. Whilst nystagmus in the vertical plane is in keeping with central pathology, horizontal nystagmus is usually due to an acute peripheral vestibular loss. The fast phase, is contra-lesional and represents the corrective ocular movement brought about to stabilize gaze.

First degree nystagmus is present on gaze deviation towards the affected ear, second degree in the neutral position and when gaze is directed towards the affected ear, and third degree nystagmus even when gaze is directed away from the lesioned ear.

An irritative vestibular lesion, although rarely encountered, will produce a fast phase nystagmus towards the affected ear.

Head thrust test

The head thrust test is an assessment of the VOR and exploits the ocular movement generated to maintain gaze stabilization in the horizontal plane during rapid head movement[3,4].

The head is turned 30 degrees in the horizontal plane. The subject is asked to fixate on a point (e.g. the examiner's nose) whilst the head is rapidly brought in to the midline. In a normal subject the eyes move and fixate in a single movement. In those with a peripheral vestibular loss the eyes move across, stop short and a single or several saccadic eye movements reposition the eyes to appropriately fixate on the target. The saccadic movements provoked by this test occur towards the affected ear. The head thrust test has a high sensitivity and specialty (originally described as 100% respectively) and may be evident even once patients may have become asymptomatic following a peripheral vestibular loss.

The head shake test

The head shake test is performed by rapidly shaking a subject's head from side to side with their eyes closed[5]. Horizontal nystagmus may be seen on eye opening if a peripheral vestibular deficit is present. The sensitivity of this test ranges from 35-94% with a specificity to 62-92%.

Romberg's test

Romberg's test was originally described to identify those patients with tabes dorsalis. Although principally a test of proprioception and the posterior column, patients who have suffered a recent unilateral peripheral vestibular loss may lean to the affected side[6]. The test may be "sharpened" by performing this test on foam (to remove proprioceptive information) or in a semianachoic chamber (to remove acoustic cues). Patients with bilateral vestibular loss are unable to stand with their feet together but rather with their feet wide apart.

Unterberger/Fukuda step test

These stepping tests are used to assess peripheral vestibular function and are largely linked to the function of the horizontal canals. The Fukuda step test involves a subject to march on the spot with their eyes closed arms extended[7]. Following 50 steps the extent of rotation is assessed with rotation of 30 degrees or greater suggestive of a unilateral peripheral vestibular deficit. This test however has a relatively low sensitivity and specificity (approximately 70% and 50% respectively) in part as the extent of rotation

Table 1: A summary of the clinical and special investigations that may be used to assess the peripheral vestibular apparatus (SCC – semicircular canal).

	Investigation
Lateral SSC	Spontaneous nystagmus
	Head thrust test
	Head shake test
	Romberg's test (note text)
	Unterberger/Fukuda step test
	Caloric testing
	Rotatory chair testing
Anterior SSC	Head thrust test
Posterior SSC	1. Head Thrust test
Saccule	Cervical VEMP
Utricle	Ocular VEMP

is largely estimated, but may be improved by accurately measuring the extent of rotation (e.g. the D+R Balance iPhone application) and by removing environmental cues (e.g. a sound localising object such as a ticking clock).

Caloric testing

Bithermal caloric testing with water or air remains the "Gold standard" method of assessing peripheral vestibular function but is essentially restricted to stimulating the lateral semicircular canal.

The external auditory canal irrigated with water at 7 degrees above and below core body temperature (i.e. 44 and 30 degrees Celsius), which results in column shift of endolymph within the lateral semicircular canal, cupula deflection and stimulation or inhibition respectively of the ampullary hair cells of the lateral semicircular canal. The strength and duration of the nystagmus provoked by these thermal changes may be recorded using videonystagmography goggles or electronystagmography. A significant difference in function may be calculated and reduced function in one or both lateral canals documented.

Additional theories to explain the nystagmus produced include thermal stimulation of the ampullary hair cells[8], endolymph/perilymph expansion[9] and changes in the specific gravity of the cupula.

Limitations of the caloric test include the age of the patient (not recommended in young children and those over 70 years) and the stimuli deemed to be non-physiological at <0.1Hz.

Rotatory chair testing

Rotatory chair testing may also be used to assess function of the lateral semicircular canals. Subjects are strapped into a chair and whilst in darkness, rapidly rotated. The chair is brought to an abrupt stop and the nystagmus produced recorded using infrared video-nystagmography goggles. A significant difference in amplitude and duration is suggestive of a peripheral vestibular deficit. Whilst standard rotatory chair testing simultaneously stimulates both lateral semicircular canals, off axis rotatory chair testing where the subject is rotated about a point directly below one peripheral vestibular organ may allow a single lateral canal to be tested in isolation.

Whilst the clinical tests discussed above are largely linked to function of the horizontal semicircular canals, the anterior and posterior canals have been more difficult to assess. However, the head impulse test in conjunction with specialist eye recording equipment can be applied to assess the function of these canals (otometrics). As with the head impulse test described above, the head is rapidly moved in specific directions whilst the subject's occular movements are recorded. Saccadic movement suggests reduced function of a specific canal depending on the direction of movement.

Saccule and utricle function

A reliable method of assessing the saccule and utricle remained elusive until the advent of vestibular evoked myogenic potential (VEMP) testing first described by Colebatch and Halmagyi in 1992[10]. This muscle reflex is evoked by stimulation of the vestibular organs with an auditory stimulus.

The VEMP recorded from electrodes placed over a tensed sternocleidomastoid muscle is referred to as cervical VEMP (cVEMP)[11] and is a measure of saccule function. cVEMP is the response, a transient release from contraction of the sternocleidomastoid muscle, recorded in response to an acoustic stimulus in the ipsilateral ear. Difficulties with cVEMP testing include reliable electrode contact and discomfort during testing. This investigation may not be possible in young children[12].

Ocular VEMP, or oVEMP, is the excitatory response elicited by contraction of the inferior oblique muscle, in response to an acoustic stimulus in the contralateral ear[13]. The pathway involves the utricle, superior vestibular nerve and contralateral inferior oblique muscle. Ocular movements are recorded by using surface electrodes on the face on upward gaze. Reduced or absent responses are hence suggestive of reduced urticle function.

The visual vertical has been used to assess the inferior vestibular nerve pathway with mixed results. A variety of methods have been reported, including that of a rotating disc[14] and bucket arrangement[15]. In each, the position of the subjective vertical axis was compared with the true vertical and used to identify pathology. A recent review of patients undergoing cVEMP testing in our unit whose ocular movements were also assessed during head tilt whilst aligning two vertical lines, would suggest saccadic ocular torsion in those with normal inferior vestibular nerve pathway function, but pendular ocular movement in those with absent cVEMP responses. This observation requires additional research and may provide a simple and efficient method of assessing inferior vestibular nerve function.

Conclusion

The peripheral vestibular system and its constituent parts may be assessed using a variety of clinical and special investigations. These allow clinicians to accurately localise pathology and hence come to an appropriate diagnosis.

As our understanding of the vestibular system develops these investigations are likely to be supplemented with additional tests of balance that may be performed on the paediatric population.

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Ossiculoplasty in current practice

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Abstract:
This article is intended to be an up-to-date summary of the recent theory and practice of ossicular chain reconstruction. We have briefly reviewed acoustic mechanics, published data for reconstruction outcomes, and the changes affecting sound conduction and biostability of implants. We have then outlined the principal practical solutions to ossicular defects according to the Austin-Kartush groups.

Key words:
Ossiculoplasty, Ossicle, PORP, TORP, Austin-Kartush

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Introduction
We present recent practice and our own experience with ossicular chain reconstruction (OCR). The senior author has over 30 years' experience in the UK and Nepal; including many hundreds of ossiculoplasties using a wide range of materials, autologous and alloplastic, utilizing new and old designs.

Acoustic Mechanics
The middle ear gain is about 20dB, mostly due to the tympanic membrane (TM) area rather than the ossicular lever. The effective stimulus to the inner ear is greater because of the critical sound pressure and phase differences between oval and round windows. An intact TM with non-intact chain can produce a loss up to 60dB. Aeration of the middle ear is crucial to free movement, but the volume has little added benefit once greater than 0.4-1 ml[1].

In OCR, TM thickness and compliance, tightness of fit, coupling (lack of slippage), and angle between drum contact and stapes (ideally less than 45 degrees) are important. Stiffness and mass play a minor part in the efficiency of sound transmission[2].

Computer modeling and laser Doppler interferometry have advanced the understanding of the normal and defective acoustic transformers[3,4,5]. Liu et al digitized spiral CT to create an ear model with over 36,000 points for finite element analysis[6].

Implant Materials

1) Cartilage
Cartilage struts have shown resorption and loss of rigidity[7,8]. Cartilage is now only used as part of TM and scutum reconstruction to resist re-perforation or retraction[9]. Conchal and tragal cartilage have similar acoustic properties. Thickness of 0.5 mm is the best compromise for TM reconstruction[10], also a cartilage shoe may help centralize a total ossicular replacement prosthesis (TORP) in the oval window (OW) niche[11].

2) Ossicle
Homologous materials have been abandoned due to concerns with virus and prion transmission though autologous ossicles are widely utilized worldwide. Extrusion is extremely rare and a healthy ossicle can be stored for a second stage in the middle ear or mastoid although we prefer primary reconstruction[12]. The goals are mechanical efficiency, stability, and avoiding ankylosis to nearby structures. Derlacki ossicle holding forceps and irrigated diamond burrs are used to shape. Residual cholesteatoma or resorption is rare in practice, so long as any visible matrix is removed and osteitic bone drilled away. Markedly eroded ossicles are discarded[13].

3) Bone
Thick cortical bone is obtained from the postero-superior part of the mastoid process; marrow and air cells weaken the graft and may lead to resorption.

4) Alloplastic partial or total ossicular replacement prostheses (PORP, TORP)
PORPs extend from the stapes capitulum to the incus, malleus or TM. TORPs are placed from the stapes footplate to the malleus or TM. Some TORPs can also be used with shoes to centralize and adapt to the angle of the footplate (FP) . Prostheses thicker than 0.2 mm have not shown risk of FP penetration[11].

a) Titanium
Now the most widely used and stable bio-inactive alloplastic material[11,15]. Lightweight, thin and rigid prostheses with an open head improves visualization and fitting. Cartilage is inserted to cover the prostheses where they contact the drum; some also hook under the malleus neck. Extrusion rates may be less than 5%[16,17,18].

b) Hydroxyapatite (HA)
HA is a bioactive ceramic with a chemical composition similar to bone compatible with direct TM contact[19]. If the top of the prosthesis lies medial to the malleus or is covered with cartilage then extrusion is less than 2%[20,21]. Disadvantages include bulk, brittleness and osseointegration, which can cause fixation. To counter this, many shapes and mixed materials are available. Failure may occur if the parts separate. HA cement can also be used on dry surfaces such as an eroded incudo-stapedial joint.

c) High Density Polyethylene Sponge (HDPS) and others
HDPS such as Plastipore has now been abandoned. Its porosity allows tissue ingrowth, and sometimes degradation with extrusion ranging from 0.89% to 10.0%[22,23]. Other materials such as non-HA ceramics, glasses, or gold have been superseded.

Results
Multiple prosthesis types and designs make adequate comparisons impossible. There is little difference in early audiometric results. Variable case mix has a large impact on series. Success is usually measured as an average air-bone gap of less than 20dB at 0.5-2, 3[24] or 4 kHz. Many authors have attempted to identify factors predicting long-term outcome. These include, mucosal thickness, ventilation, discharge, cholesteatoma, perforation, canal wall, revision, surgical complexity and presence of malleus handle. Patient's age does not affect outcome . Presence of inflammation at primary surgery is not necessarily a poor predictor for incus autografts[12]. Failure is most often caused by ossicular fixation, migration, extrusion or resorption. Placement of a long stay vent tube at primary surgery may benefit hearing outcome[26,27].

Reported success rates vary widely[18,28,29]. Generally, slightly better results are quoted for partial than total repairs[30]. Recent studies of titanium implants with over 5 year mean follow up found an air-bone gap of less than 20dB (0.5-3 kHz) in 82% of 44 PORPs (Kurz Vario bell) and 63% of 32 TORPs (Kurz Vario aerial). Extrusion rate was 5% . Another surgeon found an overall air-bone gap less than 20dB in 53%[32]. Results with incus interposition autografts generally give results comparable with allograft PORPs[33]. Titanium TORPs appear to give better early hearing outcomes than autografts when stapes arch is absent[34]. There have been many other reports of titanium implants in recent years[35,36]. There appear to be no significant differences in outcome between titanium and HA implants[37]. Patient Related Outcome Measures are currently lacking for ossiculoplasty.

Classification of OC defects and options for repair
Wullstein's classification is well known but has deficiencies, particularly type III, which may or may not include an intact stapes. The Austin-Kartush groups[38,39], are widely accepted. Disease clearance may necessitate disrupting a good conductive mechanism. The group is assessed after disease clearance. We present common situations and a few of our preferred options.

Group 0, M +, S +, I +: Intact chain

Repair TM.

Group A, M +, S +: Incus erosion

1) Loss of long process of incus (LPI).

a) Slightly short LPI or fibrous connection.

i) HA cement is useful in dry ears.

ii) Interposition between tip of LPI and stapes head. Materials that can be used include cortical bone chip from mastoid or HA prosthesis such as 'Applebaum'. This prosthesis is often unstable. Prostheses that extend the LPI as clips or springs of titanium or Nitinol are available. We have no experience with these.

b) Most of LPI absent.

i) Remove incus and reshape as interposition from stapes head to malleus handle or TM (Figures 1 and 2). Our preferred technique is as follows. Remove LPI. Make a notch in the short process of incus (SPI) and within this a 1mm 'ball and socket' hollow to fit over stapes head and arch. Make a 1.5 mm groove at 90 degrees to the notch, across malleo-incudal joint surface, to fit malleus handle or neck.

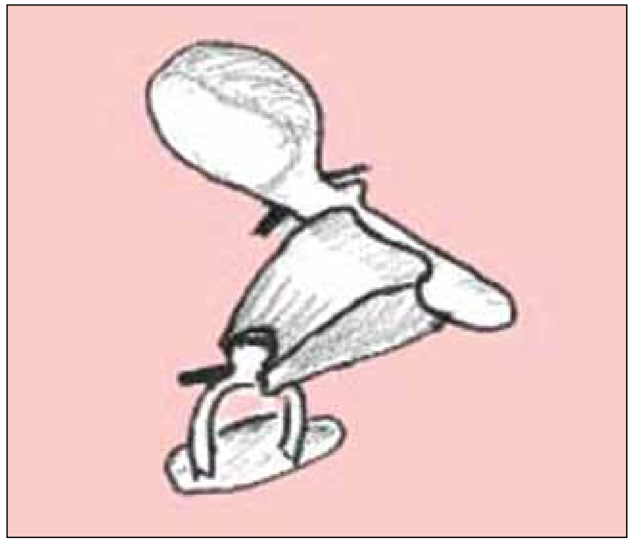

Figure 1: *Incus interposition from stapes head to malleus handle.*

ii) PORP from stapes head to malleus handle, or direct to TM, usually with cartilage cover and incus removal.

2) Incus body is absent.

Use malleus head, cortical bone or PORP. We currently favour the Kurz 'clip' PORP that sits more securely on an upright stapes than the 'bell' configuration.

Group B, M +, S –: Incus and stapes super-structure absent

1) Incus available.
Remove the osteitic LPI. Avoid removing mucosa/periosteum on incus and facial canal. Place the incus with SPI in centre of FP and grooved body under neck of malleus (Figure 3). If malleus is medialised, remove malleus head but retain tensor.

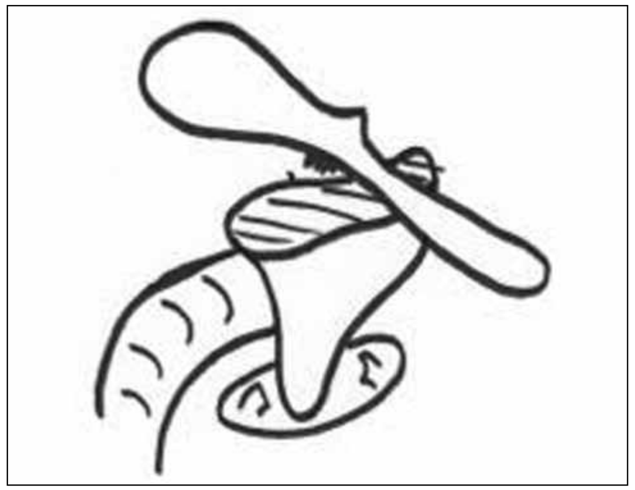

Figure 3: *Incus placed with SPI on mid FP and grooved body under neck of malleus.*

Figure 2: *Incus interposition from stapes head to malleus handle more than 5 years post operatively.*

2) No incus.
Requires TORP, either to medial side of malleus handle or direct to TM. Inherently unstable unless TORP has wide platform to lie under TM with cartilage protection (Figure 4), or malleus is relocated posteriorly.

3) No incus or TORP available.
Carve a cortical bone mushroom/umbrella shape (Figures 5 and 6). Must avoid contact with facial canal to prevent ankylosis.

Figure 4: *Extruding titanium TORP that lacks adequate cartilage cover and where the TM has retracted due to poor ventilation.*

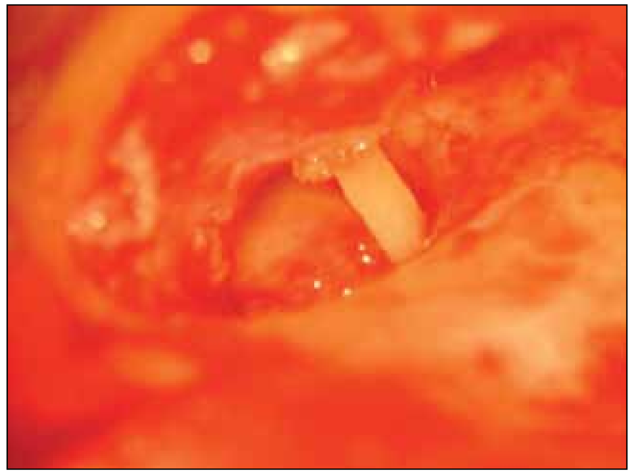

Figure 5: *Cortical bone 'mushroom' made as a TORP, carved.*

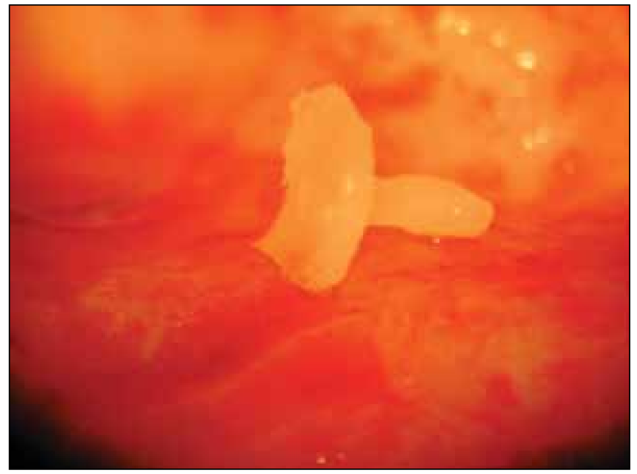

Figure 6: *Cortical bone 'mushroom' made as a TORP, in place in OW niche.*

Group C, M -, S + : Malleus and incus absent

1) Stapes upright and high.
Simply placing the TM graft over a high stapes creates a Wullstein type III. The shallow middle ear (particularly with canal wall down) is prone to retractions and recurrent disease. Thus, we prefer cartilage tympanoplasty.

2) Stapes upright but low.
In most ears the stapes head is no higher than the facial canal.

a) A small disc of cartilage placed on stapes head will improve height. A hole drilled with 1.5-2 mm diamond burr stretches over the stapes head.

b) An alloplastic 'Frisbee' type PORP of low height but wide area, covered with cartilage. This is our preferred method.

c) TORP placed between facial canal and stapes superstructure. The stapes provides support to the TORP. Additional stability can be provided by the 'silastic banding technique', technically challenging, but in the right hands can give exceptional results, usually combined with malleus relocation[40]. In the absence of the malleus, a titanium neo-malleus has been reported[41].

3) Stapes tilted down, fragile or head absent.
Use an alloplastic TORP between the crura onto the FP.

Group D, M -, S –: Malleus, incus and stapes super-structure absent

1) Round window (RW) baffle. To create an aerated middle ear segment over the RW, and leave the OW exposed is unreliable and prone to discharge. TORP required. Stability relies on wide contact with a large cartilage sheet tympanoplasty. Our preferred choice.

2) In frequently revised ears, it may be unwise to use any alloplastic foreign body. If the ear is made safe, dry and aidable by air or bone, or the other ear is good, then the patient may be very satisfied.

Group E, Head fixation in attic

This is caused by tympanosclerosis, ankylosis or extensive fibrosis. Dislocate the ISJ and check stapes mobility.

1) Fixed stapes.
Peeling away a plaque or resecting the stapedius tendon may sometimes easily free the stapes. If not, then close the ear. Freeing the attic may permit a second stage malleo-stapedotomy.

2) Mobile stapes.
Preparation requires atticotomy, removal of incus and usually malleus head, and ensure the malleus handle, if present, is mobile. Rarely the point of fixation is small and clearly defined and it is possible to free this. Make space between the surfaces and let the LPI re-adhere to the stapes head. Common points of localized fixation are tympanosclerosis of the SPI in fossa incudis or ankylosis of malleus head in the anterior epitympanum. Often the entire attic is full of tympanosclerosis. Then proceed with reconstruction as per Austen-Kartush group A or B. Alternatively, leave the fixed heads in place. Widely divide the malleus neck so that the handle is freely mobile. A PORP or TORP can then be inserted.

Group F, Stapes fixation

1) Incidental otosclerosis.
Second stage stapedotomy or malleo-stapedotomy may be appropriate.

2) Tympanosclerosis in OW niche.
Small plaques may be peeled away with care but at risk of stapes dislocation or inner ear trauma. If appropriate, a laser stapedotomy may be performed at a second stage. Because the FP is not usually fixed firmly, attempts to trephine or drill risk subluxation. Most authors consider there is a higher risk of inner ear complications than in otosclerosis.

3) Ankylosis of FP, or more commonly the crura to the promontory.
It may be possible to clear spicules of new bone with a low speed diamond burr or laser. Risk of inner ear trauma and of recurrence.

In all cases be aware that fixation could overly a dehiscent facial nerve canal.

Staging Surgery

The advantage of waiting and performing OCR during a secondary procedure is that the ear may be stable and better aerated. Not all patients need or comply for a second operation. Disadvantages of primary repair include difficulties with bleeding, oedema and visualisation, and changes during healing. We attempt primary repair in virtually every patient, whether canal wall up, down or revision. If there is a second stage and the hearing is poor then the OCR can be revised.

Complications

Sensori-neural hearing loss is rare and may be caused by footplate trauma resulting in perilymph leak or serous labyrinthitis. High frequency loss may be under-reported. Other risks are those associated with all middle ear surgery.

Conclusions

Ossiculoplasty can be challenging and long-term results disappointing. However, most series report at least 50-60% with an air-bone gap less than 20dB at over 5 years. The future of the other ear is often uncertain. Bilateral hearing is useful and hearing aids only a partial solution. Autologous ossicles are free and long lasting, with almost no risk of extrusion but require skill and time to use, and they are not available in all cases. The multiplicity of alloplastic implants and the lack of adequate long-term results make comparison difficult. Most otologists now use titanium, HA or mixed prostheses. Design is a matter of personal preference. Cartilage reconstruction of the thinned TM and covering the head of prostheses is the norm unless the malleus handle provides an effective connection.

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ENT aspects of primary ciliary dyskinesia

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Abstract

Primary Ciliary dyskinesia is a rare disorder characterised by altered ciliary structure and impaired ciliary function, resulting in mucociliary clearance abnormalities. In addition to the well-described respiratory manifestations a range of ear, nose and throat presentations co-exist, including otitis media with effusion and chronic rhinosinusitis. Diagnosis and Management by a specialist multidisciplinary team is recommended to optimise patient outcomes.

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Key words

Primary Ciliary dyskinesia, Otitis media with effusion, Rhinosinusitis

Introduction

Primary ciliary dyskinesia (PCD) is a rare autosomal recessive genetic disorder of variable penetrance. The prevalence is estimated to be around 1: 10 000 but the true prevalence is difficult to define due to differences in ethnic groups and many mild cases could be undiagnosed[1,2]. PCD is characterised by altered ciliary structure and impaired ciliary function, resulting in mucociliary clearance abnormalities[1, 3, 4]. The presence of motile cilia allows clearance of mucus, dust and debris from the upper and lower respiratory tract akin to a conveyor belt[5]. Motile cilia are also found in the paranasal sinuses, middle ear, Eustachian tube, the female genital tract and ependyma of the brain[1, 6].

Patients with ciliary defects typically present with recurrent and chronic upper and lower respiratory tract infections which may occur early after birth[1]. However, most patients also experience non-respiratory symptoms due to impaired mucociliary clearance[1] and 50% of PCD patients have situs inversus[7]. The triad of situs inversus, chronic sinusitis and bronchiectasis is known as Kartagener syndrome[8]. Biliary atresia, polycystic liver /kidney disease and hydrocephalus are all characterised by ciliary dysfunction[1]. In addition, a number of ENT manifestations have been described which will be discussed in more detail.

In England, three centres (Leicester, London and Southampton-since 2007) diagnose PCD for the NHS. Four centres based in Leeds/Bradford, Leicester, London and Southampton have been commissioned by the Department of Health in 2013 to undertake an annual multidisciplinary review of patients from England and Scotland by ENT and respiratory PCD specialists[9].

Diagnosis

The diagnosis of PCD relies on the deployment of a number of specialist tests and there is no single gold standard investigation[1]. Infection and inflammation can cause secondary ciliary defects which can result in misdiagnosis in the unwary, as such, it is recommended that the diagnostic assessments are undertaken at a specialist centre[4]. Early diagnosis is preferential to reduce the risk of irreversible lung destruction[10, 11]. However, in practice delayed diagnosis is not uncommon. Sommer et al describes how 70% of his patient population had seen clinicians more than 50 times prior to diagnosis[2].

If a child presents with symptoms suggestive of PCD (table 1), it is recommended that the clinician should have a low threshold to refer the child to a specialist diagnostic centre for further investigations. The European Respiratory Society Consensus statement recommends nasal nitric oxide measurement as a screening test for patients over 5 years of age. Nasal nitric oxide levels are very low in PCD. They also recommend that the saccharin test and radioaerosol mucociliary clearance tests are unreliable and should not be used in children[10, 12].

The European Respiratory Society Consensus statement recommends diagnostic tests should include both ciliary beat frequency analysis and transmission electron microscopy (TEM) of ciliary ultrastructure (Figure 1)[1, 4, 10]. There have been previous descriptions of normal cilia ultrastructure and hence a normal TEM alone is insufficient to exclude PCD[10, 11]. Ciliary beat frequency is useful to diagnose PCD but again, has been shown to be normal in certain cases of PCD where the beat pattern is abnormal[13]. Brush biopsy samples can be obtained from either the bronchus or nose[1, 11].

Table 1: Patients who should be referred for diagnostic testing (original)

Patients who should be referred for diagnostic PCD testing		
ENT manifestations	**Respiratory manifestations**	**Other manifestations**
Otitis media with effusion in association with airway symptoms	Neonatal respiratory distress of unknown aetiology	Situs inversus with nasal/ respiratory symptoms
	If considering testing for cystic fibrosis & presence of nasal/ ear/respiratory symptoms	Cardiac Disease with isomerism& nasal/ear/ respiratory symptoms
	Unexplained bronchiectasis	Sibling with PCD
	Daily life long wet cough	

If the diagnosis is unclear (due to epithelial infection or local inflammation) repeat ciliary brushings can be taken, ensuring that there has a 4 to 6 week period of being infection free. Genetic testing is not considered appropriate for diagnosis because approximately 30% of the genes that cause PCD have yet to be identified[1, 4].

Ear

In the normal population, otitis media with effusion (OME) is a common cause of conductive hearing loss in children. OME has an incidence of 10% to 30% of children aged one to three years and a cumulative incidence of 80% at 4 years old usually resolving by 8 years of age[14, 15].The aetiology of OME in children is believed to be multifactorial involving Eustachian tube dysfunction, childhood immunity, genetic and environmental causes[16]. Motile cilia are situated in the anterior hypotympanum and areas near the Eustachian tube opening aiding clearance of mucus and debris[17].

Patients with PCD have a high incidence of OME with up to 86% of patients affected and persisting into adulthood [2, 18]. The severity of OME in children with PCD varies widely from mild to moderately severe hearing loss [3].The clinical course of OME is more protracted in patients with PCD with hearing loss fluctuating throughout childhood typically lasting until the age of 12 or even into adulthood [3, 18]. Whilst the symptoms of OME and recurrent

Summary Text Box (Original)

PCD Key features & recommendations	
Clinical Features	
OME	Higher incidence of OME Clinical course is more protracted typically lasting until the age of 12 years
Chronic Rhinosinusitis	May present with nasal symptoms
Sinus anatomy	Increased incidence of aplastic or hypoplastic frontal and / or sphenoid sinuses
Obstructive sleep apnoea	Higher incidence of sleep disordered breathing
Respiratory distress of newborn	Consider PCD as a differential diagnosis in respiratory distress of the newborn in term infants requiring prolonged supplemental oxygen
Investigations	
Screening	Nasal nitric oxide measurement
Diagnostic	Ciliary beat frequency analysis Transmission electron microscopy of ciliary ultrastructure
Management	
OME	Non-surgical management is recommended, due to the risk of troublesome postoperative otorrhoea. Provision of hearing aids recommended as required.
Rhinosinusitis	Medical treatment with nasal douches & antibiotics Refractory cases Functional Endoscopic Sinus Surgery

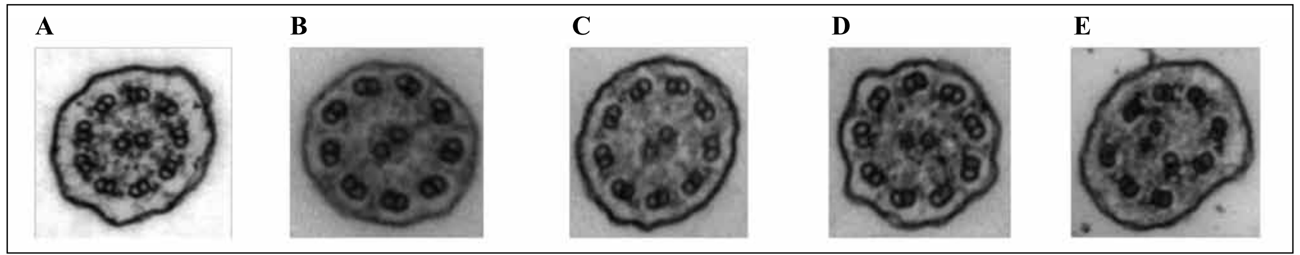

Figure 1: *Typical TEM axonemal cross sections from patients with PCD. Normal cilia (A), lack of dynein arms (B), lack of inner dynein arms (C), lack of outer dynein arms (D) and microtubule transposition defect (E).*

ear infections are a common childhood phenomenon, it is important for the ENT surgeon to consider the possibility of PCD in refractory cases particularly if there are associated recurrent or chronic nasal and respiratory symptoms.

The treatment aim for children with OME is to improve hearing and to minimise the impact of hearing loss on a child's speech and language development. In children with persistent bilateral OME, it is recommended for children to undergo grommet insertion or alternatively offer hearing aids[19]. In children with PCD however, the role of grommet insertion is controversial[3]. Several studies have shown that grommet insertion in children with PCD may result in persistent otorrhoea[20, 21]. There were also reports of minimal benefit in hearing outcomes following grommet insertion[3]. However, a team presenting their cohort of patients in Toronto, Canada argued that grommets were useful for children with more significant hearing loss and that they rarely needed hearing aids for their patients[22]. In their cohort of patients, 42% of their patients suffered from post-operative otorrhoea although they were unable to specify the exact duration or number of episodes of this due to the retrospective nature of their study but did report good otorrhoea resolution with topical antibiotic treatment with only one patient needed removal of grommet. Strategies to reduce the risk of post-operative otorrhoea in patients with PCD include peri or post- operative topical antibiotics or intra-operative saline irrigation[23, 24].To our knowledge, there are no large series looking specifically at duration and also number of episodes of otorrhoea following grommet insertion in patients with PCD. The European Respiratory Society consensus statement published in 2009 recommends non-surgical management of OME in children with PCD with hearing aids[4].

Episodes of acute otitis media should be managed with early antibiotics[4].

Nose

Patients with PCD may also present with persistent nasal blockage, discharge, chronic rhinosinusitis and very rarely, nasal polyposis with many of the patients requiring multiple antibiotic courses[2,11]. The severity of nasal symptoms reported by patients does not correspond with ultra structural defects[4]. Patients with PCD have been found to be more likely to have aplastic or hypoplastic frontal and / or sphenoid sinuses[25]. As frontal and sphenoid sinuses develop post natally with both sinuses attaining pneumatisation starting from 2 years of age with full pneumatisation by 14 years, PCD should be amongst the differential diagnosis if they are found in teenagers with persistent symptoms[26]. First line treatment for patients with chronic rhinosinusitis involves the use of long term courses of antibiotic treatment[2]. Regular nasal douching and occasionally anticholinergics are useful adjuncts for symptomatic control[4]. Functional endoscopic sinus surgery (FESS) for patients with PCD is rarely needed or effective[1]. A small series of 3 patients with PCD who had FESS were reported to have a good outcome[27]. Topical nasal steroids or antihistamines are not proven to help with symptoms unless patients also have a concurrent allergic element[1, 4].

Throat/Airway

Patients with PCD were noted to have a higher incidence of sleep disordered breathing and poor sleep quality[28]. Oktem et al describe that 52% of their population of PCD patients had evidence of obstructive sleep apnoea on polysomnography and they observed that exposure to cigarette smoke may predispose this population to obstructive sleep apnoea[28].

PCD should be considered as a differential diagnosis in respiratory distress of the newborn, in term infants, requiring prolonged supplemental oxygen. Symptoms are often attributed to chest infection or transient tachypnoea of the newborn[11]. However, over 75% of term infants with PCD require oxygen for days to weeks for respiratory distress[4]. Rhinorrhoea may also be evident at this time

Conclusion

Patients with undiagnosed PCD may present to the otolaryngologist with the common but persisting symptoms of OME or chronic rhinosinusitis. A high index of suspicion (that may include family history of PCD, consanguinity, situs inversus, recurrent chest infection and cough from birth) is necessary to identify and refer this sub-group of patients to a specialist centre for a diagnostic assessment of PCD.

Once diagnosed, with PCD, patients should be managed in a specialist centre with multidisciplinary input. ENT Surgeons should be aware of the spectrum of otorhinolaryngological disease which affects patients with PCD and the condition specific implications in managing these symptoms. In particular, the controversy surrounding the use of grommets to manage OME in this population due to the increased risk of troublesome postoperative otorrhoea. Surgical interventions should be considered carefully by an experienced team and treatment should be personalised after weighing risk benefit outcomes for the patient.

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Sinonasal malignant melanoma

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Abstract:
Sinonasal malignant melanoma (SNMM) is a rare disease, and as a consequence there is controversy surrounding the optimum mode of treatment. Prognosis is poor, usually due to the advanced stage at initial presentation, and recurrence can occur at any site sometimes many years following treatment. This review summarises the clinical and pathological characteristics of SNMM, and the existing evidence for the various treatment modalities.

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Key words
Sinonasal, Malignant Melanoma, Mucosal, Sinus

Introduction
Sinonasal mucosal melanomas (SNMM) represent less than 0.1% of all malignant melanomas, and between 1-9% of all nasal tract malignancies[1]. Mucosal malignant melanomas (as distinct from cutaneous) of the head and neck most commonly occur in the nasal cavity, followed by maxillary, ethmoid then sphenoid sinuses[2]. SNMM is therefore a very rare disease that poses a unique set of challenges to the ENT surgeon and oncologist, hampered by the lack of high-powered evidence supporting different therapeutic options.

Presentation and assessment
Presentation is similar to that of other sinonasal malignancies, namely nasal obstruction, discharge and unilateral epistaxis, although additional symptoms vary depending on exact site of origin. As for other tumours involving this region, presentation is often delayed, reflecting the lack of specificity of nasal symptoms and the usually routine referral pathway from primary to secondary care[2].

Endoscopic assessment is required for these lesions, with the characteristic pigmented appearance lending high suspicion to the diagnosis. CT and MRI are necessary to accurately stage the disease, and are essential to planning surgery. These will give details of extent of disease and bony erosion, and also involvement of adjacent critical structures such as the orbit and skull base/dura (figures 1 and 2).

Given the aggressive nature of SNMM, T staging for the disease begins at T3, and there is no recognised stage I or II SNMM (Table 1). Other staging systems used in cutaneous melanoma are not appropriate for SNMM - Breslow thickness has not been shown to have a bearing on the disease, although increased tumour thickness is associated with a worse prognosis[3]. The histological features of cutaneous melanoma that signify more aggressive disease, such as tumour thickness and ulceration, are relatively common in SNMM[4], and additionally high mitotic index and de-differentiation are associated with a poorer prognosis[5,6]. Distant metastases occur in up to 44% and is the commonest mode of recurrence, with loco-regional, regional, and local being 22%, 17% and 17% respectively[7].

Pathophysiology
The mitogen-activated protein kinase and phosphatidylinositol 3-kinase-Akt pathways have both been strongly associated with malignant melanoma, both cutaneous and mucosal. The three commonest genetic

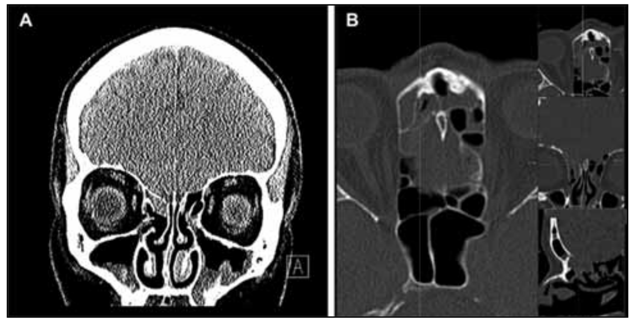

Figure 1: *Coronal (A) and cockpit view (B) CT scan demonstrating a right ethmoidal mucosal melanoma, with invasion through the skull base lateral to the cribriform plate.*

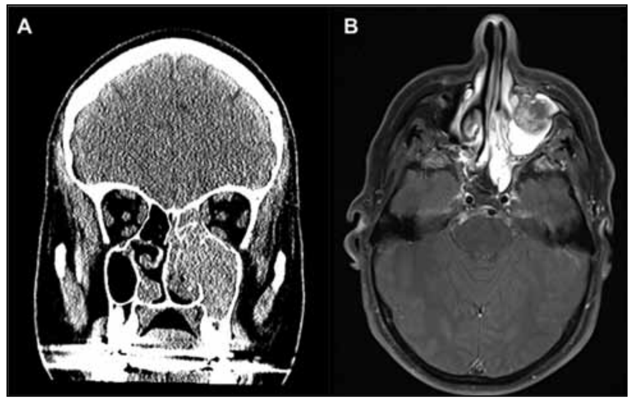

Figure 2: *Coronal CT (A) and T1 gadolinium enhanced transverse MRI (B) of a left nasal mucosal melanoma, abutting the lamina papyracea with possible breach, and extending throughout the maxillary sinus and eroding its anterior wall.*

mutations found in melanoma are activating mutations of the BRAF, NRAS and KIT genes. Whereas BRAF and NRAS mutations are commonly found in cutaneous melanomas (50% and 20% respectively[8,9], the genetic basis of SNMM is less clear. KIT and BRAF mutations, which are accessible for targeted therapy, vary depending on site of mucosal melanoma, however in SNMM are present in less that 10% of cases, with some finding no BRAF mutations at all in this group. NRAS mutations occur in around 14-22%[10]. SNMM is also associated with loss of the tumour suppressor genes PTEN, p16/INK4a (55.2%). Overall, although improving, the current understanding of the exact genetic drivers behind SNMM remains poor.

Table 1: TNM staging for mucosal melanoma			
T – Primary tumour			
T3	Epithelium and/or submucosa (mucosal disease)		
T4a	Deep sift tissue, cartilage, bone, overlying skin		
T4b	Brain, dura, skull base, lower cranial nerves (IX,X, XI, XII), masticator space, carotid artery, prevertebral space, mediastinal structures		
N – Regional lymph nodes			
NX	Regional lymph nodes cannot be assessed		
N0	No regional lymph node metastasis		
N1	Regional lymph node metastasis		
M – Distant metastasis			
M0	No distant metastasis		
M1	Distant metastasis		
Stage grouping:			
Stage III	T3	N0	M0
Stage IVA	T4A T3, t4A	N1 N1	M0 M0
Stage IVB	T4b	Any N	M0
Stage IVC	Any T	Any N	M1

Management
Given the rarity of the disease, and its poor prognosis, large scale clinical trials of the optimum treatment modality are unfortunately lacking. All cases should be discussed in either the head and neck or skin Multidisciplinary Meeting (MDT).

Surgery
This will depend on the accurate staging of the disease and also its involvement of other structures. For disease confined to the nasal cavity, en bloc resection may be possible and this may be achieved via an open or endoscopic approach. Endoscopic approaches may still be possible for diseases of the paranasal sinuses although resection may be piecemeal and therefore the assessment of margins difficult; in these cases mapping biopsies post-resection may enable the pathologist to determine any residual marginal disease. The surgeon should be ready to convert to an open approach should endoscopic resection prove impossible. The survival rates for open and endoscopic resection are comparable[11]; although by virtue of their selection the endoscopically treated cases may be less advanced therefore some selection bias may be evident[12,13]. The 3cm margins aimed for with cutaneous melanoma may not be feasible, although 1cm should be aimed for as a minimum. SNMM may spread sub-mucosally therefore it is important to be as aggressive as possible at first operation. Inevitably, the disease will often affect the skull base or lamina, and in these cases a decision should ideally be made pre-operatively as to how much resection will take place, and the patient counselled as the potential for skull base resection, CSF leak and orbital exenteration. A combined ENT/neurosurgical approach may be necessary and this highlights the need for close cooperation between specialties in the management of these patients.

In contrast to oral mucosal melanoma, given the commonest route of spread is distant metastasis, treatment of the N0 neck with surgery or radiotherapy is not routine and has not been shown to confer any benefit.

Radiotherapy
Historically, malignant melanoma has been considered a radio-resistant disease. However, this view is changing in relation to SNMM, with radiotherapy being employed as both as a radical and adjuvant treatment. The potential of radiosensitising agents may increase its effectiveness further. As discussed above, the lack of large-scale trials make the direct comparison of survival rates difficult. A

recent meta-analysis (of non-randomised retrospective series) demonstrated a non-significant increase in survival between surgery + radiotherapy vs. surgery alone (34.12 vs. 24.15 months), with an additional reduction in loco-regional recurrence rates (OR = 0.36, p<0.001), although selection bias makes these results difficult to extrapolate[14].

As well as these controversies in the effectiveness of either primary or adjuvant radiotherapy, other difficulties include minimising exposure of surrounding radiosensitive tissues (particularly when there is involvement of the orbit and dura/brain) and the relatively radiopaque bony structures that encase the sinonasal area. Intensity-modulated radiation treatment (IMRT) is the method of choice for both radiotherapeutic options, but is associated with complications. Despite the more targeted nature of the therapy, erythema, mucositis and conjunctivitis are common, with optic atrophy and osteonecrosis also described[15].

Newer options are becoming available that may deliver similar results to photon therapy without the side effects. Particle therapy using either protons or carbon ions has shown promising results in early studies. While the latter appears to be more effective, it has a higher spread of dose penetration than protons and therefore may cause more damage to the surrounding structures. Although only being available in a small number of centers worldwide, particle therapy may represent a potential curative option for patients who have recurred following either surgery or conventional radiotherapy[16].

In contrast to surgical excision, patient treated with primary radiotherapy may benefit from adjuvant radiotherapy to the uninvolved neck to improve survival and loco-regional recurrence[17,18].

Other adjuvant therapies

As with cutaneous melanoma, there is no role for primary chemotherapy alone in the management of SNMM, although there may be benefit when combined with other treatments. Table 2 summarises the results of the systematic review by Gore and Zanation demonstrating that combination therapy with surgery and chemotherapy is better than either modality alone, and that the addition of radiotherapy improves overall survival further still[7].

For adjuvant chemotherapy, dacarbazine is often used for metastatic melanoma[19]. Combination therapy with agents such as carmustine, cisplatin, tamoxifen, vinblastine and various cytokines did not have any benefit in terms of overall survival over dacarbazine alone, although recurrence free survival was improved[20]. Temozolomide is used for patients with un-resectable metastatic malignant melanoma and there is some evidence that combination with cisplatin after surgery confers an advantage in recurrence free survival compared to surgery alone[21].

Table 2: Comparison of overall survival between different treatment modalities[7]

Modality	Two-Tailed p-Value for Overall Survival
Surgery survival vs. surgery + radiotherapy survival	0.1895
Surgery survival vs. triple therapy survival	0.8925
Surgery + radiotherapy survival vs. triple therapy survival	0.2921
Surgery survival vs. radiotherapy survival	0.3421
Surgery + radiotherapy survival vs. triple therapy survival	0.1474
Triple therapy survival vs. radiotherapy survival	0.5182
Chemotherapy + radiotherapy survival vs. chemotherapy alone survival	0.3305
Surgery + chemotherapy survival vs. chemotherapy alone survival	0.0205*
Surgery survival vs. chemotherapy survival	0.3242
Triple therapy survival vs. chemotherapy survival	0.4615
Surgery + chemotherapy survival vs. surgery alone survival	0.0112*
Triple therapy survival vs. surgery + chemotherapy survival	0.0387*
Chemotherapy + surgery vs. chemotherapy + radiation survival	0.9907

*statistically significant

Immune therapy

The other class of drugs gaining prominence in the treatment of melanoma is immune modulators. Adjuvant high-dose interferon alfa-2b (HDI) has been shown to improve recurrence free survival and overall survival[22], although its main benefit may be in those that have clinically palpable nodes[23]. Checkpoint inhibitors such as CTLA-4 and PD-1, which essentially enhance the function of T cells and therefore increase the immune response, are also promising novel options[24].

Targeted therapies

These can be divided into those that specifically target the driver mutations involved in melanoma and those that target angiogenic drivers.

Mutation targeting

Vemurafenib, a potent BRAF inhibitor, improved progression free survival (5.3 vs. 1.6 months) and OS (84% vs. 64% at 6 months) when compared to dacarbazine[25]. Dabrafenib, another BRAF inhibitor, had similar effects with a lower adverse effect profile than dacarbazine[26]. MEK lies downstream to BRAF - MEK and BRAF inhibition may be used in combination to improve survival[27], and there is evidence that combining the MEK inhibitor trametinib with dabrafenib may increase time to treatment resistance[28]. Although the frequency of KIT mutations in SNMM is not clear, the competitive KIT inhibitor imatinib has had promising results in phase II trials, which although were targeted at all metastatic melanomas with cKIT mutation or activation, did include a cohort of mucosal melanomas[29]. There are no specific NRAS inhibitors under trial at the moment, although in a recent phase II trial the inhibitor MEK162 led to response in 20% of patients with NRAS mutated advance melanoma[30].

Angiogenic targeting

These drugs target the process of neovasculature formation in rapidly growing tumours, thereby reducing the supply of nutrients and oxygen and also limiting the route for blood borne metastasis. Bevacizumab is a monoclonal antibody to VEGF and when used in combination with carboplatin and paclitaxel may lead to an improvement in progression free survival (PFS) and OS[31]. Endostatin, an endogenous angiogenesis inhibitor, led to an improvement in OS and PFS in patients without BRAF or KIT mutation positive metastatic melanoma in a phase II trial[32].

With all of these therapies, larger phase III trials are needed to fully determine their effectiveness. In addition, given the low number of patients that develop SNMM this group is included in the wider group of all malignant melanomas in clinical trials. Considering the different genetic profiles between mucosal and cutaneous melanomas, further studies are needed to understand their potential in the most rare form of the disease.

Conclusion

Sinonasal malignant melanoma is a rare and aggressive disease with a very poor prognosis. The early recognition and treatment of the disease is associated with improved results, although the nature of sinonasal neoplasms means that this is not always possible. While the mainstay of treatment is surgery, the use of adjuvant radiotherapy may be beneficial. Further research is needed into the use of targeted therapies in SNMM, although these will be difficult to conduct due to the rarity of the disease, and large multinational collaborations may be needed to determine true effectiveness.

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Complex nasal reconstruction

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Abstract:
The vast majority of nasal defects following nasal trauma or surgery involve skin or skin and cartilage loss only. These can be reliably repaired with simple, well-described techniques, which will only be briefly mentioned in this article. We consider complex nasal reconstruction to be those cases that involve a loss of nasal lining in addition to skin and cartilage or bone. The level of complexity of the reconstruction required increases relative to the volume of missing nasal lining. We hope to provide the reader with a greater understanding of the range of techniques available for reconstructing the nasal lining through a series of case studies.

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Key words
Nasal reconstruction, nasal lining, facial plastics

Introduction
The nose is a complex three-dimensional structure, which when disrupted either traumatically or surgically, poses a significant reconstructive challenge. The aim of any reconstructive procedure is not just to repair the deformity, but also to maintain function. To successfully reconstruct the nose it is crucially important to assess two factors: the location of the defect and the extent of tissue loss.

Location of the defect
There are two classification systems to help describe the location of the defect. One is the 'subunits of contour'[1] and the other is the 'zones of skin thickness'[2]. The subunit principle divides the nose along boundaries between convex and concave areas (see figure 1). If tissue is inset along the subunit boundaries of convex areas (tip, dorsum, alae, columella), the resultant scar will be maximally disguised. Such is the cosmetic advantage to this, if more than 25-50% of one of these subunits is lost, it is preferable to excise the remainder of the subunit and replace it entirely. The subunit involved also affects the preferred type of tissue transfer: Collagen in a flap contracts centripetally, making flaps a good choice for reconstructing convex areas as the convexity will be enhanced; however concave areas of the nose such as the side wall are better suited to skin grafts which tend to flatten as they heal.

The second system of zones highlights the fact that the type of skin covering the nose varies (figure 2). It is important to match both colour and texture of missing skin; thus grafts taken from the preauricular area may be suitable for defects in zone one or three, whereas the forehead is a much more appropriate donor site for reconstructions involving zone two.

Extent of tissue loss
The nose is composed of three layers; the lining, the bony-cartilaginous support structure, and the soft tissue envelope. When evaluating a defect, it is important to be

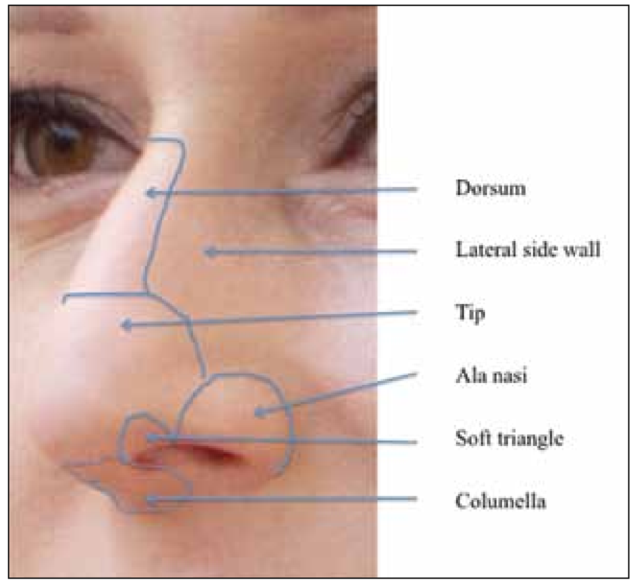


Figure 1: *Subnits of the nose.*

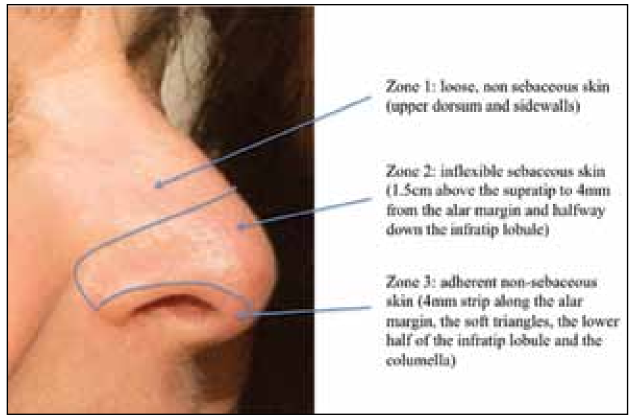


Figure 2: *Zones of skin thickness.*

accurate in identifying which of these layers is missing: each layer needs to be replaced with similar tissue, to ensure correct shape, support and adequate function.

Single layer tissue loss – skin resurfacing

These are the simplest reconstructions to perform. However, obtaining an aesthetically pleasing skin envelope will require consideration of different techniques depending on where and how large the defect is.

1) Zone one defects

Leaving superficial wounds to heal by secondary intention yields excellent results in the medial canthal area. Smaller defects in the lateral nasal wall, especially in fair-skinned patients, can also produce acceptable results when good wound care is employed.

As there is some skin laxity in this area, defects of less than 5mm can also be closed primarily. Full thickness skin grafts are a good option in concave areas, taken from the pre or postauricular area ideally, but the supraclavicular or melolabial regions are alternative sites. Small defects of less than 1.5cm can be covered with a local advancement flap, but over 1.5cm a forehead flap will be required.

2) Zone two defects

Because the skin in this area is thick and tightly adherent to the underlying cartilaginous framework, primary closure is not appropriate for any but the smallest areas of tissue loss. Skin grafting does not provide acceptable contouring here. The Zitelli modification of the bilobed transposition flap is useful in tip and alar defects up to 1.5cm in size[3].

Larger defects of over 1.5cm are best addressed with a regional flap: either the paramedian forehead flap, or a nasolabial flap if the area is limited to the alar lobule and adjacent sidewall.

3) Zone three defects

Any skin placed in zone three to cover tissue loss is prone to retraction and distortion. Therefore composite flaps are often utilized, even if the defect is small and superficial. Composite ear grafts provide a good skin match and the auricular cartilage is conveniently contoured to match the alar rim. Full thickness skin grafts can also be used, particularly in the soft triangle. Larger defects are covered in a similar way to zone two defects, with a nasolabial or forehead flap in addition to cartilage for structural support.

Two layer defects - Reconstructing the nasal skeleton

Deeper defects require not only skin resurfacing but also framework reconstruction as the integrity of the nasal skeleton is crucial to securing a long-term favourable outcome both functionally and aesthetically. Soft tissue flaps placed directly in a defect involving loss of cartilage or bone will lack structural support. The centripetal contractile force caused by the stiffening of collagen during scar maturation will subsequently result in airway collapse and deformity, therefore to prevent this missing bone or cartilage also needs to be replaced. Both bone and cartilage require a well vascularised tissue bed to ensure survival. Local flaps used for single layer defects usually provide this and can support free grafts without problems, allowing the reconstruction of the nasal skeleton and the skin resurfacing procedure to be performed contemporaneously.

Suitable donor sites for bone harvest include the nasal septum, ribs, outer table of the cranial vault (split calvarial bone grafts) or osseous free flaps. The cartilaginous nasal septum provides good quality, carveable but strong material, although its quantity is limited. Rib cartilage is more plentiful in the younger patient, although in the older patient, or in any patient with previous rib fractures, its supply might be restricted as the cartilage progressively ossifies. The patient does also incur a small risk of pneumothorax during harvest and is left with a scar on the chest wall. Carved rib cartilage does have a tendency to warp, however in clinical practice the graft's ability to warp is minimized by securing it with slowly absorbing sutures. The surgeon should not be deterred from using this donor tissue if strong, straight grafts are required. Conchal cartilage is weaker and it cannot support a scarred nasal envelope, however its shape does make it particularly suitable for alar cartilage reconstruction, or extra-anatomical alar rim grafts.

The use of permanent synthetic materials such as silicon, polyethylene or Gortex, or titanium implants for framework reconstruction should be strongly discouraged. Extrusion or infection of synthetic implants, which are frequent complications, is a surgical disaster requiring in almost all cases removal of the implant and full revision of the reconstruction. The argument that donor site morbidity is avoided with implants in our opinion is irrelevant given the risks associated with their use, and given that abundant amounts of autologous donor sites (rib, ear, calvarium) exist, the use of these types of implant can almost never be justified.

Complex defects – Replacing missing lining

Complex defects are those that involve all three layers of the nose – skin, framework and inner lining. It is important to replace the inner lining completely, otherwise any cartilage or bone grafts placed for structural support are at risk of becoming infected and resorbed or extruded, placing the whole integrity of the reconstruction in peril. The degree of complexity in these situations is dictated by the surface area of the inner lining defect, and a stepwise approach to reconstruction is used. Options available to recreate the nasal lining layer include:

- Primary closure using local advancement
- Skin or composite grafts
- Hinge-over flaps
- Septal flaps
- Folded forehead flaps
- Free flap reconstruction

These will each be discussed in turn, with cases to illustrate the techniques. Once the nasal lining has been reconstructed, techniques described in earlier sections are also often required in combination to replace the missing framework and skin.

1) Primary closure

In very small defects (1-2mm), primary closure is an option after wide undermining of the vestibular lining under the nasal bones. This can develop a few millimetres of laxity to allow primary closure, however if used to close defects over 3 mm twisting of the nasal vault and narrowing of the nasal airway will occur.

2) Skin or composite grafts

Skin grafts have a tendency to contract although can be used successfully as a staged procedure. A skin graft can be placed directly on the undersurface of a skin flap at the first stage of reconstruction, with cartilage placed in a pocket made between the graft and the flap at a second stage. The pedicle is divided as a third stage, providing cartilage size, shape and placement is acceptable. This technique does carry a 10-20% risk of graft failure. In most modern nasal reconstructive practices skin grafts are used for salvage rather than as a primary reconstructive methods as better options exist.

3) Hingeover flap

Using the external nose as a donor site to create nasal lining makes use of the excess healthy skin which would be otherwise discarded if following the subunit principle discussed earlier. Following initial lesion excision and healing of the edge over a 6-8 week period, the remainder of the subunit skin is divided into radial sections and flaps elevated from the edge of the subunit towards the defect.

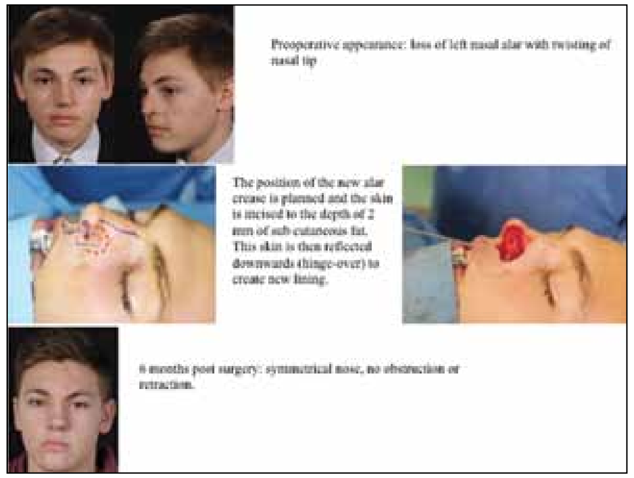
These leaflets are then folded inwards and sutured together to form a thin stiff lining. Because these flaps are hinged on scar tissue created from the initial excision margin, their blood supply is poor. If skin grafts were placed to provide temporary skin cover at the time of resection, these can also be used as part of the hingeover flap and tend to have a higher survival rate than using scar tissue alone.

The hingeover flap works best on inner lining defects smaller than 5mm, although are generally safe to use where each flap length is less than 5mm. Flaps between 5 and 10mm may benefit from a staged procedure where the leaflets are initially elevated, but then laid back down in their original position to stimulate increased neovascularisation across the scar tissue before hinging them over to create the lining 3-4 weeks later. Hingeover flaps greater than 1 cm are not advised and must be done with caution. Care must also be taken in previously irradiated skin and as the flap can be bulky, pre-existing nostril stenosis can lead to a poor functional outcome and alternative methods should be considered.

The case below (case 1), illustrates the outcome of a child who sustained complete loss of his nasal alar following a dog bite, resulting in twisting of the nasal tip. Here a hingeover flap was used to reconstruct the nasal lining before using conchal cartilage to reconstruct the nasal skeleton including a columella strut. Vestibular releasing incisions and lining rotation straightened the nose and a paramedian forehead flap used to resurface the skin.

4) Septal flaps

Flaps available to reconstruct the nasal lining can come from within the nose, from the septum or turbinates. Septal flaps are an attractive option as they replace like with like tissue. Their blood supply is adequate if they are used appropriately, for medium-sized defects 0.5-1.5cm measured cephalocaudally. A deficiency in the lining larger than this will often require two septal flaps that will result in a septal perforation and as such other methods are chosen preferentially.



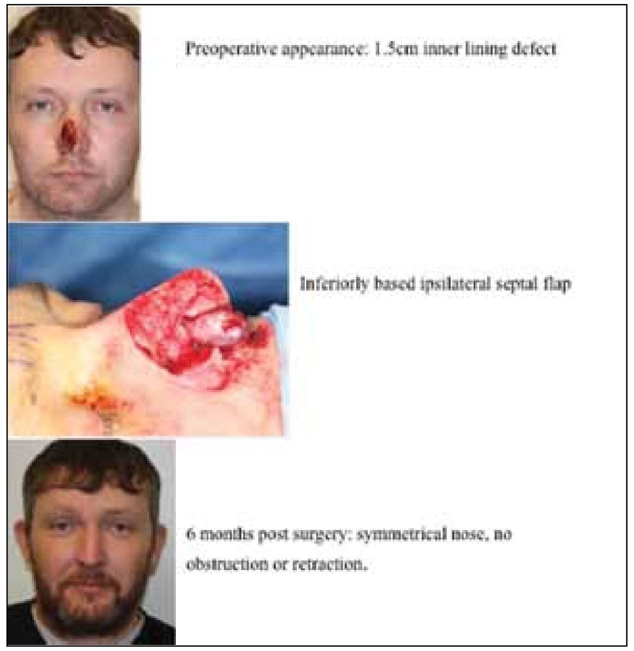
Case 1: *Hingeover flap.*

Anteriorly based ipsilateral septal flaps are the most commonly used. They are based on branches of the superior labial artery and the subsequent antero-inferior pedicle can be divided at a second stage to restore the nasal airway if required. Defects of an appropriate size in the lining of the nasal tip, alar, or middle third of the sidewall can be repaired using this flap. Case 2 shows how a 1.5cm lining defect in the alar was repaired using an inferiorly based ipsilateral septal flap. Conchal cartilage was also used to reconstruct the framework with a forehead flap for skin resurfacing.

5) Folded forehead flaps

This is the ideal method for reconstruction of inner lining defects greater than 1.5cm up to full hemi nasal reconstruction. It was first described by Menick[4] and helps to overcome the difficulties with using stiff, poorly vascularised scar tissue like in hingeover flaps, or causing damage to the internal nose from intranasal sources. It does however require more stages than other reconstructive options.

An extra paddle is created whilst elevating a standard paramedian forehead flap; this is secured intranasally and then the flap is subsequently folded back on itself to resurface the skin. A free cartilage graft can be placed primarily in between the two layers of folded forehead flap, or can be introduced at a later stage. Once all reconstructive components are in place and adjusted to the surgeon's satisfaction, the folded rim of the forehead flap is divided and the flap thinned to create an adequate airway. Case 3 illustrates this technique in more detail. A template is made of the lining defect and the forehead flap fashioned. Following the first stage the flap is bulky and contains no cartilage, which is required to give form to the nose. Thus at the second stage, once the lining has gained

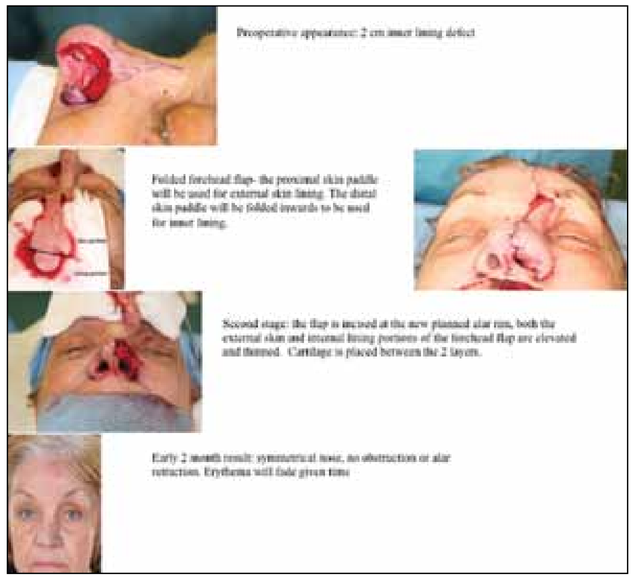


Case 2: *Ispilateral septal flap (inferiorly based).*

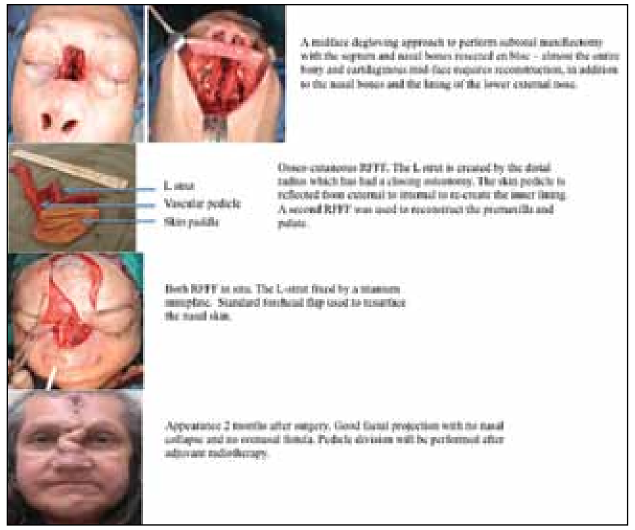
a blood supply, thinning of the flap and placement of cartilage via an alar rim incision occurs to give the nose both form and function.

6) Free flap reconstruction

Where large defects affecting greater than 50% of the inner lining exist free flap reconstruction is the optimum choice[5]. This is more common following resection of sinonasal malignancy than in cutaneous malignancies or trauma. Often these defects will have co-existing skeletal defects of the maxilla, palate, or frontal bone that require



Case 3: *Folded forehead flap..*



Case 4: *Osseocutaneous free flap using radial forearm free flap (RFFF)*

reconstructive consideration. The decision to use vascularized bone grafts in the form of an osseocutaneous free flap instead of cutaneous free flaps with free bone grafts depend on whether there is a need for adjuvant radiotherapy. In our experience most of these aggressive midface malignancies will require adjuvant radiotherapy and therefore osseocutaneous free flaps are preferred such as those deriving from the fibula, radial forearm or scapula.

Case 4 involves a septal carcinoma eroding through the palate and nasal bones at the glabella. A midface degloving approach was used and subtotal maxillectomy was performed with the septum and nasal bones resected en bloc, including almost all of the nasal lining of the lower external nose. The pre-maxilla/palate was reconstructed with an osseo-cutaneous radial forearm free flap, and a second radial forearm free flap was used to create an L-strut and a skin paddle harvested to serve as nasal lining. The external nasal skin was then reconstructed with a standard forehead flap.

Summary and conclusion

The complexity of a nasal reconstruction is not dictated by the surface area of the skin defect. Skin and framework defects of any size are generally reliably repaired with forehead flaps and ear cartilage grafting. Complex nasal deformity results when there is a deficiency of inner lining, with or without surrounding skeletal deficiency. These base layers are the most important layers to reconstruct as without a solid foundation any reconstruction will fail over time. If significant unrepaired inner lining defects exist infection and subsequent scarring and retraction of the remaining nose will follow and progressively collapse any framework no matter how robust over 2 - 3 months. What results from this scenario is a stenotic airway, retracted alar and a collapsed nose. Correction in this setting will require a complete revision.

There exists a hierarchy of complexity within full thickness nasal defects, which can be based on size. The options for repair have been discussed above and are summarised in table 1.

Table 1: Strategies to replace nasal lining defects

Size of full thickness defect	Type of lining replacement
Small (< 5mm)	Mucosal advancement, Hinge over
Medium (5-15mm)	Septal flap
Large (from 15mm up to hemi nasal)	Folded forehead flap
Subtotal	Fasciocutaneous free flap
Subtotal + skeletal deficiency.	Osseocutaneous free flap

The various options presented are proven methods of reconstruction and are to be recommended. Nasal reconstruction utilises skills from cosmetic rhinoplasty, functional rhinoplasty, skin cancer surgery, craniofacial/cleft surgery, and microvascular reconstruction of the head and neck. It is a fascinating and challenging area that is continuing to evolve.

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Grafts in septorhinoplasty

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ABSTRACT

Septorhinoplasty is not a set piece operation, rather it is the result of a variety of different techniques applied in a carefully selected way, tailored to an individual nose to effect change. A surgeon needs to be *au fait* with many of these different techniques and needs to understand which techniques to apply in different situations. Applying grafts to the nasal skeleton is one of these techniques. We review the types of grafts available, their advantages and disadvantages, their sources and their application.

J ENT Masterclass 2015; 8 (1): 86 - 91.

Key words
Septorhinoplasty, Septal reconstruction, Graft

Introduction

Septorhinoplasty is one of the most challenging and demanding procedures performed by the ENT Surgeon with both functional and aesthetic considerations being of equal importance during the reconstructive process. Without attention and correction of septal deformities either the functional outcome or the end cosmetic result will be compromised.

A strong and straight substructure is essential to allow the external nasal structures to be supported and sit in the mid-line correctly. Septoplasty thus forms an essential part of many rhinoplasty procedures. The old adage 'As the septum goes, so goes the nose' applies now just as it did several decades ago when it was first pronounced by Dr Irving Goldman[1].

In this review we plan to concentrate on commonly used graft materials, their uses, and application. We will concentrate on structural, functional and cosmetic grafts of the nasal skeleton.

Table 1 – examples of different graft types

Graft type	
Autologous (from the same patient)	Septal cartilage Conchal cartilage Costal cartilage Temporalis fascia Fascia lata Ilaic crest bone Calvarial bone
Homologous (from another human)	Irradiated costal cartilage Irradiated fascia lata Alloderm
Xenografts (from another animal)	Permacol Irradiated bovine cartilage
Allografts (synthetic)	Silicone Goretex Medpore

Grafts

Biological grafts consist of tissue removed from the body, without a blood supply, being inserted into a patient to augment other structures already present. Allografts are synthetic man made materials used for the same purpose (see Figure 1)

Application of grafts

Due to congenital abnormality, trauma or previous surgery, a patient may be deficient in certain areas of the nasal skeleton and these areas may benefit from grafting. Graft material used to replace/augment normal (but weak or absent) structures are termed anatomical grafts whereas grafts placed in other areas are non-anatomical grafts. Such non-anatomical grafts may be used to strengthen potentially weak areas and support them postoperatively. Examples include columellar grafts to mitigate possible de-projection following an open septorhinoplasty approach, or a rim graft to prevent rim retraction.

Grafts may be used to give support, give bulk or aid in function, as well as help with cosmesis.

Preoperative considerations

Preoperative assessment is key in planning septorhinoplasty surgery and external inspection and palpation give indications of which parts of the nasal skeleton may require grafting, with airway/septal assessment helping this. Assessment of the skin envelope thickness is vital as it affects the prominence of the underlying bones and cartilages. Thicker skin may camouflage minor dorsal imperfections, but will also mean that tip sculpting is more difficult and grafts used to aid tip definition may not be as visible.

Patient ethnicity requires consideration as this too may significantly affect surgical techniques, the graft selection used and the eventual outcome. The Caucasian nose has greater projection at the tip and nasion compared to the Oriental nose which may have thicker skin, weaker cartilages, a widened alar base and shorter nasal bones[2,3].

Pre-operative assessment allows the surgeon to plan which grafts may be needed in any particular case and this will inform which approach will be optimal (whether open or closed). It will also inform what additional areas of harvest site preparation may be needed (e.g. ear or rib) and what additional equipment may be necessary.

Grafting Materials

Autologous grafts

Septum

Nasal septal cartilage is the workhorse graft in septorhinoplasty surgery. It is generally straight, strong and often of good thickness. It can be used for structural support as well as for camouflage applications, with resorbtion being minimal. Scoring or light crushing can increase its malleability allowing better contouring, although over enthusiastic crushing increases its resorbtion rates[4]. Harvest is easy and local in the nose and a large amount may often be harvested by traditional SMR techniques. When harvest is undertaken before reduction rhinoplasty, the surgeon should be mindful to leave an additional thickness in the dorsal strut to allow the necessary 10-15mm to be maintained following the hump reduction. Any superfluous cartilage can be returned to the septal pocket as a 'cartilage bank' for future use.

Pinna

Large areas of the conchal bowl (cymba and cavum) can be harvested without affecting the size/shape or support of the pinna. The yellow elastic cartilage is less good for structural purposes than septal cartilage, being thin and relatively brittle. The natural curves of the cartilage may limit its application. Laminating two pieces face-face can increase its structural integrity and thickness. Crushing of this cartilage is generally not well tolerated. Harvest may be undertaken via an anterior approach, where it is easy to remain oriented but leaves an anterior scar. Posterior harvest leaves no visible scar but allows less easy orientation of the possible harvest site. The curvature and springiness makes this graft particularly suitable for use as a Butterfly graft[5].

Costal Cartilage

The abundant amount available makes this suitable when larger amounts of cartilage are needed for structural support purposes such as where there is a large dorsal defect with little septal support. Subperichondrial dissection minimizes the risk of pleural damage when harvesting ribs.

The cartilage is strong but has inherent curvature. Asymmetric splitting or cortical shaving to give straight grafts increases its tendency to twist postoperatively, especially in the under 35 age group[6,7]. In the older age group the possibility of calcification of the cartilage can cause problems. Oblique sectioning of the cartilage gives multiple thin slices (each with layers of cortex and medulla intact), which can then be laminated into a new more stable septal construct[8].

Fascial grafts

Fascia Lata or Temporalis Fascia can be used in single layers to help cover and smooth dorsal irregularities or may be used in multiple layers for dorsal augmentation.

Bone

Iliac crest bone grafts have mostly been abandoned due to unacceptable post implant resorbtion rates[9]. Calvarial bone may be used, but there is a small risk of intercranial morbidity during harvest, and gives a very rigid and often prominent graft. This may be difficult to attach, usually needing screw/miniplate fixation and may be susceptible to fracture/movement following any future trauma

Homologous grafts

Irradiated cadaveric costal cartilage and fascia lata are both available commercially. When making a decision whether to use these, the additional cost of purchase needs to be offset against savings in theatre time and reduction in possible patient harvest site morbidity. Sheet like materials of acellular human dermis such as Alloderm are also available.

Xenografts
Bovine cartilage use has previously been described though is now commonly avoided due to resorbtion rates of up to 44%10. Acellular porcine dermal preparations, such as Permacol, have become popular with some surgeons for augmentation[11].

Allografts
Synthetic grafts have the advantage of being in abundant supply and reduce both operating time and donor site morbidity. Previous cartilage depletion or a patient's apprehension regarding surgical morbidity from the harvest site may contribute to the decision to use these[12].

A huge array of different shapes and sizes of such grafts are available but some health systems can find the cost prohibitive and find difficulties keeping a wide/ varied stock available to allow suitable implants to be available for all patients. Some authors have had great success using these, however possible post-op infection/extrusion is feared by many[13].

Medpor® (Porous high-density polyethylene, PHDPE)
The porous internal architecture of this allows fibroblast ingress during the healing process and contributes to an increase in mechanical stabilisation, with less risk for infection and extrusion. It incites minimal foreign body reaction compared to silicone implants and no encapsulation occurs but is associated with significant adherence to subcutaneous tissues[13-15]. It is available in many preformed shapes and sizes for a variety of nasal applications[15].

Gortex®
Microporous Gore-Tex (fibrillated polytetrafluoroethylene -PTFE), is highly biocompatible and allows tissue ingrowth with minimal inflammatory response, and low rates of infection, extrusion and resorption. However, with its soft consistency, it does not provide much robust structural integrity for augmentation[15].

Silastic
Silastic, a non porous silicone-based implant, can have high rates of infection and extrusion, especially in thin-skinned individuals[16]. Other complications such as graft migration and dorsal cyst formation have also been documented and complications can occur many years after implantation[17].

Graft Fixation
Graft mobility post op can reduce its utility for support and can give adverse cosmetic features. The dense extracellular matrix and low vascularization means that cartilage grafts do not integrate with the host tissue and other methods of fixation are required. Pocketing in snugly tailored skin envelopes may be possible but often other types of fixation are needed. Suture techniques employing either absorbable or non-absorbable materials are widely used although tissue adhesives and cyanoacrylates can also been utilised to secure graft materials.

Grafting Techniques
With the appropriate selection of graft material or combinations the surgeon has a number of techniques available for augmenting the nose[14]. Septorhinoplasty requires precise pre-operative diagnosis to select which approach is best in any one individual[18]. Closed approaches allow skin envelope continuity with positioning of the graft in a precise pocket, avoiding any distortion or displacement. Healing time is comparatively short and the general structure can return to its previous elasticity and mobility[19].

External approach septorhinoplasty offers superior exposure of anatomy allowing better inspection of the deformity and allows more extensive grafting procedures to be undertaken under direct vision[20].

Septal Assessment and Correction
Assessment and correction of the septum is undertaken initially. Minor septal deviations may be corrected with traditional septoplasty techniques via a closed approach and septal cartilage can easily be harvested with sub mucous resection.

For more grossly deviated septums an open approach is preferred as this allows better visualization and access, and with this increased access septoplasty in-situ may still be possible. If this is not possible then the septum should be removed, assessed outside the body and a neo-septal graft can then be constructed and reinserted. Such extracorporeal septoplasty was first postulated by King and Asley in 195220, though was not performed until 1981[21].

An ascending ladder of reconstructive possibilities can be followed according to the damage found on the septum. Following removal of the septum an area of straighter/ intact cartilage from further back in the septum can be brought forwards and used as a new L-shaped strut to replace the excised/ deviated anterior septum. The size/

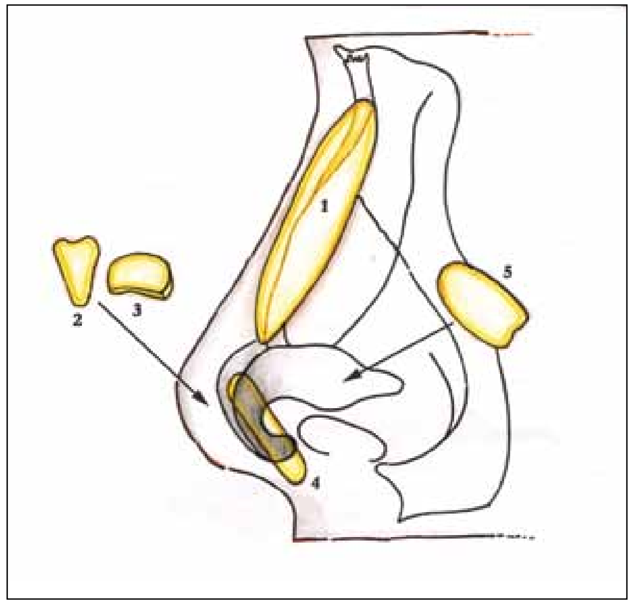

Figure 1: *showing : 1-Dorsal graft, 2- Shield graft, 3- Tip graft, 4-Columellar strut graft & 5-Alar batten graft.*

shape of the construct needs tailoring to the patient. If a single piece septal graft is not possible, a new L-strut can be constructed from 2 pieces of straight cartilage overlapped and sutured together. Where this is not possible, and a septum is found to be composed only of multiple smaller fragments, then a neo-septal construct can be made supporting these separate fragments on PDS foil (Ethicon ZX[8])21, 22. With each of these techniques two-point graft fixation with non-absorbable sutures to the Upper Lateral Cartilages and to the Nasal Spine is required for stability. Where reusable septal cartilage is totally lacking, a rib graft may be necessary

Where a straight septal cartilage is present, but it is too short, a caudal septal extension graft should be considered. This allows alteration of nasal projection and length and plays a part both in function and aesthetics. A portion of posterior septal cartilage can be harvested by SMR and be secured end to end to the caudal portion of the existing septum to add length[23].

Specific Grafting situations

Functional Grafts

Alar Batten Grafts
Alar batten grafts are used to support/strengthen the lateral crurae of the Lower Lateral Cartilages (LLCs) to prevent alar collapse. The collapse site varies, though is often at the internal valve area, underlying the supra-alar crease[24]. Septal cartilage is usually used. The grafts are not intended to create major changes in resting anatomy and can be placed either deep to the LLCs through an open approach or superficial to them in tailored pockets via a closed approach. (See Fig 2.)

Spreader Grafts
These widen the dorsal septal angle between the septum and nasal sidewall in order to improve the airway. Septal cartilage is used, however more recently in-folding and suturing of the excessive anterior edge of the Upper Lateral Cartilage following hump removal has been described to form 'auto spreader grafts' in situ[25]. Spreader grafts may also assist in cosmetic improvement in noses with middle-third narrowness/asymmetry and can also be useful in the cosmetic improvements of inverted-V deformities[26-28]. (See fig 3.)

Butterfly Grafts
Butterfly grafts are used to splint and resist more severe nasal valve collapse. The inherent curve and elasticity of the concha makes it the ideal graft. The curved cartilage is positioned over the dorsum with the graft's lateral edges placed under the lateral crurae of the LCC to stent them open. An open approach is often needed. The graft may add bulk to the nasal tip but this can be useful for improving both the functional and cosmetic results in revision rhinoplasty[29,30]. (See figure 4)

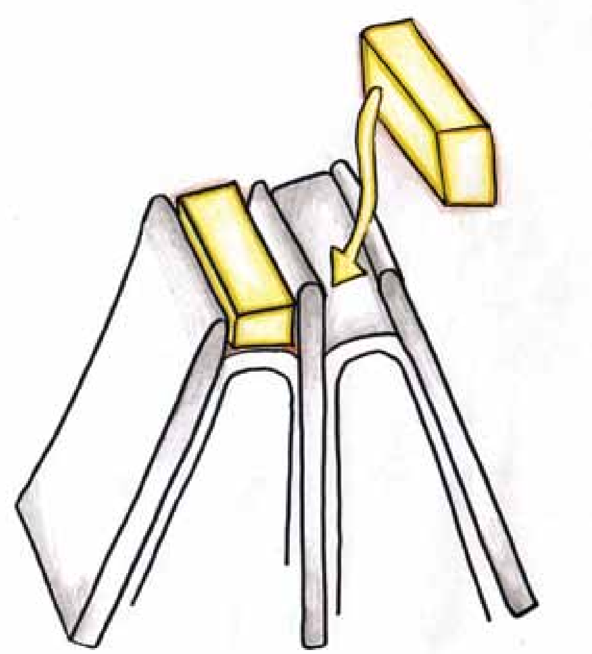

Figure 2: *Spreader grafts.*

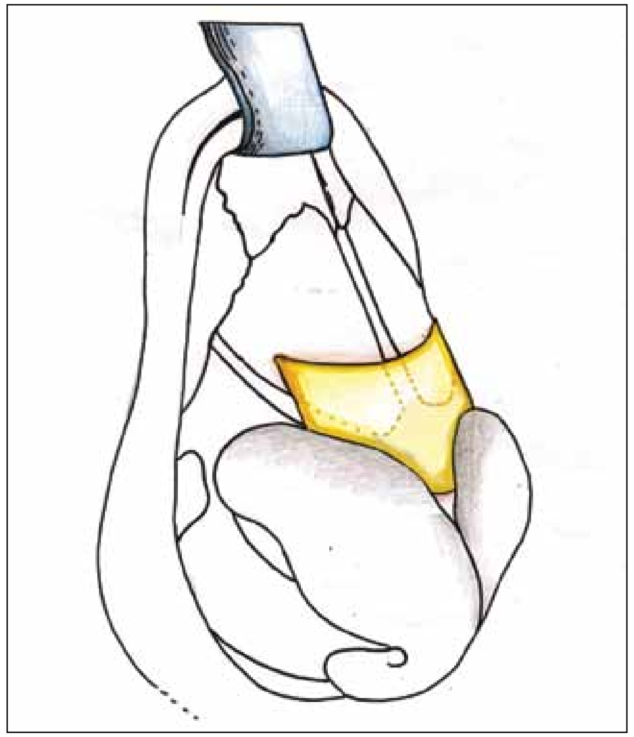

Figure 3: *Butterfly graft.*

Cosmetic grafts

Dorsal grafting

The material chosen for dorsal grafting depends on the amount of augmentation needed. Minimum augmentation (or dorsal smoothing over deeper irregularities) can be achieved with one or more layers of sheet material such as fascia, Alloderm or Permacol[11]. Septal cartilage grafts offer more augmentation but large defects may need rib cartilage. (see figure 2)

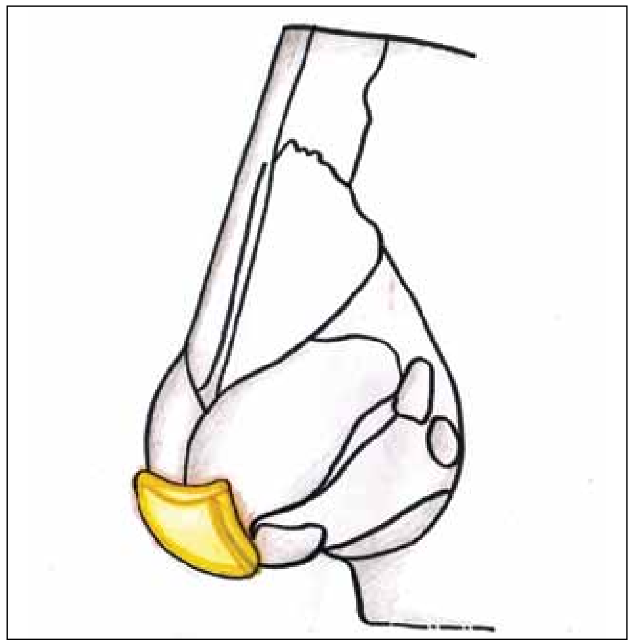

Figure 4: *Tip graft.*

'Turkish Delight' Graft

Diced cartilage (0.5-1.5mm dice) can be wrapped/sutured in a layer of fascia or Surgicel to form a malleable cylindrical 'sausage' which makes an excellent dorsal graft where larger pieces of other graft material is elusive. Resorbtion rates are low and good cosmetic results are achieved[31].

Tip/Shield Grafts

A tip graft is generally a small beveled rectangular or trapezoid graft sutured over the domes to give tip projection, symmetry and definition.

Shield grafts (named as their shape resembles a shield) are useful in patients lacking prominence of the nasal tip lobule[32]. Septal cartilage is carved and edge-bevelled to obtain the appropriate shape. The graft is inserted at the tip-columellar junction, anterior to the intermediate crura, to define the "double-break" columellar profile[33]. A larger graft placed more anteriorly may be used to contribute to tip projection whereas a graft placed more posteriorly may be used primarily to add length to the nose. (See figures 2 & 5)

Camouflage Grafts

Small pieces of sculpted or crushed cartilage may be applied to various areas of the nose to help smooth and regularize the nasal contours. These may be sutured in place or tissue adhesive may be used to secure them.

A 10-15mm beveled trapezoid of septal cartilage inserted into a pocket over the upper lateral cartilage via an intercartilaginous incision is a useful method of effacing the mid-third shadow caused by traumatic evulsion of an upper lateral cartilage on one side.

Conclusion

Septorhinoplasty is not a 'set piece' operation, rather it is a combination of different manoeuvres applied and tailored to an individual patient's needs. A surgeon thus needs an armamentarium of different techniques and an understanding of which to apply in differing situations. Varied grafting techniques make up an important part of this.

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Immunotherapy in allergic rhinitis

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Abstract
Allergic rhinitis (AR) has a significant impact on an individual's productivity and quality of life and is an important public health issue. Allergen avoidance and pharmacotherapy with steroids and antihistamines are the mainstay of treatment for AR. Immunotherapy, however, is establishing itself as a modality of treatment with the potential to alter the natural course and biology of AR. Both subcutaneous and sublingual specific allergen immunotherapy are being used in the management of AR. This review aims to discuss the principles, advantages and disadvantages of subcutaneous and sublingual immunotherapy for AR.

J ENT Masterclass 2015; 8 (1): 92 - 96.

Keywords
Allergic rhinitis, Subcutaneous immunotherapy, Sublingual immunotherapy.

Introduction
Allergic rhinitis (AR) is characterized by nasal symptoms including sneezing, nasal pruritus, nasal obstruction, rhinorrhoea (clear nasal discharge) and ocular symptoms of conjunctivitis. These occur as the consequence of an IgE mediated reaction, to inhaled allergens, in a sensitised individual[1]. It can be triggered by seasonal pollens and moulds, as well as perennial indoor allergens, such as dust mites and pets. Sensitisation to various allergens begins in the first year of life. The prevalence of allergic rhinitis peaks in the second decade of life and then gradually diminishes[2].

AR is an important public health concern and affects >20% of the population in the UK[3]. It causes considerable morbidity and loss of work productivity and poorer performance at school[4]. AR is often co-prevalent with asthma and if uncontrolled is associated with asthma exacerbations and increased medication usage[5].

The standard therapy for AR includes allergen avoidance, intranasal corticosteroids and intranasal and systemic antihistamines. In spite of a plethora of pharmacological agents available, a third of children and almost two thirds of adults with AR report only partial or poor relief with pharmacotherapy. In the UK approximately 40% of patients with AR may be poor responders to pharmacotherapy[6]. The reasons for this are multi-factorial but include poor nasal inhaler technique, poor compliance, under-treatment by physicians and intolerance of treatment. Even if these issues were addressed it is important to recognize that none of these pharmacological treatments actually have any disease modifying roles and merely offer symptom relief. Allergen immunotherapy is the only disease-modifying treatment for AR.

What is allergen immunotherapy?
Allergen immunotherapy is a form of treatment that involves administering repetitive doses of allergen over time to induce immunological tolerance - the ability to inhale the antigen without allergic symptoms after discontinuation of the therapy. The two common methods of allergen administration are the subcutaneous route (subcutaneous immunotherapy, SCIT) and the sublingual route (sublingual immunotherapy, SLIT).

Allergen immunotherapy was first formally described in the early part of the 20th century. Noon and Freeman described the procedure of inoculation with grass pollen for the treatment of hay fever and laid down the initial protocol for subcutaneous immunotherapy[7,8].

Mechanisms of action
AR patients exhibit a predisposition to develop a T helper (Th)2-predominant immune response in response to inhaled allergen. Th[2] cells secrete interleukin (IL)-4, IL-5 and IL-13, which stimulate B cells to switch to producing IgE class allergen-specific antibodies. These IgE antibodies bind to the high affinity Fc (Fragment crystallisable) epsilon receptors on the surface of mast cells and basophils. Exposure to allergen cross-links the surface-bound IgE molecules on mast cells and basophils, which then degranulate releasing mediators such as histamine, leukotrienes, cytokines and prostaglandins. These mediators lead to symptoms of allergic reactions (reviewed in Wheatley et al.[9]). Although the exact mechanism of immunotherapy is not fully understood there is a significant literature describing the impact on all the stages of the allergic immune response described above. The predominant effect observed is a skewing from a Th-2-mediated response to a Th-1-immune response. Also reported is an increase in T regulatory cells, a specialized subset of T cells that have immune-suppressive functions and produce the immunosuppressive cytokines IL-10 and transforming growth factor-β (TGF-β)[10]. Moreover, there is a reduction in the reactivity and sensitivity of peripheral basophils to antigens. The allergen specific IgE levels show an early increase followed by a decrease while the levels of allergen specific IgG^4 increase over time[11]. A summary of the immune changes that accompany allergen immunotherapy is given in Table 1. The reader is referred to a comprehensive review on the mechanisms of action of allergy immunotherapy by Akdis et al[12].

Patient selection, indications and contraindications
Patient's preference plays a large role in the decision to proceed with immunotherapy. This is because the treatment is prolonged (usually 3 years) and the results are not immediately obvious. Additionally there are adverse effects associated with immunotherapy that could be life threatening. Patients should be also be made aware that immunotherapy with any allergen may not be curative. Most clinical trials report a 30–40% reduction in symptoms as well as pharmacotherapy requirements in the first year of treatment[13].

Table 1. Immunological changes induced by allergen immunotherapy (AIT)

Cell type/ Immunoglobulin	Action
Mast cells/Basophils	1. Decreased mediator release in the early phase of AIT 2. Decreased numbers in tissue in the late phase of AIT
Dendritic cells	1. Release of TGF-ß and IL-10 2. Induction of regulatory T cells
T cells	1. Induction of allergen-specific regulatory T cells 2. Suppression of allergen-specific Th1 and Th2 cells
B cells	1. Induction of IL-10 producing regulatory B cells 2. Induction of $IgG4^+$ B cells
IgE	Early increase followed by late decrease in allergen-specific IgE
IgG4	Increase in allergen-specific IgG4

Patients with a definite diagnosis of IgE-mediated AR confirmed on allergy tests (skin test or specific IgE levels) are candidates for immunotherapy. Objective confirmation of IgE sensitivity should be established using skin test or specific IgE testing to the relevant antigen. The recently published Clinical Practice guidelines in USA on AR recommend immunotherapy in patients who have failed allergen avoidance and pharmacotherapy or tolerate it poorly[14]. Immunotherapy for AR in the UK is mainly offered for IgE- mediated seasonal pollen induced rhinitis that has not responded to medical therapy and in selected patients with animal dander or house dust mite allergy that has not responded to allergen avoidance and adequate pharmacotherapy[15]. In addition patients should be well motivated and understand the risks and limitations of immunotherapy and be willing to invest the time in the prolonged treatment course.

The ideal candidate for immunotherapy is an individual with a sensitisation to a single allergen. Desensitisation to a single allergen (monotherapy) is the recommended practice in the UK. Certainly multiple allergen immunotherapy is not recommended and this is supported by evidence in literature that desensitisation is allergen specific and more efficacious when used alone rather than in combination with multiple unrelated allergens[15]. In Europe and the USA multiple desensitisations are more commonly attempted.[16]

Immunotherapy is not recommended in patients with moderate to severe or unstable asthma, patients on beta-blockers, patients with other medical and immunologic disease, small children (<5 years) and pregnancy. Patients with asthma have been reported to develop more severe systemic reactions with immunotherapy if a reaction occurs. Beta blockers counteract emergency treatment with adrenalin (which may be required for treatment of a reaction to immunotherapy), and therefore patients are asked to be switched to an alternative class of drug before commencing desensitisation therapy[17]. Initiation of immunotherapy is contraindicated in pregnancy although most centres in the UK do not stop immunotherapy in pregnant women once maintenance (stable dose) therapy has been reached. The perceived highest risk to the foetus is if the mother has anaphylaxis, which is more likely during the up dosing period[18].

Delivery of immunotherapy - subcutaneous and sublingual

Subcutaneous immunotherapy (SCIT)

SCIT was introduced in early 1900s and has been widely studied and applied since. The allergen is introduced subcutaneously and several doses are administered over a period of 2-3 years. The usual standard SCIT protocol comprises an up dosing phase and a maintenance phase. In the up dosing phase a series of weekly doses of increasing strength and/or volume of the allergen solution is administered. Once the maintenance dose or highest tolerated strength has been achieved, this dose is repeated every 4 weeks for approximately 3 years. The schedule for increasing the allergen dose is not fixed and is tailored according to the tolerance of the patient. Similarly the length of treatment should be cut short if clinical improvement is not apparent after 2 years of treatment or extended if there have been breaks in treatment or up dosing is particularly prolonged.[19] An alternative approach is pre-seasonal immunotherapy. Pollinex is licensed in the UK and has preparations against grasses and rye or tree pollen. Four to six incremental dosages of allergen are administered at weekly intervals before the start of the specific pollen season, for three consecutive years.[20,21] The efficacy of Pollinex compared with the more regular injections is not yet known. There are significant cost and capacity advantages of this shortened regimen.

Several reports affirm the clinical efficacy of SCIT and its ability to modify the body's immunological response to allergens long term. The onset of improvement in symptoms is variable but can be seen from 12 weeks of commencement of therapy and increases over a period of 1-3 years of treatment. The clinical effect of SCIT continues even after cessation of treatment and has been reported to last for as long as ten years[22]. The benefits of SCIT are not limited to improvement in symptoms of AR. It has been reported to prevent development of new sensitisations in mono-sensitised children. Allergic children who received immunotherapy against house dust mite over a 3-year period went on to develop new sensitisations in only half the group in contrast to the group of allergic children who did not receive immunotherapy, all of whom developed new senstisations[23]. Additionally, SCIT reduces development of asthma in children treated for rhinitis. Immunotherapy of children with pollen allergy for 3 years resulted in reduction of conjunctivitis and rhinitis symptoms as well as an improvement in bronchial hyper-reactivity[24].

One of the challenges with monitoring the efficacy of immunotherapy is the lack of good immunological biomarkers that would measure the patient's response or lack of therein, to the desensitisation regime. Durham et al. reported prolonged clinical remission with reduction in late skin response and associated CD^3+ T cell infiltration and IL-4 mRNA expression 3 years after discontinuation of therapy[25]. Other possible markers that have been suggested include an increase in allergen-specific serum IgG^4, increased serum functional IgG responses, as well as changes in cytokine and proliferative responses of peripheral blood mononuclear cells to allergens. However, none of these have been shown at an individual level to correlate well with the clinical response to immunotherapy.

Adverse effects of SCIT include local reactions (swelling, itching, skin necrosis) and systemic effects (anaphylaxis). Reported incidence of local reactions range from 0.6% to 58% and that of systemic reactions from 0.06% to 0.9%[26]. Possible risk factors for severe reactions during immunotherapy include uncontrolled asthma, injections administered during exacerbations of symptoms, high degree of hypersensitivity, use of beta-blockers, injections from new vials, and dosing errors[27]. The fatality rate, however, is low at one per 2 million injections. In the UK this risk is managed by limiting SCIT treatment to specialist centres with the facilities and personnel available to manage anaphylaxis and a waiting period for 60 minutes after administration of the allergen.

Sublingual immunotherapy (SLIT)

In 1986, the British Committee for Safety of Medicines reported 26 deaths connected with SCIT, so newer modes of allergen administration such as sublingual and intranasal routes began to be more actively explored[28]. SLIT involves placing an allergen extract (aqueous or tablet form) under the tongue to allow absorption. The allergen should be taken daily, and the currently recommended length of therapy is 3 years, similar to SCIT.

SLIT took a while to establish itself as an accepted modality of immunotherapy and was considered a poorer alternative to SCIT; the WHO position paper from 1998 considered it a viable alternative to SCIT but did not recommend it. SLIT achieved 'accepted' status in the management of AR in the Allergic Rhinitis in Asthma (ARIA) guidelines published in 2001 and recommended status for pollen allergy in adults and children and mite allergy in adults in the ARIA 2010 update.[29,30] Several systematic reviews have confirmed the benefits of SLIT in management of AR in the Allergic Rhinitis and its Impact on Asthma (ARIA)[31,32]. The meta-analysis by Lin et al. included 63 randomised control trials of SLIT and reported a moderate grade level of evidence that SLIT improves AR symptoms[33]. As is the case with SCIT, SLIT improves the control of asthma, conjunctivitis and disease specific quality of life[14,34]. The optimum dosage, duration of treatment and frequency of administration of SLIT have not yet been established. However the doses of allergen extracts required for successful treatment with SLIT are at least 50 to 100 times higher than those administered with SCIT[1,26].

The advantages of SLIT include the ease of administration and superior safety profile to SCIT. The daily doses are taken at home, following the administration of the first dose in a medical setting, and this reduces the number of outpatient appointments required. As the doses are administered at home the patient must be well informed about adverse effects, how to deal with them and when to seek medical advice[35]. Local adverse effects with SLIT include itching and swelling of lips and sublingual oral mucosa that resolve spontaneously and happen in the range of 0.2-97%[26]. Antihistamines can be used to ameliorate these symptoms and they usually settle within a couple of weeks of commencing treatment. Systemic reactions have been reported with SLIT but are extremely uncommon and no deaths have been reported in literature to date. It is thought that lack of efficacy in SLIT can often be attributed to poor compliance as the patient is not supervised in their daily treatment. Review appointments during treatment are focused around encouragement and compliance to ensure patients remain motivated to complete the course.

Grazax is the only licensed SLIT product in the UK. The preparation is only for grass pollen allergy. However, several unlicensed vaccines are being prescribed to individual 'named patients', depending on clinical indications and are reviewed in Walker SM et al.[15].

SCIT versus SLIT

The jury is still out as to which mode of allergen administration is more efficacious. Dretzke et al. stated in their systematic review that the superiority of one modality over the other could not be demonstrated by indirect comparison[36]. Chelladurai et al. reported low-grade evidence to support SCIT as superior to SLIT for reduction in asthma symptoms and moderate-grade evidence for reduction of allergic rhinoconjunctivitis[37]. They concluded however that additional studies were required to strengthen this evidence base for clinical decision making[37]. A meta-analysis by Di Bona et al. concluded that SCIT is more effective than SLIT in controlling symptoms and in reducing the use of anti-allergic medications in seasonal allergic rhinoconjunctivitis to grass pollen[38]. Further direct comparison of SCIT versus SLIT in randomized control trials is warranted to answer the question of efficacy definitively.

Future directions

The field of immunotherapy for AR is wide open for further research and improvement in treatment modalities. Some key research areas include:

1. Research around the efficacy of SCIT versus SLIT and other exploring other delivery mechanisms.
2. Further understanding of the immunological mechanisms that induce tolerance to allergens following immunotherapy and the development of biomarkers to measure the patient's response to treatment.
3. Improvement of patient adherence to long-term immunotherapy protocols
4. Development of new recombinant or component based allergens to tailor treatment to match a patient's allergen profile.

Declaration

The authors have no competing interests.

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Management of acute and chronic parathyroid insufficiency after total thyroidectomy

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Parathyroid insufficiency management, Parathyroid splinting, Permanent Hypoparathyroidism, Postoperative Hypocalcaemia.

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Abstract
Acute and chronic parathyroid insufficiency are the most common complications after total thyroidectomy. Their true prevalence, has been understimated. The aim of this review is to propose management strategies through the understanding of the three different syndromes of parathyroid failure: postoperative hypocalcaemia, protracted and permanent hypoparathyroidism. Selective management of postoperative hypocalcemia (s-Ca <2 mmol/L at 24h) with calcium and calcitriol at discharge is recommended. The number of parathyroid glands remaining in situ, iPTH and serum calcium levels one month after surgery should be taken into account to assess the likelihood of recovery from protracted hypoparathyroidism. Permanent hypoparathyroidism is managed with calcium and vitamin D analogues supplementation or calcium salts alone according to iPTH levels, s-Ca levels and patient's symptoms, with the aim of keeping the s-Ca concentration in the lower limit of the normal range (2.1-2.2 mmol/l).

Introduction
Postoperative parathyroid insufficiency is the most common complication after total thyroidectomy[1-4]. The prevalence of transient hypocalcaemia and permantent hypoparathyroidism according to a recent review and meta-analysis ranges from 19% to 38% and 0% to 3% respectively[5]. The true prevalence, however, is being underestimated due to a lack of clear definitions[6,7], inadequate follow up and conflicts of interest 8. Actually, national registries and large multicenter studies show that the problem of permanent hypoparathyroidism is worse than usually reported in the literature with a prevalence ranging from 6.4% to[12]%[9-13].

Regarding the aetiology, the majority of the authors agree that the main cause of hypocalcaemia after total thyroidectomy is an acute parathyroid insufficiency due to a combination of factors: intraoperative injury to the parathyroid glands, devascularization, gland autotransplantation and inadvertent removal of parathyroid tissue, all leading to a reduction of the functional parathyroid parenchyma[1]. Less than four parathyroid glands remaining in situ due to accidental excision or autotransplantation is a crucial factor leading to acute parathyroid insufficiency and chronic[1,10,14-22] and requires a most meticulous surgical technique when identifying and preserving the parathyroid glands intraoperatively. Hemodilution, urinary calcium excretion induced by surgical stress, calcitonin release during thyroid mobilization, vitamin D deficiency and hungry bone syndrome have been also suggested as contributing factors to post-thyroidectomy hypocalcaemia[6] but iPTH sampling after thyroidectomy has clearly demosntrated that, by far, parathyroid failure is the most relevant and perhaps sole factor leading to hypocalcaemia.

Although it may seem that permanent hypoparathyroidism can be easily managed with calcium and/or vitamin D supplements, long-term treatment of hypoparathyroidism has not been standardized and its long-term negative impact on patients' wellbeing has been underestimated[23,24]. In addition to uncomfortable symptoms, such as paresthesiae and muscle cramps, when target calcium levels are not reached, patients may be affected also by renal function impairment, calcification of basal ganglia, and are more likely to have neuropsychiatric diseases and infections[25,26] . A recent survey carried out on 374 patients suffering from permanent hypoparathyroidism, showed that 75% of those polled, experienced more than 10 symptoms despite appropriate treatment. Approximately 80% required admission to hospital. Disability to perform household activities was reported by 85% of the patients. Ultimately, patients experience a generally decreased of their quality of life[23].

The aim of this current review is to propose a therapeutic strategy based on three different syndromes of parathyroid failure.

Postoperative hypocalcaemia

There is general consensus that serum calcium and/or PTH levels should be monitored after total thyroidectomy and treatment of postoperative hypocalcaemia must be started before symptoms occur. According to the more widespread proposal, we define postoperative hypocalcaemia as a s-Ca <2mmol/L (8 mg/dL) at 24 hours after total thyroidectomy[8] .

Broadly speaking, post-thyroidectomy hypocalcaemia has been traditionally managed by implementing one of the three following therapeutic strategies:

- Selective strategy, which consists in starting treatment when hypocalcaemia is diagnosed within 24 hours postop.
- Preventive strategy, which consists in giving calcium and/or vitamin D to all patients at discharge independently of biochemical parameters.
- Reactive strategy, only treating patients who develop signs and symptoms of hypocalcaemia

We prefer a selective therapeutic strategy, since it allows for patients to be safely discharged home early, avoids overtreatment and prevents symptoms. It is very uncommon for patients to develop symptoms of hypocalcaemia within 24 hours of surgery. Preventive treatment may be indicated in high-risk patients in whom hypocalcaemia is most likely (extensive lymphadenectomy, concomitantnt parathyroidectomy for primary hyperparathyroidism, double parathyroid autotransplantation). Selective strategy[27-29] has also been supported also by other leading groups. As an example, De Pascuale et al. propose to avoid treatment in patients with less than 70% PTH decay and less than 12% calcium drop 24 hours showing no symptoms and in whom parathyroid autotransplantation has not been performed[28]. Other authors have found selective approach with only one iPTH measurement on the morning of

Table 1: Definitions and management of the three syndromes of parathyroid insufficiency after total thyroidectomy

Syndrome	Definition	Recommended treatment	Management
Postoperative hypocalcaemia	s-Ca <2 mmol/L within 24 hours after surgery	Calcium carbonate 1.5-3g/d Calcitriol 0.5-1.5 μg/d	Selective therapeutic strategy If symptomatic hypocalcaemia add i.v. calcium s-Ca target: 2.35-2.45 mmol/L (parathyroid splinting) Follow-up one week and one month after surgery
Protracted hypoparathyroidism	iPTH <1.1 pmol/L and/or need for calcium/vitamin D replacement at 4-6 weeks after surgery	Calcium carbonate 1.5-3g/d Calcitriol 0.5-1.5 μg/d	s-Ca target: 2.35-2.45 mmol/L Follow-up: re-check s-Ca, s-P, s-Mg and iPTH every two months until recovery or until 1 year
Permanent hypoparathyroidism	iPTH <1.1 pmol/L and/or need for calcium/vitamin D replacement one year after surgery	Calcium carbonate 1.5-3g/d Calcitriol 0.5-1.5 μg/d or Calcifediol or 1-alpha-calcidol 0.5-4 μg/d Switch calcitriol to high dose 25OHD3 (calcifediol 10.000 IU/ twice a week), particularly if s-Cr >120 mmol/L	s-Ca target: 2.1-2.2 mmol/L *Aparathyroidism* (undetectable iPTH): Calcium and Vitamin D *Hypoparathyroidism* (detectable but subnormal iPTH): Calcium +/- Vitamin D *Relative parathyroid insufficiency* (hypocalcaemia with inappropriately "normal" iPTH levels): treat associated condition and adjust calcium and vitamin D treatment Assess addition of thiazides and/or 1-84PTH if difficulty in reaching target s-Ca. Follow-up: twice a year if stable. Close monitoring if intercurrent disease, pregnancy or lactation

postoperative day 1 to be a safe and cost-effective strategy[29]. On the other hand, some studies have found that routine supplementation with calcium and calcitriol appear to be a less expensive approach and more beneficial to patients[30].

Our current protocol for total thyroidectomy calls for a serum calcium sampling obtained 24 hours after surgery and oral treatment with calcium and calcitriol is started if s-Ca <2 mmol/L (Table 1). Our management of postoperative hypocalcaemia has been slightly modified over time since we realized that a more intensive medical treatment may improve the outcome of parathyroid insufficiency[14] by putting the parathyroid glands at rest (parathyroid splinting). Thus, we advocate for high dose of calcium carbonate, ranging from 1.5 to 3 g/day, and calcitriol (Rocaltrol®) 0.5-1.5 μg/day. Should symptomatic postoperative hypocalcaemia occur, i.v. calcium should be started together with oral calcium and calcitriol supplements (Figure 1).

An iPTH determination the next day (12-24h after thyroidectomy) is desirable in order to have a baseline value at the time of the first patient's postop visit the following week. In the presence of undetectable levels of PTH at 24 hours, treatment is better continued after this initial visit and s-Ca and iPTH re-checked at four postoperative weeks.

Protracted hypoparathyroidism

About two thirds of patients with postoperative hypocalcaemia will recover the parathyroid function within one month after total thyroidectomy[15] and medical management can be stopped. If by then, iPTH is still low or undetectable and treatment is required, the probability of recovery from parathyroid insufficiency within the following year is 75%. Thus, about 25% of patients with protracted hypoparathyroidism will eventually develop permanent hypoparathyroidism. Protracted hypoparathyroidism is defined as a subnormal iPTH concentration (<13 pg/mL) and/or need for replacement therapy at 4–6 weeks after thyroidectomy[15]. We consider this 4-6 weeks time point a key moment to assess parathyroid function and to provide useful information to the patient. No variable can predict the likelihood of permanent hypoparathyroidism before this time period.

Replacement therapy can be tapered at one month if iPTH levels are normal (Table 1); if parathyroid insufficiency persists, supplements should be maintained.

Recovery from protracted hypoparathyroidism

Findings in our cohort of total thyroidectomy patients suggest that a normal-high serum calcium concentration at the time protracted hypoparathyroidism is diagnosed is a favourable factor for iPTH recovery[14,15]. This led us to formulate the hypothesis that injured/ischaemic parathyroid

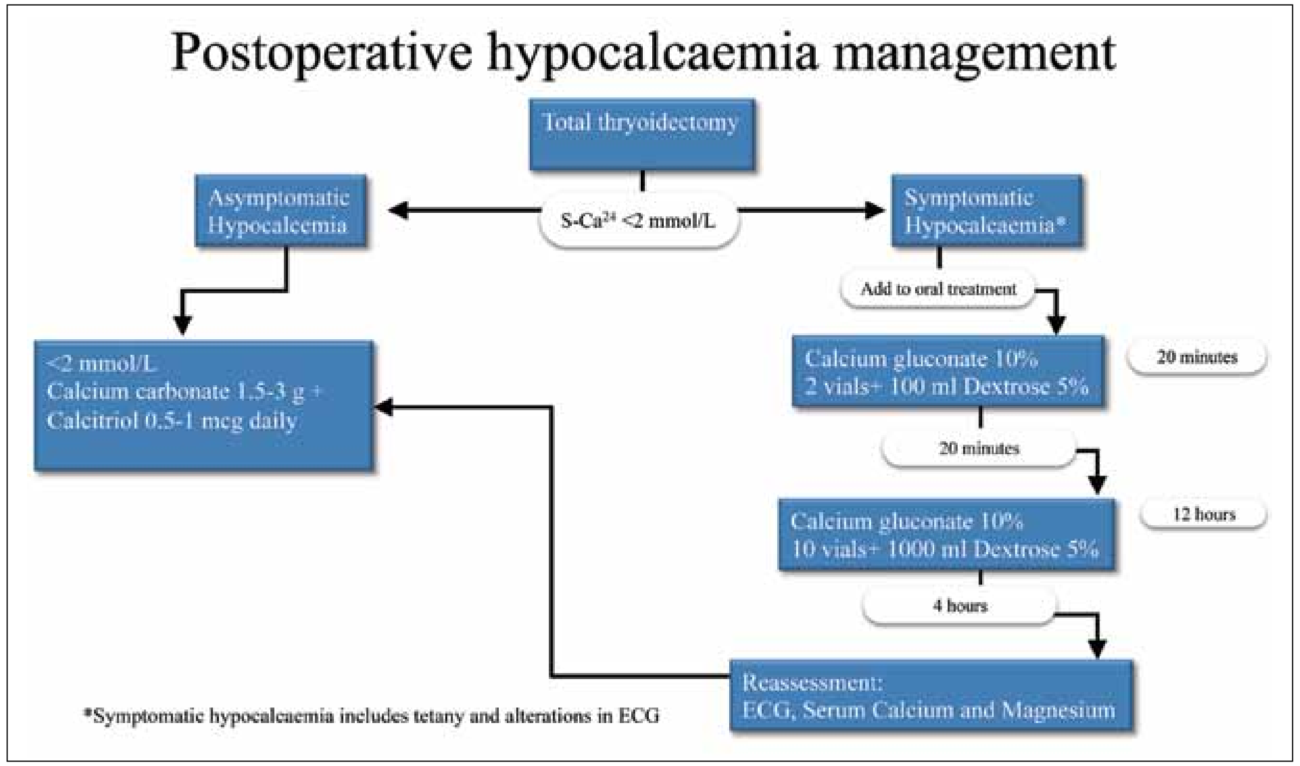

Figure 1: *Management of postoperative hypocalcaemia after total thyroidectomy.*

glands resting in a normal-high serum calcium environment from the very beginning after thyroidectomy, may recover better that if s-Ca is kept in the low normal of even subnormal range to "stimulate" iPTH secretion. If this is substantiated in further studies, replacement treatment initiated at the time postoperative hypocalcaemia is diagnosed should be targeted to keep s-Ca levels in the 2.35-2.45 mmol/L range (parathyroid splinting).

In addition to intensive medical treatment, the number of parathyroid glands remaining in situ (PGRIS = 4 minus autotransplanted minus accidentally resected glands) plays a critical role in parathyroid insufficiency and has a synergistic effect with s-Ca concentrations (Figure 2) in furthering parathyroid function recovery. The higher the number of preserved parathyroid glands, the more likely the patient will recover from protracted hypoparathyroidism. The relevance of a high delayed s-Ca concentration and of parathyroid in situ preservation, was already suggested in the seminal paper of Pattou et al.[1]. Our studies have largely confirmed their findings and have cast serious doubts about the efficacy of autotransplantation of fragmented normal parathyroid tissue to prevent permanent hypoparathyroidism.

Permanent hypoparathyroidism

Permanent postoperative hypoparathyroidism can be defined as a subnormal iPTH concentration (<13 pg/mL) and need for calcium replacement with or without vitamin D supplements 1 year after total thyroidectomy. Although some studies suggest a 6-month period as the limit for parathyroid function recovery, it is a common observation that some patients will recover the parathyroid function between 6 and 12 months after surgery and even later[31].

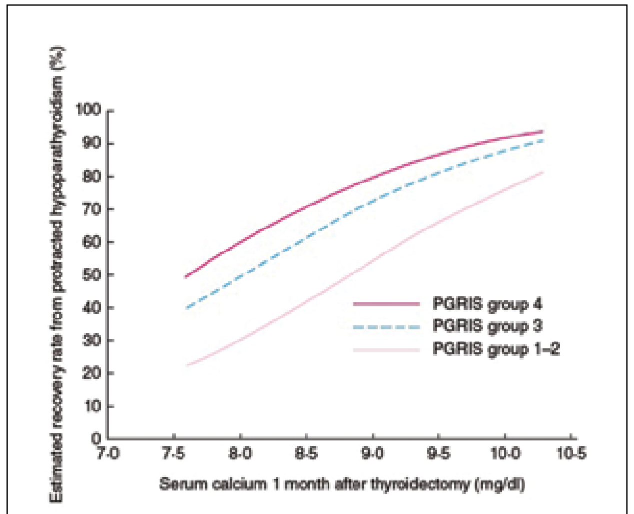

Figure 2: *Estimated recovery rates from protracted hypoparathyroidism according to the number of parathyroid glands remaining in situ and the s-Ca concentration 1 month after total thyroidectomy (previously published in 15).*

In case further treatment is needed beyond one year, we recommend to maintain calcium carbonate as required but switch calcitriol to calcifediol. Calcifediol is cheaper, non-nephrotoxic and easily managed by the patient because it usually is started as one ampoule (Hidroferol ® 266 mg, 10,000 UI) twice a week. Initial observations in our unit, confirm that impaired renal function is more commonly seen in patients receiving calcitriol than in those treated with calcifediol

Three different syndromes of permanent hypoparathyroidism should be differentiated:

- Aparathyroidism (undetectable iPTH levels with high phosphate): should be managed with both, calcium and vitamin D supplements. Addition of thiazides could be assessed in certain cases in which normal stable calcium levels are difficult to maintain. The chance of recovery in this case is really unlikely.
- Hypoparathyroidism (low but detectable iPTH levels with normal phosphate): can be often managed with calcium salts alone.
- Relative parathyroid insufficiency. Normal basal iPTH levels but insufficient iPTH reserve to maintain s-Ca within the normal range under some circumstances such as gastroenteritis, chronic malabsorption, gastric bypass or treatment with biphosphonates. In patients with malabsorption, high TSH values are often seen despite "appropriate" thyroxine dosage, giving a clue that a g.i. problem is the main underlying cause of hypocalcaemia.

Once permanent hypoparathyroidism is stabilized, patients should be monitored twice a year with regular determinations of serum calcium, iPTH, phosphate, magnesium, 25-hydroxivitamin D and 1,25-hydroxivitamin D in addition to renal function. It should be desirable to perform also a densitometry and kidney ultrasound to assess possible complications derived from long-term parathyroid insufficiency. Monitoring should be more closely performed in case of intercurrent severe disease, lactation or breastfeeding.

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DISCLOSURE

The authors have no financial disclosures to declare and no conflict of interest to report.

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Management of second primary tumours in head and neck

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Abstract
This review aims to give an overview of the management of second primary tumours (SPT) in the head and neck with an emphasis in metachronous SPT.

The appearance of a SPT in the head and neck has a negative impact in prognosis. Every successive head and neck tumour produces a 10% decrease in adjusted survival and treatment options are determined by previous treatment and by the extension of the SPT. In this scenario, prevention and early detection of SPT are paramount.

Persistence in tobacco smoking and alcohol drinking has significant influence on the appearance of a second neoplasm, and would be responsible for one-third of these tumours. The patient should be informed about the risk of SPT and the need to consult early in case of any suspect symptom.

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Key words
Head and neck cancer, second primary tumour, squamous cell carcinoma, metachronous second primary tumour.

Introduction
The treatment of head and neck squamous cell carcinoma (HNSCC) is in constant evolution and has achieved definite improvements in loco-regional control of the disease. However, these improvements have not been accompanied by a parallel increase in survival. This divergence has been attributed to several reasons: co-morbidities, complications or toxicity associated with treatment, development of distant metastasis, and the development of second primary tumours (SPT)[1].

Distant metastases and loco regional failure are important causes of mortality in the first two years after the initial tumour treatment, while SPT become important as limiting factors of survival past this first two years. The risk of developing a SPT remains constant throughout the follow-up.

The index tumour is the first diagnosed tumour and a SPT is any malignant tumour discovered thereafter. The most common location for SPT after an index HNSCC are the lungs and the head and neck[2,3,4,5].

From a chronological point of view, a SPT is classified as synchronous if it is diagnosed within 6 months after the diagnosis of the index tumour or metachronous if it is diagnosed after this period. The accepted criteria that define a SPT were established by Warren and Gates[6], as follows:

- Both tumours must be diagnosed as malignant on histological examination.
- The two neoplasms must be anatomically separated by normal mucosa.
- The possibility that one tumour is a metastasis of the other must be excluded.

More recently some clarifications have been added to these criteria, usually related to the distance that should separate the two lesions or the interval between two events. The minimal distance between two lesions to be considered independent tumours is 1.5 to 2 cm. The minimal time to exclude the possibility of local recurrence varies between 3 and 5 years according to different authors,.

Geneti analysis techniques could now be used to increase the accuracy of diagnosis of SPT. Leong et al studied the allelic imbalance that occurs in tumour cells due to the loss of genetic material in tumour suppressor genes. This phenomenon, known as loss of heterozygosity is present in tumour cells but not in normal cells, and occurs in each tumour with a distinctive pattern. Thus, the finding of two tumours with a similar pattern is consistent with a diagnosis of metastasis, while a different pattern would suggest a SPT.

Incidence
Numerous studies have demonstrated that patients with HNSCC have an increased risk of SPT, both synchronous and metachronous. Synchronous SPT can be studied by cross-sectional studies of prevalence. Metachronous SPT, however, appear throughout the follow-up period with a constant rate risk, so is better to use the annual incidence[5].

Incidence of Synchronous SPT
The incidence of synchronous SPT varies greatly among different series, probably due to variations on the diagnostic strategy. Haughey et al[2]. found a higher incidence of synchronous tumours in studies which included systematic panendoscopy. Table I shows the frequency of synchronous SPT in different studies[5,7,10-14].

Incidence of Metachronous SPT
The annual risk of metachronous SPT in patients with HNSCC ranges from 1.5% 11 to 6% . This risk seems to be constant throughout the follow-up period[4,5,10,11,12]. Table 2 shows the annual incidence of metachronous SPT in different studies[3,4,10,11,15-20].

Patients that survive the SPT are at risk of the appearance of a third, fourth, or consecutive malignant tumour. In a retrospective study of 3631 patients with head and neck carcinoma, we showed that patients with SPT had an increased risk for developing subsequent tumours[21]. The annual incidence of a second tumour after a head and neck index tumour was 3.8%, rising to 5.1% for third tumours and to 7.8% for fourth tumours. Interestingly, these risks of subsequent neoplasm remained constant throughout all the follow-up period.

Table 1. Incidence of Synchronous SPT in different studies.

Author	Year	Number patients	Number SPT (%)
Jones et al.[10]	1995	3436	37 (1.1%)
Barbone et al.[11]	1996	380	28 (7.4%)
León et al.[5]	1999	1845	86 (4.7%)
Cianfriglia et al.[12]	1999	200	13 (6.5%)
Esposito et al.[13] [a]	2000	877	10 (1.1%)
Erkal et al.[14] [b]	2001	1112	77 (7.0%)
León et al.[15]	2002	2307	127 (5.5%)

[a] Only laryngeal tumours as index tumour.
[b] Only patients with an index tumours treated with radiotherapy

Risk factors.
SPT have been associated with the consumption of toxic substances such as tobacco and alcohol. The risk of SPT doubles for smokers and drinkers. Moreover, in patients with tumours related to tobacco and alcohol (oral cavity, oropharynx and larynx), 80% of SPT appear in these same areas, while for non toxic patients less than half of SPT appear at such locations[5]. In the series of Laccourreye et al.[4], only smoking showed statistical correlation with the occurrence of metachronous tumours.

In most studies the most common metachronous tumours are located in the head and neck, followed by lung tumours, tumours outside of the H&N and oesophageal tumours, in that order. This association suggests a common pathogenic pathway for these tumours. Overall, tumours of the head and neck, lung and oesophagus represents more than three quarters of the SPT. Not surprisingly, bladder tumours are the most common tumours out of this group, given their association with tobacco consumption. In some series bladder tumours reach frequencies between 5% and 14%.

Attempts have been made to identify patients with a higher susceptibility of developing SPT, but to date there

Table 2. Incidence per year of Metachronous SPT in different studies.

Author	Year	N patients	Index Tumour	% metrachronous SPT / year
Jovanovic et al[17]	1994	740	Oral C.	2.8%
Day et al [18]	1994	1090	Oral C Orophrx.	4.0%
Barbone et al.[11]	1996	380	Oral C.	
Pharynx				
Larynx	3,3%			
León et al.[5]	1999	2128	H & N	3,8%
Cianfriglia et al.[12]	1999	200	Oral C.	1.5%
Yamamoto et al.[19]	2002	1639	H & N	3.2%
Laccourreye et al[4]	2002	410	Glottis	2%
Lin et al[16]	2005	662	Larynx	2%
Lin et al[16]	2005	595	Oral C.	6%
Dikshit et al[3]	2005	876	Larynx Hypophar.	2.1%
Sjögren et al[20]	2006	359	Glottis	3%
Rennemo et al [21]	2008	2063	H & N	4%

is no easy and clear marker. A special scenario is the case of early-stage HNSCC where a high cure rate is achieved with adequate treatment. In these patients, long-term prognosis mainly depends on SPT development. In one study of our department, the risk factors for SPT in early-stage cancers were heavy alcohol use and the location of the index tumour in the oropharynx[22].

Finally, for related to human papillomavirus (HPV) the incidence of SPT is lower than for HNSCC related to tobacco and alcohol[23].

Management

Prevention

Despite multiple attempts and several clinical trials, there is no effective drug to reduce the incidence of second tumours nowadays. Tobacco and alcohol cessation is the only intervention likely to prevent SPT. In a study performed in our centre[23], the persistence in tobacco smoking and alcohol drinking showed significant influence on the appearance of a second neoplasm, and would be responsible for one-third of these tumours. In our opinion, tobacco and alcohol cessation should be a major goal after diagnosis and treatment of a HNSCC, in order to decrease the incidence of second neoplasms and to improve survival in this group of patients.

Diagnosis.

Early diagnosis of SPT is one of the major goals in the management of these patients. Synchronous tumours must be ruled out in the initial staging of the index tumour. In this context, PET-CT is becoming a standard in the evaluation of HNSCC patients. Early detection of metachronous tumours appears more controversial but it has a great interest for these patients. There are multiple strategies based on repeated screening tests and this focus on the need for post-treatment monitoring of patients with HNSCC. The most usual strategy in the follow-up consists in a periodic systematic examination of the upper aerodigestive tract and annual chest radiography for five years. Other tests such as bronchoscopy, esophagoscopy, or FDG-PET are used in a complementary manner, depending on clinical findings. The main problem is that the risk of second malignancies is constant throughout all the life of the patient, so follow-up tests should be repeated indefinitely. On the other hand, some studies have demonstrated than SPT are mainly diagnosed by their clinical signs or symptoms rather than by routine tests[24]. Furthermore, some studies have demonstrated that survival was not influenced by the diagnostic method of the SPT[25]. Adequate information and health education of the patient is of paramount importance to address prevention. The patient should be informed about the risk of SPT and the need to consult early in case of any suspect symptom.

Prognosis.

The appearance of a SPT is a cause of decreased survival and appears as the main cause of treatment failure and death in patients with HNSCC. In our experience[5,10] the survival at 15 years was 22% for patients with SPT, significantly lower than 54% for patients with a single tumour.

The location of the SPT has also prognostic influence. The SPT in the head and neck have a higher survival than those in the lung or the oesophagus. Our data[5,10] showed a 5-year survival of 58% for SPT in the head and neck location, 12% for lung tumours, and 6% for oesophageal tumours. Tumours outside the aero-digestive tract showed a 36% survival.

In the case of successive head and neck SPT, patients had a progressive decrease in survival with every new tumour[26]. The decrease in adjusted 5-year survival corresponding to every successive head and neck tumour was about 10% (Figure 1).

Treatment of SPT in Head and Neck Region

Treatment selection for SPT in the head and neck can be challenging, and should be addressed in a multidisciplinary tumour board. The choice depends not only in tumour extension and location, but also in previous treatments in the area and patient co-morbidities and sequelae.

When surgery is used for the treatment of SPT, there is some controversy about the management of the N0 neck. In a study done in our hospital, we found than the risk of occult neck nodes was low for patients with a second glottic tumour (0%), and for patients with non-glottic T1-T2 tumours who had received previous radiotherapy in the neck (5.3%). Patients with non-glottic locally advanced tumours (T3-T4) and non-glottic T1-T2 tumours who had not received previous radiotherapy in the neck had a risk of occult neck nodes of 28.1 and 33.3%[27], respectively . Therefore, elective neck dissection could be omitted only in patients with glottic tumours and in patients with an early tumour (T1-T2) who had received previous radiotherapy in the neck. In all other cases it is advisable to perform an elective neck dissection.

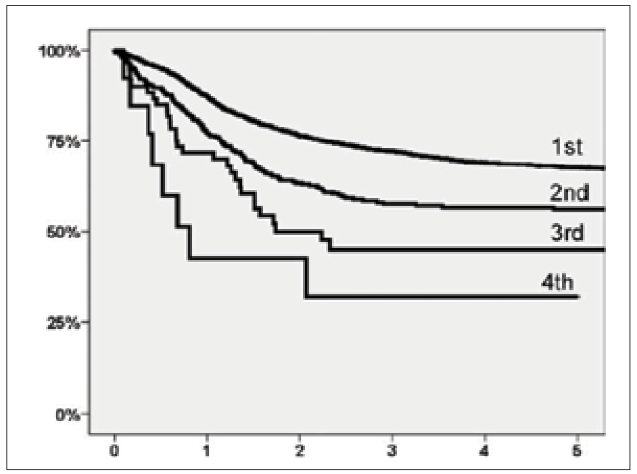

Figure 1: *Adjusted survival of HNSCC by chronology of appearance.*

In the case of successive HNSCC[28], the percentage of patients that were not considered candidates for radical treatment increase with the appearance of successive tumours, particularly in the case of the advanced-stage tumours. For patient candidates to radical treatment, surgery was increasingly used with each newly diagnosed tumour.

Conclusions

As loco-regional control for HNSCC improves, others problems appear. The metachronous SPT are one of the most important factors limiting survival of patients with HNSCC. The most important risk factor for SPT is tobacco and alcohol consumption. The patient should be informed of the risk of metachronous SPT and be aware of symptoms to allow early diagnosis. Once a SPT is controlled, the patient has a higher risk for a consecutive tumour.

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Problem solving after complications of tracheo-oesophageal valve (voice prosthesis) insertion

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Abstract
This paper focuses on the complications after tracheo-oesophageal voice prosthesis insertion based on our experience of providing a multidisciplinary national problem solving clinic between 1996 and 2015. 135 patients were seen during this time period. The identification and problem solving of voice issues after laryngectomy requires the skills of a multidisciplinary team of Head and Neck surgeons, Speech and Language Therapists, Gastroenterologists, Clinical Nurse Specialists, Dieticians, Radiologists and Radiographers. The most frequent problems seen in the clinic were difficulties related to tonicity (including spasm), and voice prosthesis issues such as leakage and candida. Stomal problems are also outlined. Each of these problems is discussed along with proposed solutions.

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Key words
Surgical voice restoration, voice prosthesis, problems

Anatomical and physiological changes after laryngectomy
Outlining the anatomical and physiological changes that occur after laryngectomy provides a context for some of the common problems that arise post surgery.

In 1979, Dr Eric Blom, a Speech Pathologist and Dr Mark Singer introduced a surgical endoscopic technique enabling the formation of a puncture between the trachea and oesophagus and the subsequent placement of a one way silicone voice prosthesis[1]. The valve allowed expired air to be shunted from the lungs into the oesophagus and then across the reconstructed segment whilst not allowing saliva and food to flow from the oesophagus to the trachea[2]. The flow of air over the mucosa of the pharyngo-

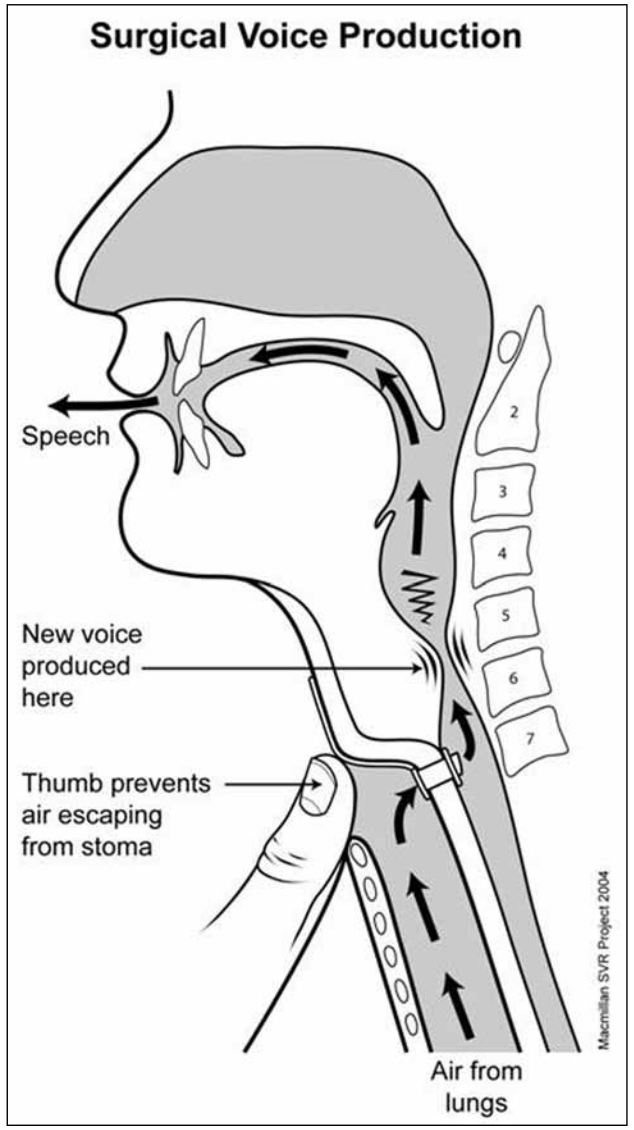

Figure 1: *Surgical Voice Restoration.*

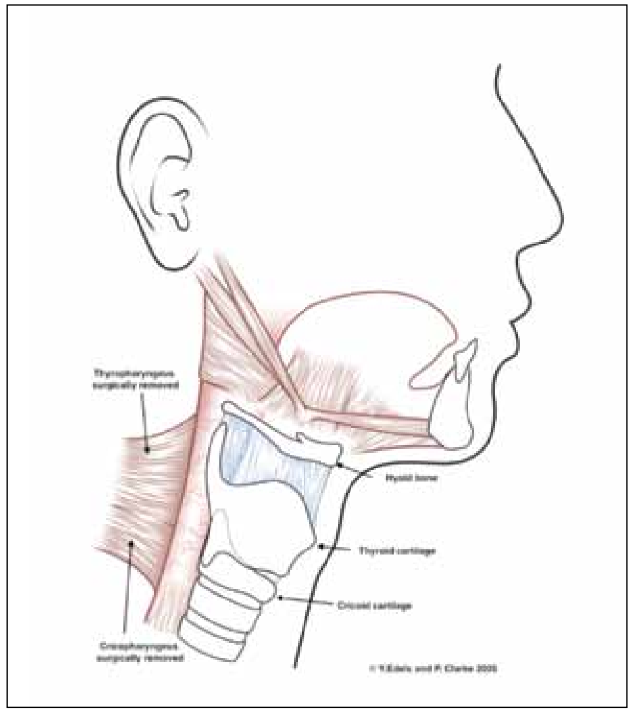

Figure 2: *Skeletonisation of the larynx.*

esophageal (PE) segment causes vibration of the mucosa and hence sound which is then articulated into speech, (figure 1).

The procedure and the Blom Singer prosthesis rapidly became the intervention of choice for voice restoration after laryngectomy and valve speech is the method of communication post laryngectomy that most closely approximates normal laryngeal voice[3].

A standard total laryngectomy usually involves an initial separation and "skeletonisation" of the larynx from the jugular and carotid vessels on either side of the neck. The suprahyoid muscles are dissected off the hyoid bone. The inferior constrictors are dissected off the laryngeal skeleton (Figure 2). These muscles are later reconstructed to form the PE segment, which allows for optimum voice and swallow function.

Once the larynx is removed, a surgical puncture can be performed between the trachea and oesophagus (TEP) to permit voice prosthesis placement. This usually takes place at the time of laryngectomy surgery (primary puncture) but may also take place at a later date (secondary puncture). A myotomy of the upper oesophageal muscles is also performed[4-7] (Figure 3). This reduces the risk of reflex muscular spasm in this area in response to the injection of air into this area through the valve. Any spasm[8-9] disrupts the movement of air across the PE

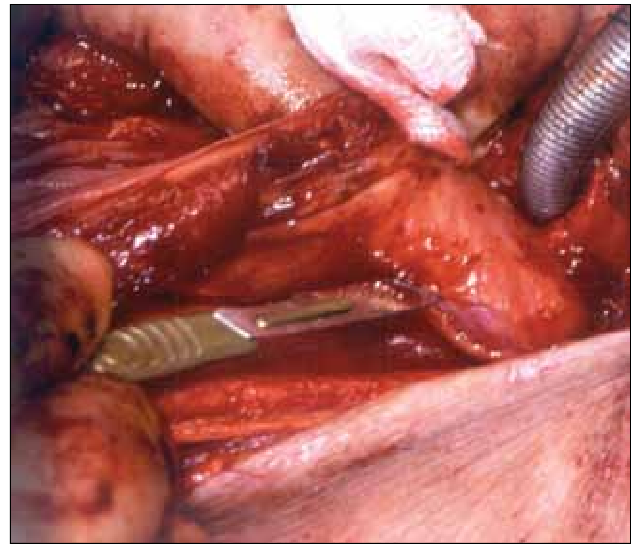
Figure 3: *caption caption*

segment and the consequent vibration and sound production. In our centre, 52% (n-70) of patients referred for problem solving between 1996 and 2015 had evidence of an incomplete myotomy observed on videofluoroscopic examination. An incomplete myotomy often directly results in complications related to voicing including spasm and voice prosthesis leakage.

After closure of the pharynx the thyropharyngeus and cricopharyngeus muscles are repaired as the initial stage of a second level of closure over the repaired pharynx which also creates a tonic muscle layer that allows apposition of the mucosa and mucosal vibration when air is passed over this area. This PE segment can be seen on videofluroscopy as a narrowing which closes (in the same way that the glottis closes) on voicing. The muscle tone of the thyropharyngeus and cricopharyngeus muscles will influence voice quality post-surgery.

Reconstruction of the suprahyoid muscles by suturing them onto the superior margin of the repaired thyropharyngeus[10] prevents the formation of a pseudodiverticulum (mucolised pouch at the base of tongue). Repair of these suprahyoid muscles, in particular the middle constrictor, probably also helps swallow efficiency. Figure 4 illustrates completed reconstruction of the pharynx after laryngectomy.

Complications related to voicing
The reconstructed segment has the potential to vibrate and produce sound and become a physiological replacement for the vocal folds. In order for vibration to occur post laryngectomy, air needs to be redirected from the trachea to the reconstructed segment to produce sound.

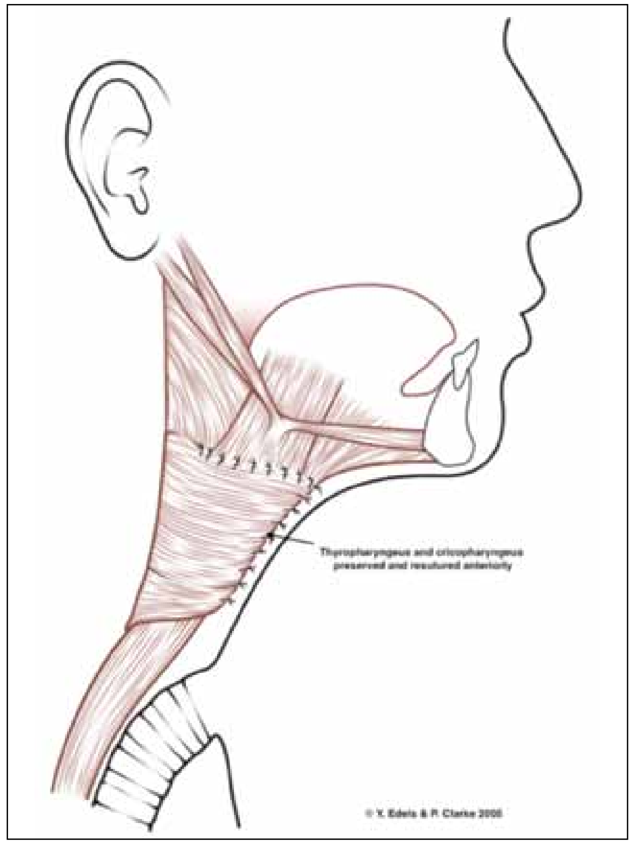

Figure 4: *Completed reconstruction of neopharynx*

Tonicity

In the early days of surgical voice restoration, it was reported that up to 12% of patients were unable to achieve tracheo-oesophageal voice[11]. Use of video fluoroscopic imaging of the reconstructed segment attributed this failure to excess tone in the muscles of the reconstructed segment. Tonicity difficulties represented the most frequent problem observed in the patients attending our problem solving clinic with an incidence of 69% (n-93).

Tonicity is the amount of pressure used to produce alaryngeal voice. Tonicity reflects the laryngectomised patient's ability to produce fluent sound of adequate intensity without effort. A tonic voice has been variously described as the ability to produce 10-15 syllables per breath and sustain /a/ for a minimum of 10 seconds at intraoesophageal pressure levels less than or equal to 20mmHg on a pressure manometer[12] or the ability to sustain /a/ for minimum 8 seconds and count 1-15 on one breath[13]. In pioneering work, a tonicity continuum was developed based on videofluoroscopic and aerodynamic findings[14].

Videofluoroscopy imaging and perceptual analysis can be used to evaluate both the PE segment and tonicity of voice quality. The continuum of tonicity is reflected in Table 1 below along with suggested behavioural and surgical interventions.

Spasm and hypertonicity are often the result of an incomplete myotomy. Both spasm and hypertonicity can be corrected by the injection of Botulinum toxin into the upper oesophageal sphincter[15-16]. The precise area of spasm can be identified during video fluoroscopy and by showing that voicing can be very significantly improved with the injection of local anaesthetic into the tissues around the neopharynx. Having confirmed the area of spasm by this method and the diagnosis of hypertonicity/spasm the surgeon can proceed to the injection of Botulinum toxin. The authors utilise 200-500 units of Dysport (Ipsen Biopharm Ltd) (equivalent to 60-100 units of Botox (Allergan)). This needs to be injected accurately into the muscle and is best undertaken under X-ray control to ensure accurate delivery. The author's results in 52 patients diagnosed with spasm between 2000 and 2015 indicated an 88% (n – 46) success rate following injection of Dysport. 6% (n-3) failed to achieve voice after Dysport injection while a further 6% (n- 3) were lost to follow up.

Table 1 Continuum of tonicity (adapted)

	Tonic	Hypotonic 8-40mmHg	Hypertonic 32-72mmHg	Spasm 38-100mmHg
% of problem solving clinic patients		22% (n-30)	16% (n-21)	31% (n-42)
Swallow	Pharynx to oesophagus dilates	Pharynx to oesophagus dilates	Mildly reduced pharynx to oesophagus dilation	Mildly reduced pharynx to oesophagus dilation
Videofluoroscopic PE segment appearance	PE segment visible, ideal tone	PE segment widely dilated with too little tone	PE segment narrowed with increased tone	PE segment long and narrow with excess tone Distension of upper oesophageal air reservoir
Voice quality	Easy, loud, minimal effort	Weak, whispery, breathy, soft	Voice tight, effortful, intermittent	No voice or difficulty sustaining voice
Behavioural treatment	None required	Digital pressure on external neck, head turn	Low pressure voice prosthesis	None
Surgical treatment	None required	None	Botox	Botox

Voice prosthesis issues

The voice prosthesis may leak through the centre of the prosthesis (central leakage) or around it (peripheral leakage) posing a risk of aspiration into the trachea. In our sample, 25% (n-34) presented with central leakage and 7% (n-10) with peripheral leakage. Leakage, if present, can usually be observed by asking the patient to drink water containing food colouring. Leakage may also be observed on radiological imaging by magnification of the area where the voice prosthesis is located. Figure 5 illustrates central voice prosthesis leakage.

Central voice prosthesis leakage

Leakage through the barrel of the prosthesis most commonly occurs when the prosthesis reaches the end of its natural lifespan as a consequence of deterioration of the valve. In some cases, the pressure generated by peristalsis whilst swallowing causes the valve to be forced open, resulting in central leakage. An increased pressure voice prosthesis may correct this problem. If leakage persists, injection of Botulinum toxin into the upper oesophageal muscles at the level of the prosthesis may help eliminate this. Sometimes, patient technique may result in the use of excess pressure to achieve stomal occlusion during voicing. Excess stomal pressure can result in contact between the oesophageal flange of the voice prosthesis and the posterior oesophageal wall. The resulting suction effect may trigger central leakage. A stenosis above the level of the valve can cause a jetting effect of liquids passing through and stenosis below the valve can cause pooling of liquids, both of which can cause leak though or peripheral to the prosthesis. These problems may require dilation of the stenosis.

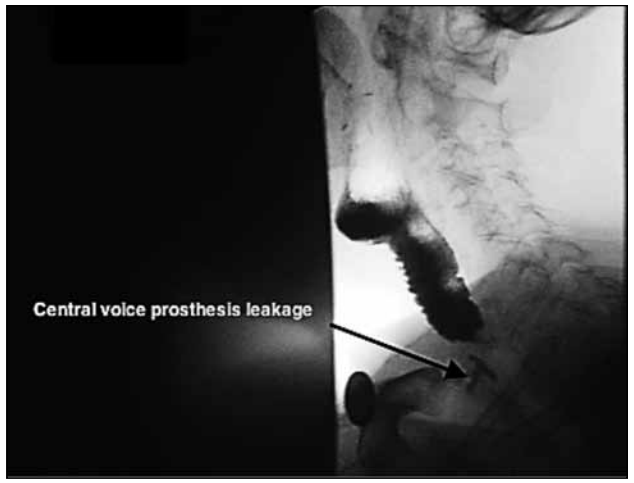

Figure 5: *Video fluoroscopic image of central voice prosthesis leakage.*

Peripheral voice prosthesis leakage/enlarging TEP

Several factors may contribute to peripheral voice prosthesis leakage. A too short voice prosthesis or one not fully through to the oesophagus may result in peripheral leakage. In this case, peripheral leakage occurs as a consequence of swallowed liquid flooding the posterior tracheo-oesophageal puncture. A prosthesis that is too long can "piston" within the tracheo-oesophageal wall and pull liquid through the fistula. Accurate sizing and placement of the voice prosthesis generally solves these issues.

Loss of elasticity of tissue in the tracheo-oesophageal or "party wall" may result in a gap between the prosthesis and the puncture causing peripheral leakage. This enlargement of the TEP may be related to use of wider diameter prostheses, particularly with short prosthesis length, advanced or metastatic disease, prior radiotherapy, preoperative nutritional status, and presence of hypopharyngeal disease[17].

The treatment of persistent peripheral leakage in the past has included placement of a larger diameter voice prosthesis[18]. However, this strategy tends to produce over dilation of the tracheo-oesophageal puncture which ultimately exacerbates peripheral leakage. Alternate strategies therefore include: the sequential placement of progressively narrower catheters, to accommodate a narrower gauge voice prosthesis or the placement of a large oesophageal flange voice prosthesis. Prophylactic strategies to prevent peripheral leakage include placement of a voice prosthesis in a gel cap to minimise tissue trauma. In some cases, anterior removal of the voice prosthesis may excessively traumatise fragile tracheo-oesophageal tissue and exacerbate already significant peripheral leakage. Patients with exdwelling voice prostheses may benefit from compromised party wall management. This technique involves cutting the anterior flange of the voice prosthesis leaving the barrel and posterior flange in situ. The new gel capped voice prosthesis can be placed in the tracheo-oesophageal puncture displacing the remnants of the previous voice prosthesis into the oesophagus and maintaining tracheo-oesophageal puncture patency.

If such methods fail to stop peripheral leakage, surgical interventions such as injection of autologous fat around the puncture, cauterisation of the tissue around the TEP or use of a purse string suture[19-20] can help. In persistent cases surgical closure of the fistula is required. Careful two layer closure may work, but frequently breaks down if the tissues have been subjected to prior radio or chemoradiotherapy. Often the oesophageal defect is larger than expected and direct closure results in stenosis so augmentation of the oesophageal lumen and the party wall is recommended with either a free radial forearm flap or pectoralis major flap if the patient has previously received radiotherapy.

Candida

Silicone voice prostheses can become covered in a biofilm containing different types of organisms with Candida Albicans having been identified as the fungus which typically causes most harm to the voice prosthesis and its surrounding tissues[21]. Candida along with other organisms, forms plaques which start to damage the voice prosthesis as they grow. These plaques may be visible as a surface discolouration on the voice prosthesis. Candida may distort any part of the voice prosthesis causing early failure of the prosthesis and leakage. In addition, candida may infiltrate local tissue causing inflammation of surrounding tissue and possible granulation. Where possible a patient can be encouraged to become proficient at self changing their voice prosthesis. Regularly rotating two prostheses allows the removed one to be sterilised to slow candida proliferation. It may also be appropriate to treat candida using the appropriate antifungal medication[22]. In some cases, cost benefit analysis will justify the use of specialised anti fungal voice prostheses. Finally there is some evidence to support the use of probiotics to minimise antifungal colonisation[21,23].

Conclusions

Problem solving of tracheo-oesophageal voice prosthesis issues benefits from a multidisciplinary team focus. An understanding of the anatomical and physiological changes post laryngectomy provides a foundation for understanding complications following tracheo oesophageal valve insertion. The most frequent complications include disorders of tonicity and voice prosthesis issues (leakage and candida). In addition, consideration of factors relating to the stoma may enhance problem solving of tracheo-oesophageal voice prosthesis complications.

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Deep neck space infections - a literature review and management algorithm

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Abstract

Deep neck space infection (DNI) is an important otolaryngology emergency. This article provides an overview of DNI and review of the relevant literature. We also present an evidence-based algorithm for managing DNI in clinical practice.

Methods

A Medline literature search was performed using the following keywords: deep neck space infection, complications, incision and drainage. Patients with peritonsillar abscess, intra-oral abscess, cellulitis of the neck, trauma and superficial skin abscess were excluded.

Results

Twelve retrospective studies were found between 1981-2014. A summary of the results follows; patient age- 2 months-96 years, commonest known cause of DNI- odontogenic infection (8/12 studies), commonest identifiable location for DNI- parapharyngeal space (6/12 studies), commonest bacteria isolated from culture- Klebsiella Pneumoniae and polymicrobial (4/12 studies), commonest form of treatment- surgical drainage (mean average 73%). Complications occurred in up to 30% of patients.

Conclusion

Patients with DNI should be managed in a systematic and safe way in order to prevent avoidable morbidity and mortality.

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Keywords

Deep, neck, infection, complications

Introduction

Deep neck space infection (DNI) is an important otolaryngology emergency. Despite the widespread use of antibiotic therapy and improved imaging techniques, DNI still has the potential to cause serious complications including airway obstruction and death[1]. The purpose of this article is to provide an overview of DNI and review the relevant literature over the past 35 years. We also present an evidence-based algorithm for managing DNI in clinical practice.

Methods

A literature search using the online Medline database was performed using the following keywords: deep neck space infection, complications, incision and drainage. The author screened One hundred and twenty one abstracts and full text versions were retrieved for 12 relevant studies carried out between 1981-2014. Patients with peritonsillar abscess, intra-oral abscess, cellulitis of the neck, trauma and superficial skin abscess were excluded. The following parameters were examined in each review article; location of study, study size, patient age, commonest deep neck space involvement, commonest source of infection, most frequent species grown from bacterial culture, significant co-morbidities, surgical management and life-threatening complications.

Overview of DNI

Anatomy

Knowledge of the anatomy of the deep neck spaces is paramount to understanding the spread of DNI. The neck is divided into 5 main fascial spaces; submandibular, parapharyngeal, retropharyngeal, prevertebral and carotid. The boundaries and contents of these spaces are illustrated in Table 1 and Figures 1a and b.

Table 1. Summary of International Retrospective Reviews for children and adults with DNI's between 1981-2012[1-12].

Year	Author (country)	Age group	No. of patients	Commonest single deep neck space	Commonest known cause	Commonest bacteria grown from culture	Significant co-morbidities	Surgery (inc. FNA)	Life threatening complications
2008-2012	Chi et al. (Taiwan)	>18 years	148	Parapharyngeal (78%)	Odontogenic (34%)	Klebsiella pneumonia (29%)	DM (22%) HIV(1%)	47%	Airway obstruction (1.3%) IJV thrombosis (2%) Septic shock (1.3%) GI bleed (2.6%)
2003-2010	Bakir et l. (Turkey)	3-69 years	173	Submandibular (26%)	Odontogenic (49%)	Polymicrobial (58%)	DM (2%)	60%	Mediastinitis (6.3%) Airway obstruction (3.4%)
2004-2009	Lee et al. (Singapore)	<16 years	131	n/a	Odontogenic + URTI	Klebsiella pneumoniae (27%)	DM (34%)	95%	Not stated
1996-2007	Eftehkarian et al. (Iran)	1-65 years	112	Submandibular	Odontogenic	Peptostreptococcus (35%)	DM (21%)	80%	Death (1.7%)
2001-2006	Daramola et al. (USA)	3 months- 86 years	106	Submandibular (48%)	Odontogenic (49%)	Streptococcus spp (44%)	DM (6%) IVDU (13%)	80%	Airway obstruction (7.5%)
1997-2003	Suehara et al. (Brazil)	2 months- 94 years	80	Submandibular (45%)	Odontogenic infection-27%	Staph. Aureus (38%)	DM (24%) IVDU(4%) HIV(3%)	98%	Death (11.2%) Airway obstruction (7.5%) Septic shock (8.8%) Mediastinitis + necrotising fasciitis (6.3%)
1999-2003	Mazita et al. (Malaysia)	2-75 years	36	Parapharyngeal (31%)	Unknown (69%)	No growth (53%)	DM (33%) Cancer (8%)	100%	Airway obstruction (5.6%) Recurrent deep neck space abscess (5.6%)
1995-2003	Boscolo-Rizzo et al. (italy)	2-96 years	177	Parapharyngeal	URTI	Coagulase –ve staphylococcus (37%)	DM (12%)	24%	Airway obstruction (10.1%) Mediastinitis (3.3%) IJV thrombosis (2.2%)
1997-2002	Huang et al. (Taiwan)	11 months-88 years	185	Parapharyngeal (38%)	Odontogenic (23%)	Streptococcus viridans (34%) and Klebsiella pneumonia (34%)	DM (30%)	73%	Death (1.6%) Airway obstruction (10.2%) IJV thrombosis (0.5%)
1996-2002	Wang et al. (Taiwan)	1-86 years	196	Parapharyngeal (67%)	URTI (17%)	Klebsiella pneumonia (33%)	DM (11%) Cancer (2)	73%	Airway obstruction (4%) Mediastinitis (2.6%) Sepsis (3%) IJV thrombosis (1%)
1986-1995	Flanary et al. (USA)	<16 years	39	Retropharyngeal (82%)	n/a	Beta haemolytic streptococcus (24%)	n/a	54%	Airway obstruction (30.7%)
1981-1998	Parhiscar et al. (USA)	2 months- 80 years	210	Parapharyngeal (43%)	Odontogenic (43%)	Streptococcus viridans (39%)	IVDU (10%) DM (16%) HIV (15%)	95%	Death (1%) Airway obstruction (5.2%) Mediastinitis (1%)

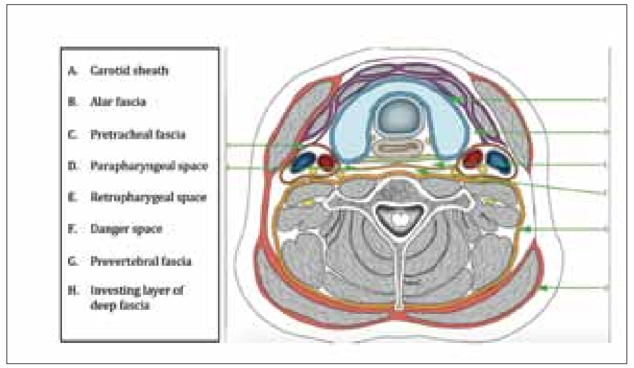

Figure 1a: *Schematic representation of the deep fascial neck spaces.*

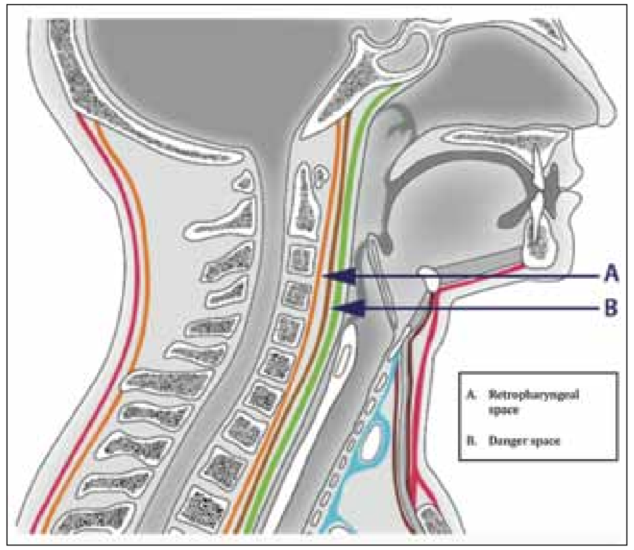

Figure 1b: *Schematic representation of retropharyngeal and danger spaces within the neck.*

In DNI, infection often spreads to the adjacent deep neck space (e.g. peritonsillar infection migrates to the parapharyngeal space), but occasionally this relationship is unclear. For instance, in odontogenic infections, the spread is dictated by the relationship of the effected tooth to the mylohyoid line (a line delineating the insertion of the mylohyoid onto the medial border of mandible). Infection that begins posterior to the 2nd molar tooth typically migrates to the submandibular space or parapharyngeal space, whereas infection arising anterior to the 2nd molar tooth spreads to the floor of mouth[13]. This is important, as infection of the floor of the mouth, (such as Ludwig's angina), has a far greater potential for airway compromise compared to that in the submandibular space. Other deep neck spaces such as the 'danger space' also carries a high chance of morbidity and mortality. The danger space is a potential space between the alar fascia (anteriorly) and prevertebral fascia (posteriorly). Infection can enter this area from the surrounding deep neck spaces and spread inferiorly into the thorax (Figure 1a and b.).

Bacteriology

The source of DNI may remain unidentified in up to 67% of patients[12,16,17] and infections are often polymicrobial[1]. Responsible organisms generally relate to the source of infection (e.g. anaerobic bacteria in odontogenic infection and streptococcus in pharyngo-tonsillar infection). In diabetic patients, Klebsiella Pneumonia tends to occur more commonly. This is thought to be secondary to diabetes-related complications such as impaired neutrophil function and complement activation and a higher prevalence of Klebsiella Pneumonia bacteria existing in the oropharynx[18]. The retrospective review series in Table 1 reflects these findings, where Klebsiella Pneumonia was more commonly isolated from bacterial cultures in Asian countries where the incidence of diabetes within the study population was relatively high.

In paediatric patients, a high prevalence of Staphylococcus Aureus has been reported. One study has shown that staphylococcal infection was present in 79% of children aged less than 1 year with DNI[19]. Another study has shown that children under 16 months with DNI were 10 times more likely to have a staphylococcal infection than non-staphylococcal infection, most of which were Methicillin-Resistant[20]. Staphylococcus Aureus is also thought to lead to a higher complication rate amongst pediatric patients with DNI and therefore is often covered with empirical antibiotics such as clindamycin+/-tazocin[20,21]. These findings seem contrary to the review data in Table 1. However, many of the studies did not describe age distribution within the study population.

Clinical presentation of DNI

Children

The most common cause of DNI in children is cervical lymphadenitis, often following an upper respiratory tract infection[13]. The retropharyngeal and parapharyngeal lymph nodes act as a drainage pathway for the upper respiratory tract. Suppuration in these nodes results in abscess formation and resultant DNI. Retropharyngeal infections are more common in younger children. A large study by Novis et al involving over 40,000 paediatric patients from the U.S 'Kids Inpatient Database' showed a significantly lower age average for retropharyngeal abscess compared to peritonsillar or parapharyngeal abscess[14]. Children typically present with rapid onset neck mass, pyrexia, dysphagia, 'hot potato' voice and dehydration. Severe trismus, torticollis or dyspnoea are 'red flag' signs for impending airway obstruction. Even in the absence of an external neck swelling, a high index of suspicion should prompt early imaging.

Adults

The commonest DNI in adults is of the parapharyngeal space (typically caused by pharyngo-tonsillar infection),

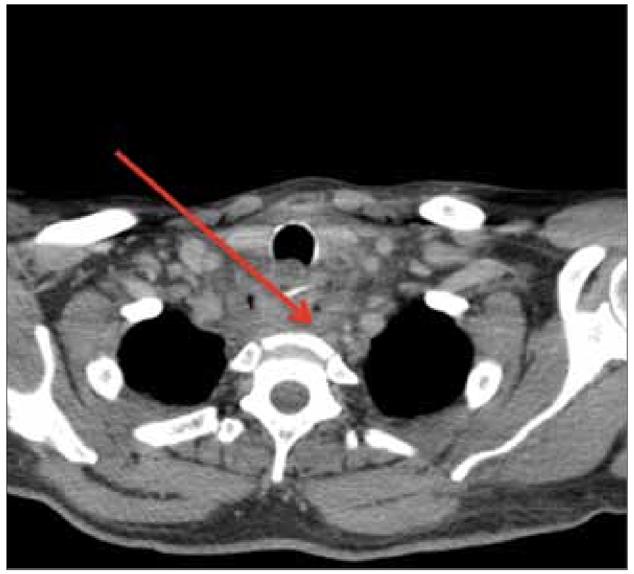

Figure 2a: *An axial view of a contrast-enhanced computer tomography at the level of the neck demonstrating a bone perforating both sides of the oesophagus with surrounding locules of gas.*

followed by submandibular space (odontogenic infection). These findings are demonstrated in Table 1[1-12]. Immuno-compromised patients (diabetes mellitus, HIV, a history of intravenous drug use), are more likely to have multiple and/or extensive deep neck space infections[15]. In adults, clinical features are similar to that in children, though often patients will present with a history of dental infection, trauma or upper respiratory tract infection.

The aim of clinical assessment in both adults and children is to establish a diagnosis, identify the source of infection and assess for airway compromise.

Imaging studies

Contrast-enhanced Computer Tomography is the modality of choice for DNI and can be up to 100% sensitive for infection[22,23]. It is important to include chest imaging up to the level of the aortic arch to assess for mediastinal spread from the retropharyngeal, danger and prevertebral spaces (Figure 1a and b). Reviewing images in a lung window is also helpful at helping to identify locules of gas within soft tissue (Figure 2a and b).

The typical features of an abscess on CT would show a rim enhancing, hypodense lesion with possible central necrosis. It is important to note that up to 25% of ring enhancing lesions are not drainable during surgery (as mentioned in the retrospective review by Flanary)[11]. The use of post contrast images can help to identify poorly enhancing soft tissue lesions (such as phlegmons), which are less amenable to surgical drainage[24]. Fluid and fat

Figure 2b: *A coronal view of a contrast-enhanced computer tomography demonstrating a bone perforating both sides of the oesophagus with surrounding locules of gas.*

stranding along the fascial plane often represent areas of cellulitis only[25]. Ultrasonography has a useful diagnostic and therapeutic role in superficial neck space infections, though often for DNI's, this technique does not provide sufficient access[21,26]. Some studies advocate the use of

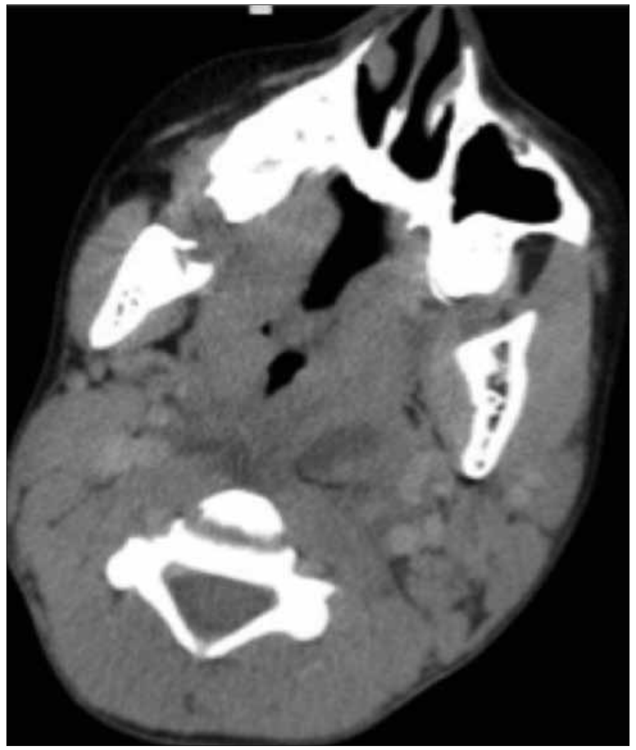

Figure 3: *An axial view of a contrast-enhanced computer tomography of the neck demonstrating a left parapharyngeal abscess extending to the contralateral neck caused by a left peritonsillar abscess in a child.*

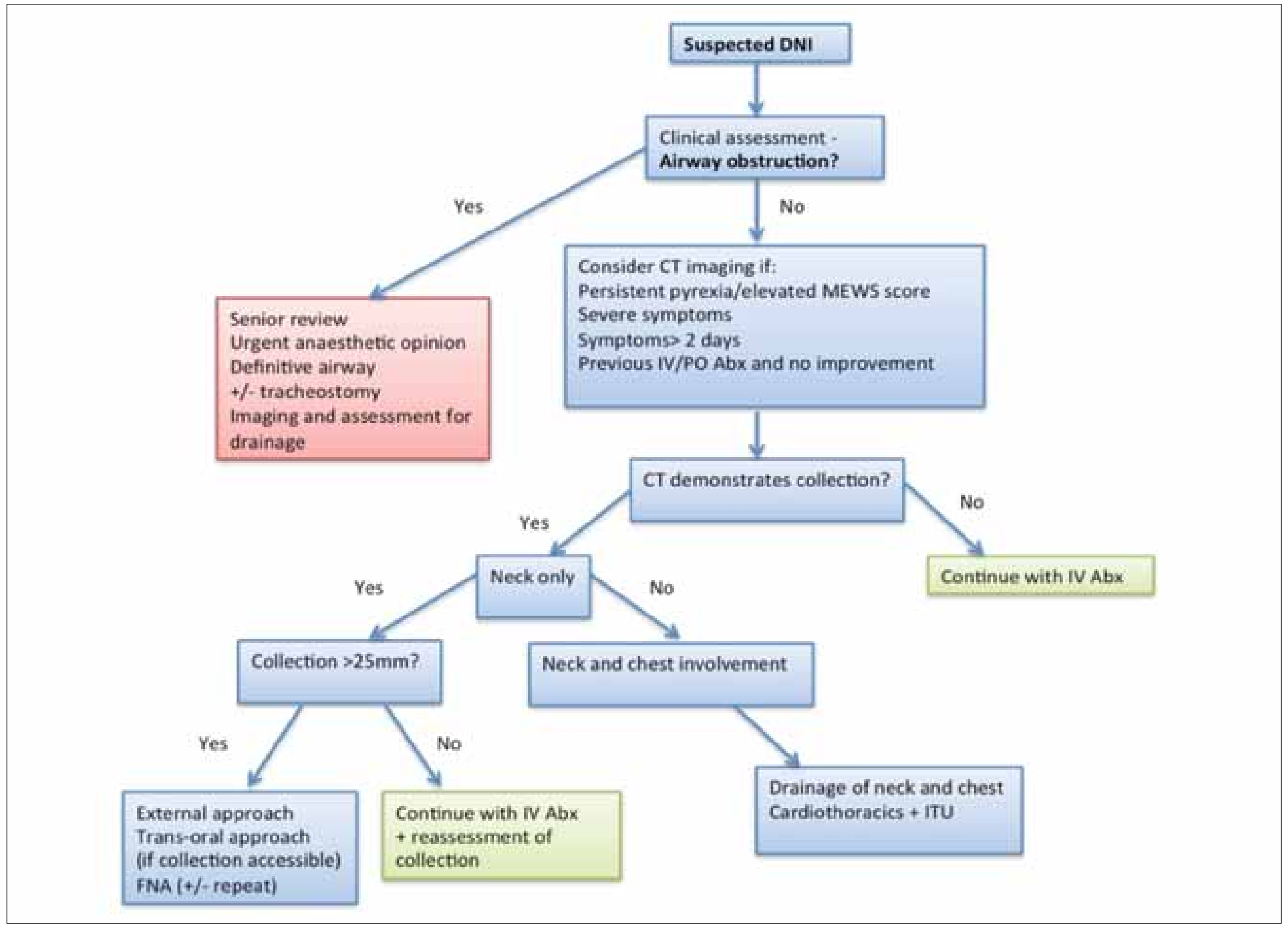

Figure 4: *Guideline for the management of DNI*

Table 2. Boundaries of the deep neck spaces

Boundaries	Submandibular space	Parapharyngeal space	Retropharyngeal space	Prevertebral space	Carotid space
Superior	Oral mucosa	Skull base	Skull base	Skull base	
Inferior	Mylohyoid + anterior belly digastric	Superior mediastinum	coccyx		
Anterior		Ptergomandibular raphe	Pharynx + oesophagus	Prevertebral fascia	SCM
Posterior	Posterior belly digastric + stylomandibular ligament	Prevertebral fascia	Alar fascia	Vertebral bodies	Prevertebral space
Medial	Hyoglossus + mylohyoid	Superior constrictor, pharyngobasilar fascia			Visceral space
Lateral	Skin, platysma, mandible	Deep lobe parotid + mandible	Carotid fascia		SCM
Contents	Sublingual gland Submandibular gland	Fat Lymph nodes Pterygoid muscles contents of carotid sheath CN IX, XI, XII Sympathetic chain	Lymph nodes	Alveolar tissue	Carotid artery IJV Ansa cervicalis CN X

radiographs to help identify the source of odontogenic infection (e.g. orthopantogram)[27] however, lateral soft tissue neck x-rays have been found to be inferior to accurately identifying other deep neck space infections (e.g. retropharyngeal and parapharyngeal) compared with CT[28] (Figure 3). Magnetic Resonance Imaging (MRI) with the use of gadolinium and fat suppression using T^1 images can be more precise than CT in detecting multiple deep neck space involvement, but it takes time and has limited use in paediatric patients[21,25].

Management

Following detailed clinical assessment (including assessment of the airway), the principals of managing DNIs are as follows:

1. Early use of broad-spectrum antibiotics (preferably guided by culture and sensitivity of organism)
2. Drainage of collection (surgical drainage versus aspiration, if required)
3. Management of complications

Antibiotics

Broad spectrum antibiotics including anaerobic cover are usually the most appropriate choice for treating DNI, however, this will also be influenced by local microbiology guidance. For instance some hospitals will recommend the use of co-amoxiclav, others may advocate the use of amoxicillin plus metronidazole.

Drainage of collection

According to our review, formal surgical incision and drainage is the commonest form of treatment, although fine needle aspiration is becoming increasingly popular and can be useful in older paediatric patients to avoid unnecessary surgery. Evidence has shown that small abscesses (defined as being <25mm) can be effectively treated with antibiotics alone and may not require surgical drainage[30]

Complications

Our review demonstrates a complication rate of up to 30% following DNI (Table 1). The highest reported complications include; upper airway obstruction (31%), mediastinitis (6.3%), internal jugular vein thrombosis (2.2%), sepsis and septic emboli (<8.8%)[1-12,31]. A rare reported complication has also included pseudoaneurysm of the internal carotid artery[32] which is though to be due to the close proximity of the parapharyngeal and retropharyngeal spaces to the carotid sheath[33] (Figure 3). According to a review by Boscolo-Rizzo the incidence of life threatening complications is significantly higher in patients who are older than 55 (p=0.04), have a white blood cell count >14’000/mm^3 (p=0.01), associated systemic disease (p<0.001) and pretracheal space or multi-space involvement (p<0.001)[8].

Management algorithm

Based on our review and our own clinical experience, we propose a pragmatic approach to the management of paediatric and adult DNI by using the pathway outlined in Figure 4.

Conclusion

The most important aspect in the management of DNI is rapid assessment of the airway and early diagnosis. Patients should be approached in a systematic and safe way in order to prevent avoidable morbidity and mortality. Anatomical knowledge of the fascial planes within the neck are imperative to understanding how infection propagates through the different neck spaces and improves clinical management.

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Anaesthesia for the difficult airway

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Abstract
A fundamental priority in patient management involves securing the airway. This may be challenging in a subset of patients, particularly in the context of patients with head and neck pathology. There are a number of techniques anaesthetists may use to manage patients with difficult airways, including face mask ventilation, the use of supraglottic airway devices, direct laryngoscopy, videolaryngoscopy, fibreoptic intubation and finally front of neck access.

Each technique has its context with which to be used, and close cooperation between surgeons and anaesthetists is required in the management of patients with difficult airways.

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Anaesthesia, airway, difficult airway

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Aims of anaesthesia
The traditional aims of anaesthesia are the triad of unconsciousness, inhibition of pain and muscle relaxation. The process of achieving these parameters renders patient airways susceptible to a loss of protective reflexes, a loss of patency and a requirement to supplement ventilation.

Securing the airway is the ultimate goal and there are countless techniques that can be used to achieve this. The choice of technique must be guided by a combination of patient anatomy and pathology, acuity, surgical requirements and anaesthetic skills.

Definition of a difficult airway
Ventilation can be challenging in a subgroup of patients with difficult airways. To date, there is no standard definition of a "difficult airway" in the literature. However, the American Society of Anesthesiologists attempt to define a difficult airway as one where a 'conventionally trained anaesthetist experiences difficulty with facemask ventilation of the upper airway, difficulty with tracheal intubation, or both[1].' This definition however does not specify the underlying reasons behind the difficult airway, which may include:

- Difficulty or failure to achieve facemask or supraglottic airway device (SAD) ventilation due to poor seal, excessive gas leak, high resistance to ventilation or difficulty in maintaining a patent airway
- Difficulty or failure to place a SAD
- Difficulty or failure to visualise the glottic inlet with laryngoscopy
- Difficulty or failure to pass an endotracheal tube (ETT)
- Difficulty or failure to perform front of neck access (FONA)

The problems of a difficult airway
The incidence of airway complications depends on context and severity. In the general population, the incidence of minor complications is as high as every 40 patients[2], while major complications, including brain damage and death, occurs in 1 in 21,600[3]. Although the incidence of major complications appears relatively low, the severity of outcome is significant. The 4th National Audit Project of the Royal College of Anaesthetists and Difficult Airway Society (NAP[4]) prospectively assessed all major airway complications from every UK hospital over a 12-month period[3]. It found that patients with head and neck pathology accounted for 40% of all major airway complications, with a higher frequency of brain damage, death, requirement for emergency surgical airways and poorer airway management than other groups[3]. Because difficult airway is more predictable in patients with head an neck pathology, plans must be in place and agreed upon between anaesthetist and surgeon to ensure surgical access as well as safe, continual oxygenation and anaesthesia.

Solutions to the difficult airway
There are many techniques, routes and approaches to securing the airway. One of the key deciding factors involves understanding the anatomical basis for potential difficulties encountered.

Site and cause of pathology
Disorders affecting airway management may be classified as intraluminal, extraluminal or a combination of both. These can then be subclassified according to the site of compromise, be it supraglottic, glottic or subglottic. Pathology to consider is seen in table 1, which is not an exhaustive list.

Table 1. Site of pathology leading to difficult airway.

	Intraluminal	Extraluminal
Supraglottic	Abscesses	Rhinophyma
	Quinsy	Trismus
	Ludwig's angina	Reduced mouth opening
	Diphtheria	Reduced neck movement
	Angioedema	Retropharyngeal abscesses
	Neoplasm	
	Congenital malformations	
	Airway trauma	
Glottic	Epiglottitis	Haematoma
	Neoplasm	Tumours
	Cricoarytenoid disorder	Surgical emphysema
		Trauma
Subglottic	Subglottic stenosis	Thyroid enlargement
	Tracheal lesions	Radiotherapeutic changes

Airway Management
The techniques available at the anaesthetist's disposal range from non-invasive to invasive, each with its place in the management of the difficult airway.

Facemask ventilation
Facemask ventilation (FMV) is a crucial skill for all anaesthetists and plays a fundamental role in commonly used airway management algorithms[1,4,5]. Despite the simplicity of the technique, knowledge of patient anatomy, equipment and technical skills are necessary. FMV is indicated in any scenario where spontaneous ventilation has ceased, is insufficient or alternative ventilation strategies have failed. There are very few contraindications, but difficulties may be encountered in patients with abnormal head and neck anatomy, beards, high body mass indices, poor jaw protrusion, a history of snoring and those with known sleep apnoea. The incidence of difficult FMV is 1.4%, and impossible FMV is 0.16%[6]. In these circumstances, a two-person technique, suction or adjuncts such as oropharyngeal or nasopharyngeal airways may be of use[7], but ultimately alternative airway approaches are necessary to maintain patient oxygenation.

Supraglottic airways devices
SADs play a pivotal role in both elective and emergency airway management. The classic laryngeal mask airway (LMA) was the first introduced in 1988, and modifications of this have progressively led to the features seen in SADs in use today. This generally includes a ventilating 'tube' section and a supraglottic 'mask' section. Second and third generation devices also include gastric suction tubes, bite blocks, and can tolerate higher ventilator pressures.

Due to the widespread use of SADs in the elective setting, anaesthetists are familiar with their insertion, and their use is firmly established in adult difficult airway guidelines world-wide[1,4]. The role of SADs in the paediatric difficult airway population is also increasingly being recognised[8].

The number of SADs available is increasing, and there is as yet a limited evidence base for choosing any individual device[9]. More important is the understanding of the role SADs play in the management of patients with difficult airways. This includes:

1. Ventilation rescue in failed FMV, failed intubation or both
2. Ventilation rescue in out-of-hospital settings
3. Conduit to achieve blind, assisted or fibreoptic-guided tracheal intubation in either elective or emergency settings[3].

Direct Laryngoscopy
Direct laryngoscopy has been used as a technique for orotracheal intubation for more than 100 years[10]. Laryngoscopes have been modified and improved upon since, and insertion adjuncts such as gum-elastic bougies (GEB) have been developed. However, the overarching aim remains: to obtain a direct view of the glottic inlet allowing insertion of an endotracheal tube (ETT).

Patients are placed in the "sniffing" position, with cervical flexion and atlanto-occipital extension[11]. This causes alignment of the pharyngeal, laryngeal and oral axes allowing glottic visualisation. A laryngoscope blade attached to a handle with a light source is then inserted in the right side of the mouth to sweep the tongue to the left and the blade advanced along the tongue base until the epiglottis is visualised, at which point the tip of the blade is rested within the vallecula. A 45-degree force up and away from the laryngoscopist then lifts the epiglottis forward to reveal the glottis. A tracheal tube can then be directed to rest within the trachea through the inlet, with or without the aid of a GEB or an introducing stylet.

Patients with difficult airways may be challenging to intubate with direct laryngoscopy. Intraluminal pathology may either make it difficult or impossible to obtain a view of the glottic inlet, or to insert an ETT. Extraluminal pathology tends to interfere with the ability to align the pharyngeal, laryngeal and oral axes, and therefore making it challenging to get an adequate glottic view.

If difficulties in intubation with direct laryngoscopy are encountered, three modifications have been shown to be useful:

1. Optimising positioning – attempts to align axes by changing patient positioning or manipulating the position of axes manually
2. Alternative laryngoscopes – a multitude of blades and handles could be used
3. Use of an adjunct such as a GEB

If these techniques fail, direct laryngoscopy is likely to be unsuccessful and alternative ventilation strategies must be pursued.

Videolaryngoscopy

To overcome the shortcomings of direct laryngoscopy in patients with difficult airway, cameras have been placed in laryngoscopes to produce videolaryngoscopes (VLs). VLs bypass the need to align oral, pharyngeal and laryngeal axes, thereby providing a wide field of view and allowing operators to "look around corners" with reduced head and neck manipulation[12]. These indirect views can also be displayed as video images live on screen, allowing the co-ordinated management with assistants. VLs have been shown to have a rapid learning curve for both experienced laryngoscopists and novices[13].

There are now a multitude of marketed VLs, each with its own blade design, geometry and technique for tube insertion. However, they can broadly be classified into one of three types:

1. Macintosh blade VLs

The Macintosh blade is the standard blade used for direct laryngoscopy. VLs may be designed with this blade and an embedded camera at the tip. These VLs have the advantage of being familiar to anaesthetists, allow both direct and video-assisted glottic views, and require minimal modification to intubating technique. Examples include the Storz® C-MAC™ and the A.P. Advance™.

2. Angulated blade VLs

VLs such as the GlideScope® have blades with sharp curves allowing improved glottic views with minimal head and neck manipulation. However, the degree of anterior angulation generally requires tracheal tubes to be inserted on an angled stylet, and intubation with modified techniques compared to Macintosh blade VLs.

3. Channelled VLs

These VLs have an anatomical curvature to their blades, but allow loading of an ETT into a channel that guides the tube into the glottis. When the desired glottic view is obtained, an ETT can be advanced through the guide channel then unloaded. This design overcomes the challenge of optimised view but difficulty in successfully intubating. These types of VL, including the Airtraq® and the KingVision®, require easily learned skills and have a high success rate.

Videolaryngoscopy has become a vital tool in the management of difficult airways, and the Difficult Airway Society are due to adopt the use of VL in their initial plan for predicted difficult airway. More recently, the use of VL for awake intubations has emerged, as it is an easily learned technique with good success rates if airway topicalisation and appropriate sedation are applied[14]. However, some VLs are more suitable to this technique, and there is a significant subset of patients in which this approach will not be appropriate.

Fibreoptic Intubation

It has been well established that the gold standard for managing the anticipated difficult airway is with an awake fibreoptic intubation (AFOI). However this is not always the most suitable technique, for example in children, uncooperative adults or bleeding airways. Fibreoptic intubation can also be done in the anaesthetised patient

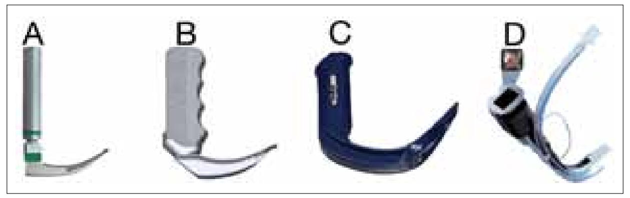

Figure 1: *Examples of different laryngoscope shape and design.* **A**. *Machintosh blade direct laryngoscope.*
B. *Macintosh blade Storz® C-MAC™ videolaryngoscope.*
C. *Angulated blade GlideScope® videolaryngoscope.*
D. *Channeled Airtraq® videolaryngoscope.*

(i.e. asleep), although it is more suited in the awake patient, as with the correct technique it allows safe intubation of the patient with minimal discomfort[15].

NAP4 recommends that every anaesthetic department should be able to offer an AFOI when indicated and that the awake option is preferred when considering fibreoptic intubation[3].

AFOI allows the safe intubation of a spontaneously breathing patient using either the nasal or oral route. Appropriate equipment includes a fibrescope, oxygenation devices, LA topicalisation devices and a variety of endotracheal tubes whilst continuously monitoring the patient. The procedure can be divided into three main stages: 1) patient preparation; 2) fibreoscopy; 3) intubation.

Patient preparation. The procedure should be discussed with the patient beforehand to establish a rapport and ensure patient co-operation. Supplemental oxygen should be established from the start of the process and appropriate conscious sedation established before LA topicalisation is attempted. It is important to adequately topicalise the nasopharynx (with LA & suitable vasoconstrictor) and oropharynx to allow for comfortable fibreoscopy and passage of the endotracheal tube.

Fibreoscopy. This involves fibreoptic navigation via oral or nasal routes to the trachea. The nasal route for fibreoscopy is usually preferred to oral, as it is better tolerated by the patient and generally allows for easier passage to the trachea.

Intubation. Once in the trachea with the fibreoptic scope, the appropriately selected and pre-loaded endotracheal should be railroaded into the trachea and its position confirmed before induction of anaesthesia.

Anaesthesia is only induced once the correct placement of the endotracheal tube has been confirmed. AFOI techniques require specialist training, skill and equipment. If the decision has been made to intubate a patient using an AFOI technique, the whole team, including theatre staff, surgeons and anaesthetic staff should be made aware.

Front of neck access

Access to the trachea may at times be impossible to achieve via the oral or nasal routes. In the most dramatic circumstances, this occurs in a "can't intubate, can't ventilate" (CICV) scenario, where a patient is not ventilatable with a facemask or SAD and intubation is impossible with direct or videolaryngoscopy. This is thought to occur with a frequency of one every 50,000 anaesthetics[3]. In more controlled scenarios, this can present as a patient who is awake and spontaneously ventilating but oral or nasal intubation is predicted to be unachievable.

There are a number of options for achieving front of neck access, as can be seen in figure 2.

Anaesthetists have favoured the cannula approach for many years due to the familiarity with the equipment and technical skills required. Narrow bore cannulae have internal diameters of ≤2 mm, are inserted through the cricothyroid membrane, and can only be used for ventilation using a jet ventilator. They are a holding measure as they are prone to kink or become misplaced, and have a 63% failure rate when placed by anaesthetists in the emergency setting. Wide bore cannulae have wider internal diameters of ≥ 4 mm and allow ventilation using conventional breathing systems. They have a lower failure rate of 43% but require specific skills and equipment.

Surgical front of neck access has a consistently higher success rate, and each approach has a place in different clinical scenarios. Surgical cricothyroidotomy is generally performed in an emergency CICV scenario, although the technique varies and there is disparity in the literature as to which is the most effective method to access the trachea. The procedure generally involves an incision, either transverse or vertical, a scalpel puncture of the cricothyroid membrane, and insertion of a 6.0 mm tracheal tube. This approach has gained particular popularity in the pre-hospital setting, where it has been consistently shown to be successful[16]. Translation to non-traumatic CICV patients is likely to be less successful, but has better outcomes than the cannula approach, and the success rate is superior when performed by surgeons as compared to anaesthetists.

Percutaneous tracheostomy can also be performed in the emergency setting[17], but requires more equipment and time to perform successfully. It generally relies on a Seldinger technique to insert a guidewire between tracheal cartilages and progressively dilate the path allowing insertion of a tracheostomy tube or ETT. As well as in emergent scenarios, this procedure is commonly performed in the critical care setting for patients requiring prolonged ventilation[18]. More recently, ultrasound guidance has been used to improve safety of this percutaneous procedure[19], which is particularly relevant to patients with difficult airway anatomy.

Finally, surgical tracheostomy is a procedure most familiar to head and neck surgeons, and is uncommonly applied by anaesthetic or critical care medicine specialists. When performed awake, local anaesthetic and vasoconstrictor

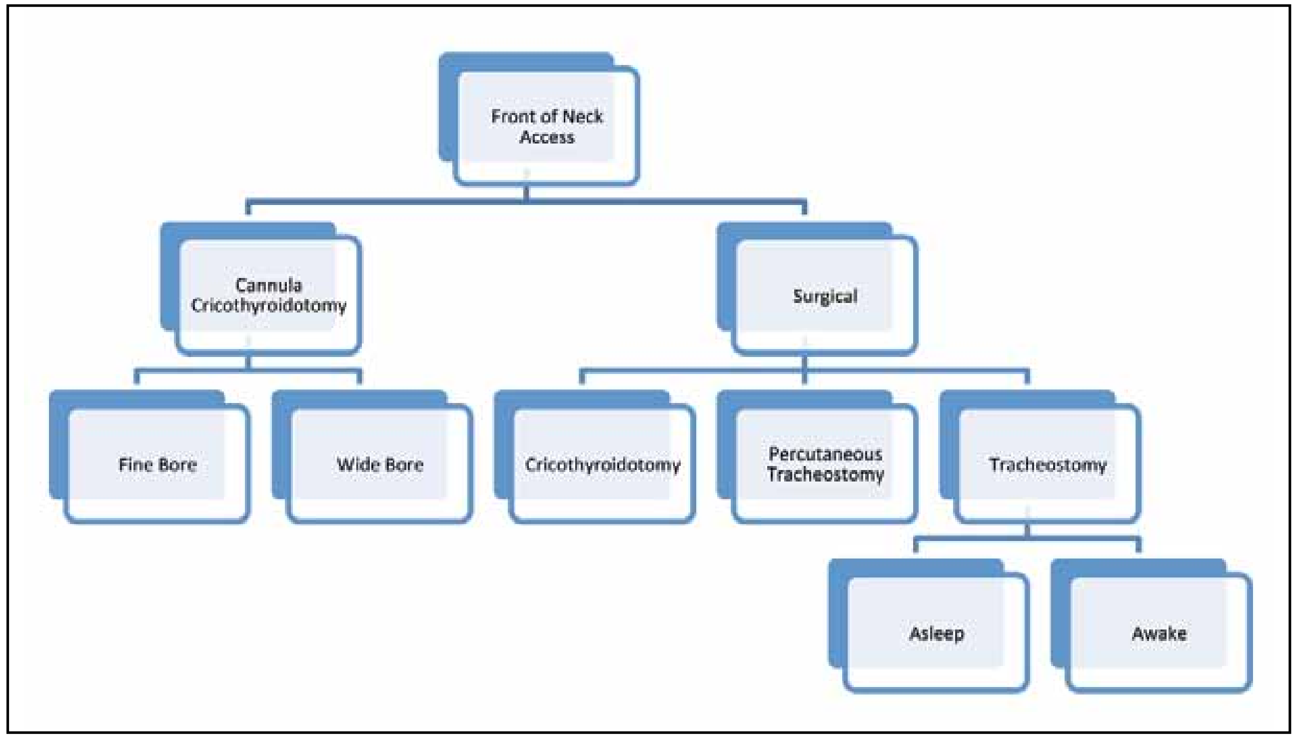

Figure 2: *Options for achieving front of neck access.*

infiltration of the front of the neck is usually accompanied by minimal sedation to allow tolerance of the procedure. It generally is less time-critical than other techniques[20]. A frequent indication for tracheostomy is for critically ill patients requiring prolonged ventilation, however it is an alternative technique in the CICV scenario.

The decision of which technique to chose in a CICV patient has been the subject of much discussion and debate. The Difficult Airway Society (UK) is expected to advocate the primary utilisation of "scalpel front of neck access," although numerous algorithms have been adopted[21]. The ultimate strategy requires technical proficiency and rapid decision making in order to secure the airway; the precise approach is likely to remain a matter of debate for some time.

Conclusion

Securing the airway is a fundamental and primary priority in the management of any patient, be they medical, surgical or otherwise. Patients with head and neck pathology in particular are at greatest risk of having difficult airways and thus airway complications[3]. It follows that close communication between surgeons and anaesthetists is vital in the management of the shared airway, be they difficult or otherwise. The anaesthetic management of patients with difficult airway is 'context-sensitive'[22], and there are a wide range of techniques and tools in the anaesthetist's arsenal. The choice must be guided by underlying patient pathology anatomy, surgical technique, and ultimately the skills and experience of the anaesthetist.

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Management of recurrent benign salivary gland tumours

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ABSTRACT

Recurrent pleomorphic adenoma (RPA) is the most common recurrent benign tumour of the salivary glands. Treatment remains a challenge with high likelihood of recurrence. We performed a review of the literature to discuss current developments in the management of RPA of the salivary glands. An Ovid Medline keyword search was performed to review the literature. Results were limited to the English language. Consistent findings are that enucleation is not indicated for the treatment of RPA. Multinodular recurrence is associated with further recurrences as some nodules may completely be void of capsule24. Thus, adhering to a wide disease free margin is essential in minimising recurrence. Facial nerve monitoring (FNM) may reduce operating time and time to recovery but does not affect the overall morbidity of facial nerve dysfunction. There is conflicting evidence regarding the benefit and risks of adjuvant post-operative radiotherapy (ART).

Conclusion RPA presents a surgical challenge with potential impacts on the patient's quality of life. We advocate the need for a more comprehensive operation than initial surgery when faced with RPA in attempt to reduce risk of further recurrence. We suggest identifying the FN away from previous surgery and scar tissue, along with routine use of a facial nerve monitor. ART is recommended for second recurrence, to be considered for multifocal disease and where further surgery is likely to impact on the function of the facial nerve. The ultimate treatment is assessed on a case by case basis.

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Key words

Recurrent Pleomorphic Adenoma, Management, Salivary Gland

INTRODUCTION

There are a variety of benign tumours that may arise within the salivary glands. The most common type is pleomorphic adenoma (PA) with the parotid gland being the most common site (80%), followed by submandibular, sublingual and minor salivary glands (7% of cases)[1-2].

Standard treatment of PA is complete surgical excision with a safe margin of normal tissue[3]. There are a number of surgical options that have been described for surgical excision of PA ranging from enucleation to total parotidectomy. However the most common approaches are those of limited parotidectomy with identification of the facial nerve described by O'Brien et al, extracapsular dissection without identification of the facial nerve described by McGurk et al and superficial parotidectomy which involves removal of the entire gland superficial to facial nerve[4,5].

Comparing reported recurrence rates in the literature is difficult as many surgeons do not routinely follow up patients with PA and recurrence may occur as late as 45 years after the initial surgery[6]. However using standard approaches such as limited or superficial parotidectomy, recurrence rates are in the order of 1-2%[7-13]. Enucleation is associated with the highest probability of recurrence, up to 43% in some series[14].

The reasons for recurrence has been attributed to a number of factors: The surrounding capsule of the tumour can vary in thickness and in some areas be completely[15-18]; The variable thickness of tumour capsules increases the risk of tumour rupture from excessive retraction which can seed tumour into multiple sites.

Pseudopodia arising from the tumour mass can perforate the capsule and extend into surrounding tissue not appreciated macroscopically[18]. In our institution, we have seen rare cases of multifocal benign pleomorphic adenoma with small satellite lesions clearly distinct from the main tumour specimen and not related to pseudopodia.

The treatment of recurrent PA (RPA) remains a major surgical challenge due to the high likelihood of multifocality, the risk of facial nerve injury and the possible requirement of reconstruction. The purpose of this study is to perform a review of the literature to discuss current developments in the management of RPA of the salivary glands.

An Ovid Medline keyword search was performed using the search terms "pleomorphic adenoma" OR "benign mixed tumour" AND "recur*". This was combined with the "AND" tool using each search term separately. Search terms included "multi-focal" OR "multifocal"; "surg*" OR "enucleation" OR "parotidectomy" OR "local excision"; "facial nerve"; "radiation"; "chemotherapy"; "hard palate"; "submandibular"; "secondary malignancy" OR "ex-recur*".Results were limited to the English language. Each title and abstract was read and included only when pertaining to recurrent pleomorphic adenomas. Reference lists were reviewed to retrieve papers not included in the initial search.

DISCUSSION

Histopathological features

PA's contain elements of epithelial and myoepithelial cells mixed with stromal cells that may be myxoid, mucoid or chondroid enclosed in an incomplete capsule[7,19,20]. Consideration of the histopathological characteristics is essential to prevent incomplete excision or breach of the tumour capsule[20]. Hypocellular tumours have a greater proportion of chondromyxoid stroma and a higher rate of incomplete encapsulation[21]. This type of tumour is softer and more friable, making it more susceptible to tumour rupture, spillage and multifocal recurrence[12,22].

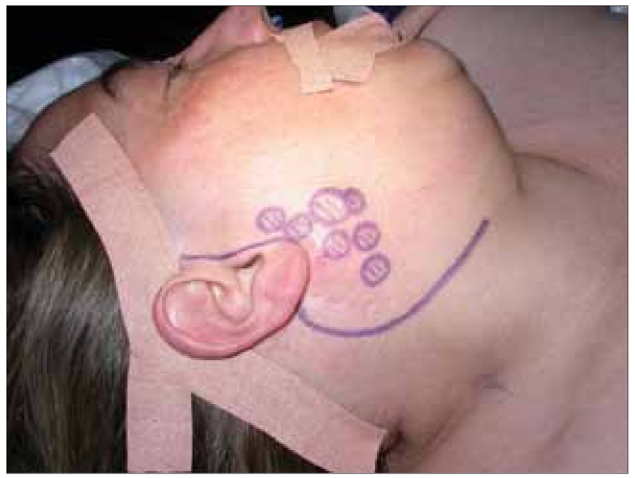

Figure 1: *Incision and areas of recurrent pleomorphic adenoma shown.*

Epidemiology and Incidence

A literature review of 1183 PA cases reported by Witt et al identified a higher incidence of recurrence after extracapsular dissection (ECD) compared to SP with recurrence rates of 3% and 0.3% respectively[23]. In contrast Foresta et al found a lower recurrence rate with ECD when compared to SP (1.4% vs 3%) and lower complications[20]. Recurrence rates following surgery for PA depend on the length of follow up, increasing from 14% at 5 years to 57% at 20 years[24]. PAs typical recur 7 - 10 years after initial surgery but can recur as early as 6 months[7,25-27].

Multi-focal vs uni-focal recurrence

RPA is associated with a high incidence of multi-focal recurrence due to tumour rupture, seeding tumour cells into the parotidectomy bed (see Figure 1). The numbers of nodules can be as high as 266 with an average number of 26, however this number depends on the mode of detection[28]. Makeieff et al reported multifocality in 39% using physical examination, 44% using MRI and 63% on pathological examination following excision in 62 patients presenting with RPA[29]. Other series report multiple foci of PA in 33 - 98%1[0,14,24,30-33].

Evaluation

Ultrasound, CT and MRI are widely utilised to asses RPA[34]. MRI is considered superior because PAs typically have high signal intensity on T^2 weighted images. However all modalities are unreliable in detecting tumour foci less than 1mm in diameter which is common in multifocal RPA[10,28,35]. MRI is useful to delineate tumour from surrounding tissue and can help distinguish malignant from benign disease on the basis of infiltrative margins and low signal intensity on T^2 weighting[36-38]. This is particularly relevant in patients with who underwent surgery more than 10 years prior as an extended length of time has the potential for malignant transformation[30].

As expected, multifocal recurrence is associated with higher rates of further recurrences[24]. To prevent such recurrence, a variety of surgical approaches have been utilised.

Surgical Intervention of RPA

Although a strong correlation exists between initial surgical technique and recurrence, standard parotidectomy approaches are often not feasible for RPA[28,39]. Recurrent nodules of tumour can occur within scar tissue, adipose tissue and remnants of the deep lobe of parotid in up to 81% of cases[10,40]. A number of factors need to be considered when approaching patients with RPA including the type of previous surgery, age of the patient, number of prior operations, location and number of tumour foci.

Age in particular is a factor that must be considered when managing RPA. Malard et al found significantly earlier recurrence in patients under the age of 25 (5.1 years ± 2.8 years) compared to those 25 years and older (15.5 years ± 10.6 years)[41]. Although young age cannot be confirmed as a prognostic factor for recurrence, it is considered to be a significant predictor of recurrence. Thus, the decision for more aggressive surgical treatment may be necessary to minimise recurrence in younger patients.

Previous Surgery

The surgical approach to treat RPA will depend on the initial surgical procedure. When enucleation has been the initial surgical intervention, most authors advocate a standard superficial parotidectomy, as the facial nerve trunk will not have been dissected. In this situation finding and dissecting the nerve should not be difficult and the deep lobe of parotid is unlikely to be contaminated by tumour cells.

In cases where the entire superficial lobe has been removed and there is multifocal recurrence, a long and difficult operation should be anticipated. Use of a nerve integrity monitor and magnification with loupes or an operating microscope can be very useful as distinguishing between branches of the facial nerve and scar tissue may be very difficult. Stennert et al in their review of 31 patients with RPA found extensive scar tissue and multifocal tumour in all cases[10]. Their recommendation was for total parotidectomy with removal of surrounding fat tissue and previous scar tissue. However, in practice, this can be very difficult and en-bloc removal of all tumour foci is unlikely to be possible. Vucak's review of 81 RPA cases found that SP and TP together had a significantly better outcome than enucleation and support the general consensus of either SP or TP[3,5,24,25,41-44]. In cases where the initial surgery was either a TP or a complete SP, surgical intervention of RPA is generally limited to local resection. This is the only option if the aim is to preserve a functional facial nerve[24,25,45]. Regardless of the initial operation, RPA must be approached on an individual basis with subsequent surgery determined by a number of factors[27,30].

Success rates following redo parotid surgery depend on the initial surgical technique. Phillips et al reviewed 126 RPA cases with previous local excision and found no further recurrences with a median follow up of 15 years 31. However, Wittekindt's review of 108 RPA patients with median follow up of 19 years found regardless of surgical approach, microscopic residual disease was unavoidable and long term recurrence occurred in 75% of patients[28].

Location

With respect to parapharyngeal space RPA, complete excision including the oropharyngeal mucosa to obtain a disease free margin is the primary objective, although this is often difficult to obtain[40]. In certain circumstances, osteotomies may be necessary to gain adequate access to the tumour in combination with either a transcervical or transoral approach[46-49].

Wide local excision via the transoral approach is recommended for RPA involving the palate with removal of associated mucosa and involved periosteum or bone[50-55]. In cases where palatal reconstruction is necessary, functional considerations to minimise impact on speech, swallowing and anterior facial projection are necessary[56].

Defects affecting only the mucosa of the hard palate can be left to granulate or local flaps used to close the defect. However, bony defects of the hard palate and/or upper alveolar ridge defects will require either an obturator or free tissue transfer to provide separation of the nasal and oral cavities and, if applicable, restore facial cosmesis[56].

Risk to the Facial Nerve

The risk of facial nerve (FN) damage increases substantially with each subsequent revision procedure for RPA[40]. The incidence of temporary facial nerve paresis ranges from 90 - 100% and 11 - 40% for permanent paresis[24,28,30,31,33,40,57]. Factors associated with this increased risk include multiple tumours, more than one operation, deep parotid lobe and parapharyngeal RPA[31]. Furthermore, ECD is twice as likely to result in permanent facial nerve damage for RPA when compared to SP[12].

Facial nerve monitoring (FNM) has been increasingly used in an attempt to protect the FN. It is especially useful when marked fibrosis surrounding the nerve is present from previous surgery. Early detection of the facial nerve and maintaining surrounding fibrotic tissue limits perineurium exposure, mechanical manipulation and attempts to avoid devascularisation[40]. Although FNM does not appear to affect the rate of facial paralysis, it does result in less severe FN palsies, faster recovery of paralysis and shorter operative time[29,57]. As identification of the nerve may be difficult when engrossed by scar tissue, both trans-mastoid and retrograde approaches can be effective to depict nerve in scar-free areas[40,59].

In cases where multiple recurrences have occurred with infiltration of facial nerve branches, the surgeon is ultimately faced with FN sacrifice with immediate microsurgical grafting[24-26,28,33,34,44,60-62]. We advocate finding the facial nerve in a previously undissected area using either a retrograde or transmastoid approach (see Figure 2 and Figure 3). We also routinely use a facial nerve monitor.

Use of adjuvant radiotherapy

The incidence of second recurrence after surgery for RPA is 35%[63]. Adjuvant radiotherapy (ART) has been utilised to reduce the rate of further recurrences. There are no specific criteria for the use of RT, however a number of papers have suggested that ART may be of benefit[24].

Three retrospective papers have compared patients undergoing surgery alone and those receiving ART. Liu et al reviewed 33 patients treated for RPA with a median of 12.5 years follow up[64]. They found 82% had local control with ART compared to just 6% with surgery alone.

Renehans' review of 114 patients treated for first recurrence of RPA revealed 92% local control with ART versus 76% with minimum 4yrs follow up[60]. They also showed lower secondary recurrence with ART compared with surgery alone (8% versus 24% respectively). This was more pronounced when recurrence was multinodular (4% versus 43%). Although not statistically significant, Carew et al showed 100% local control with ART versus 76% receiving surgery with mean 7 years follow up[26].

Other retrospective papers reviewing ART without comparison groups showed recurrence ranging from 76 - 96%[65-69]. Chen et al recommend ART when multinodular disease and positive microscopic margins are present[68]. Wallace et al in a more recent review add that ART may also be beneficial in patients with gross residual disease[69]. Furthermore, radiation does not result in clinical deterioration of FN function during or post RT making it a viable option when surgical approach would involve FN damage[67].

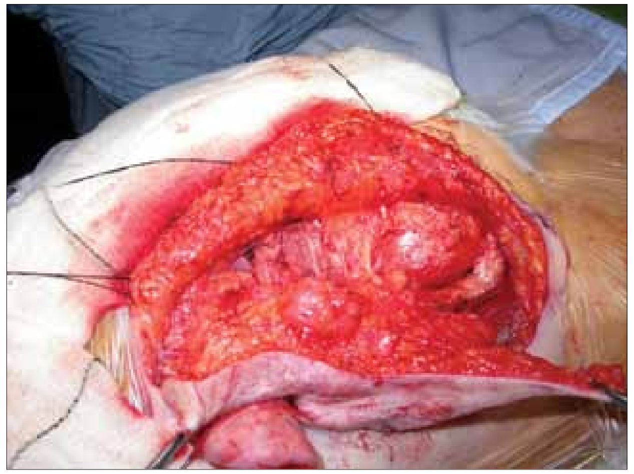

Figure 2: *Retrograde dissection of the facial nerve utilising the principle of finding the facial nerve in a previously undissected area.*

Not all papers have shown reduced recurrence with ART and the associated risks must also be considered[25]. The most common side effect is skin toxicity and other side effects include ototoxicity, fibrosis with trismus, TMJ dysfunction and secondary malignancy[14,65,68]. Malignant transformation de novo has been reported to range from 0 - 23%[28,31,33,40,65,70]. No papers however have shown an association with ART and increased incidence of malignant transformation[30,31,68].

Despite no prospective studies comparing surgery for RPA with or without RT, the available evidence supports the use of ART in certain circumstances. We recommend ART for gross or microscopic residual disease, for second recurrence, and to be considered for multifocal disease and where further surgery is likely to impact on the function of the facial nerve.

Observation of RPA

In some cases it may be appropriate to simply observe the recurrent tumour. This would be considered appropriate for patients unfit for surgery, the elderly or if it was considered that the risk of harm and morbidity associated with further treatment outweighs the perceived benefit of subsequent treatment[40].

CONCLUSION

RPA presents a surgical challenge with potential impacts on the patient's quality of life. A number of factors have been identified in the decision making process with respect to the extent of surgical resection, potential reconstruction and need for adjuvant radiotherapy. The ultimate treatment is assessed on a case by case basis.

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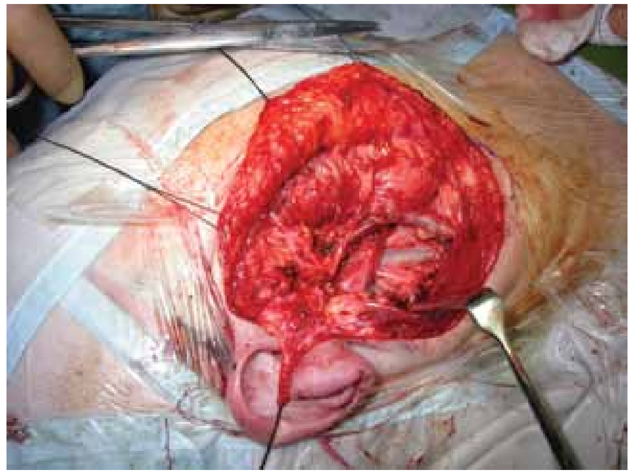

Figure 3: *Total conservative parotidectomy completed.*

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Facial nerve monitoring

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Key words
Facial nerve, electophysiology, monitoring.

Electrophysiology and monitoring

Development of facial nerve monitoring

Since the first description of intraoperative cranial nerve stimulation by Fedor Krause in 1898, the techniques have been refined, all relying on observing movement of the face in order to confirm the functional integrity of the facial nerve[1,2,3,4,5,6,7].

In 1979, Delgado and colleagues described the use of evoked compound muscle action potentials (CMAP) to monitor facial nerve function in response to stimulating the intracranial portion of the facial nerve[8]. The introduction of facial electromyography (EMG) enabled not only facial nerve identification either by electrical stimulation or inadvertent manipulation, but also the possibility of mapping its course through the temporal bone and assessing changes in function during surgical resection of tumour from the nerve's surface[9]. Facial nerve monitoring has proved an invaluable aid during vestibular schwannoma surgery[10,11,12]. The introduction of an auditory signal has enabled real-time auditory feedback to the surgeon during tumour dissection[13,14].

Three trials tested the hypothesis that facial nerve outcome improved when using intraoperative facial nerve monitoring. Harner and colleagues[12] demonstrated the usefulness of facial nerve monitoring in 91 consecutive cases of vestibular Schwannoma resection via the suboccipital route. At one year, 78 percent of those patients who were monitored demonstrated facial function, compared with 65 percent in an unmonitored group, although these data were not studied statistically. Niparko and colleagues[15] described the results of 29 patients who underwent translabyrinthine removal of vestibular Schwannoma and compared them with a similar group of 75 unmonitored patients. They demonstrated that monitoring was associated with a significant improvement of facial function at one year for tumours over 2 cm intracranial diameter. Kwartler and colleagues[16] demonstrated that monitored patients with tumours over 2.5 cm had a significant improvement of facial function when compared with a matched unmonitored group.

The benefit of facial nerve monitoring during surgery for chronic middle ear disease is less certain. Facial nerve injury after otological surgery is rare in experienced hands and there are no randomized controlled trials examining its efficacy. Silverstein and others recommend that the facial nerve should be monitored during all general anaesthetic cases where the facial nerve is at risk, although it has taken some time for the use of monitoring to become widespread and accpeted[17,18,19,20]. Hu et al. reported a survey that showed an increase in the number of surgeons who felt that facial nerve monitoring should be used as a standard of care from 32% in a similar study performed 10 years previously, to 49% in their more recent survey group[21]. This proportion is thought to be higher in the UK and Australia however[22].

Increasing usage of nerve monitors has implications for litigation cases. In general such cases question whether a reasonable body of practitioners would employ a nerve monitor during surgery (Bolam test). If any such body is likely to recommend use of monitoring, then failure to use a monitor would likely become indefensible as Breach of Duty could be established. The principle remains however that if any adverse outcome would have occurred regardless of the lack of nerve monitoring, then the claim would fail. The claimant must therefore establish causation.

Intraoperative facial nerve monitoring is no substitute for experience in the otological setting and should not replace good surgical practice, but if the operating team adopt the approach that all patients are monitored, the set up technique becomes routine and more reliable. With developments in robotic surgery, investigators have evaluated facial nerve monitoring systems which have been integrated in to the drill system, to determine whether such systems could reliably warn of impending facial nerve contact during robot-assisted direct cochlear access procedures. At present however such systems lack sensitivity and repeatability[23].

Technique for continuous facial nerve monitoring

The operating theatre is filled with electrical interference generated by the equipment surrounding the anaesthetized patient. Monitoring techniques have developed to minimize this interference and amplify only relevant information. Two sets of subdermal platinum or stainless steel needle recording electrodes are inserted into the upper and lower face. The electromyographic electrical response is biphasic. The amplifiers amplify the difference between the potentials recorded at each electrode. This arrangement has the advantage of common mode rejection; electrical interference from other sources is recorded by both electrodes equally and therefore does not create a potential difference between the two closely aligned electrodes. A number of commercial EMG cranial nerve monitoring systems are now available including the NIM-2 (Xomed Treace, Jacksonville, FL, USA) and the Neurosign (Magstim, Whitland, UK). They rely on recording facial muscle activity and delivering the information as a visual and audible representation of the CMAP response. The audible response is either presented as raw EMG activity or a characteristic sound when EMG activity reaches a set threshold.

All systems are isolated and self-contained electrical nerve stimulator and monitoring units. The electrodes are connected to a preamplifier pod, which is attached to the operating table. The recorded electrical signal is filtered through high- and low-pass filters and either rectified and displayed on a logarithmic bar chart or presented as a CMAP waveform. Different systems use different methods of presenting the same information to the surgeon.

The logarithmic bar chart has a delayed response decay to enable calculation of rectified CMAP amplitude. Systems that present a CMAP waveform present it as visual and audible real-time information or utilize image capture strategies that also give waveform amplitude information. This allows the surgeon time to examine the waveform and size of the CMAP. So called 'repetitive responses' occur as a result of repetitive depolarizations after surgical manipulation has ended. They can be used as a measure of nerve irritability as a result of early damage, for example from thermal injury. Compare this with non-repetitive responses which are indicative of direct mechanical stimulation of the nerve.

Familiarity with the set up and function of a chosen monitoring system is essential. The senior surgeon must take responsibility and should check that the equipment is functioning normally. Tapping the skin overlying the two sets of subdermal electrodes will generate a recorded response on the monitor. This confirms that electrodes are connected to the preamplifier pod and in turn the preamplifier pod is connected to the monitor, which is switched on. The volume should be checked so that a response is audible over background theatre noise.

Facial nerve stimulation is delivered as a short (0.1 ms) electrical pulse. This is the default setting for most monitors. The stimulating electrode is either monopolar or bipolar. The monopolar electrode is favoured because it is simple to use, but has the disadvantage of stimulating a larger area. The bipolar electrode requires careful positioning of both electrode tips on to the tissue surface; this can prove difficult in the tight confines of the temporal bone. The use of constant voltage stimuli has an advantage over constant current stimuli because it delivers a relatively reliable current to the nerve whatever the medium that surrounds the nerve. In 2013 The American Society of Neurophysiological Monitoring established a position statement on intra-operative motor evoked potential monitoring, based upon best available evidence, which included guidelines on proper usage, interpretation and general anaesthesia use in a variety of clinical settings including facial nerve monitoring[24]. Regarding general anaesthesia, Choe et al. also concluded that induction of total intravenous anaesthesia with propofol and remifentanil provided reliable conditions for facial nerve monitoring during complex ear surgery[25].

Predicting postoperative facial function

A number of studies have described an objective technique that correlates parameters of the evoked CMAP to eventual facial outcome[15,26,27,28,29]. The test gives nondichotomous results and therefore a retrospective cut-off point is used to predict those patients who have a good prognosis. Results indicate that a low stimulation threshold, across the site of tumour dissection, is a valuable prognostic indicator of good long-term facial function. The technique, which is simple to perform, assesses the minimum current required to evoke a muscle response after tumour resection. The drawback to the described technique is that the majority of patients have some degree of facial function immediately after surgery. This group will almost certainly have good long-term outcome[30]. It is the small group of patients with poor facial function immediately after surgery that will benefit most from a sensitive and specific predictive test. Axon and Ramsden compared post-dissection minimal stimulation thresholds with immediate postoperative facial function for predicting long-term facial function in 184 patients undergoing vestibular Schwannoma surgery[30]. Post-dissection stimulation thresholds demonstrated only a moderate relation to eventual outcome, which was of limited clinical value. The test criteria were then applied to patients with poor immediate postoperative facial function for predicting long-term outcome, the predictive accuracy fell, further reducing test validity.

Some studies compared the supramaximal CMAP to either facial nerve stimulation proximal and distal to tumour dissection or before and after tumour dissection. These techniques have been advocated as more accurate methods of analysing data, because they remove absolute amplitude comparisons and rely on comparison of ratios[31,32].

Difficulties of monitoring facial function

All otological procedures rely on a facial muscle response, warning the surgeon that the facial nerve is near. A simple audible noise is all that is required. Recent monitoring systems have increased the amount of information available to the surgeon, stimulating the desire to expand monitoring techniques and so improve patient outcome. This information is superfluous to most procedures and of benefit to only a few. Facial CMAPs represent a complicated interplay between groups of muscle fibres depolarizing in response to facial nerve stimulation. The muscles of the face are very different to those found in the limbs. The facial motor units are small, often having only 25 muscle fibres supplied by each motor neuron compared with many thousands in more peripheral muscles. As a consequence, each muscle has a wide ill-defined motor end-plate zone. The muscles are also arranged in an almost haphazard arrangement, overlying each other and aligned in different directions. This makes meaningful electrophysiological recording difficult. Intrasubject variability (test–retest variability) is high and intersubject comparison almost impossible. The CMAP waveform is usually multiphasic instead of the well-recognized biphasic responses recorded from peripheral muscles, a consequence of phase cancellation. Calculation of maximum amplitude or area under the waveform bears little relation to the number of motoneurons innervating the muscle fibres that create the response.

Monitoring facial function for non-otological procedures

The facial nerve is at risk of iatrogenic injury in the cerebellopontine angle and parotid. Intraoperative facial nerve monitoring has been advocated during microvascular decompression and superficial parotidectomy[33,34]. Arguments for adopting its use for all surgical procedures are the same as those for otological surgery.

Conclusions

Monitoring facial nerve function is straightforward and neither hampers nor impedes surgery. There is evidence that these techniques offer benefit in improving facial nerve outcomes in surgery that may challenge the facial nerve. Further work is required to develop an intraoperative technique that enables accurate assessment of clinical facial nerve function at any point during skull base procedures. Only accurate estimation of motorneuron function will give the surgeon a true representation of immediate facial function and hopefully then enable development of a valid predictive technique.

The speciality as a whole requires a better evidence base to support the use of intraoperative montoring

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Developing a comprehensive enhanced recovery protocol for head & neck cancer - challenges for the future

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Abstract
Enhanced recovery after surgery (ERAS) has been developed over the last two decades to provide improved outcomes and hasten post-operative recovery in a variety of surgical settings. The department of health has identified the extrapolation of Enhanced Recovery after Surgery (ERAS) concepts to the field of oncology as a strategic pillar to improve cancer outcomes.

Oncological treatment is often multimodal and ablative. Outcome measures include treatment related morbidity, and mortality which are often confounded by the natural history of the cancer under treatment. This article describes our experience of developing a broad based Enhanced recovery programme (ERP) specifically for head and neck cancer patients and a guide to adapting the protocol for local use.

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Introduction
There is an increasing burden on public sector oncological services necessitating implementation of high quality low cost health care. Enhanced recovery after surgery (ERAS) or an Enhanced Recovery Programme (ERP) is a concept pioneered in Denmark during the 1990s[1] with the goal of improving patient related outcome, reducing complications and length of stay, by engaging and treating patients holistically and ensuring care is delivered in a systematic fashion to all within the programme.

The overall strategy is 4-fold; to fully involve the patient in their care; to bring patients to the best possible health status before surgery; to co-ordinate systematic protocolised treatment throughout their hospital stay and offer the best possible rehabilitation to facilitate return to normal function as quickly as possible.[2] Critical to the enhanced recovery concept is increased patient understanding of the process of care delivery and active commitment to their optimisation for and rehabilitation from surgery.

Each ERP care package include multiple small interventions that individually may have only a small undetectable impact but together through a summation of each marginal gain improve outcome.

Established ERP have evolved over the last 20 years and allow systematically deliver of a bespoke cost effective, patient centred care package. The sub-speciality with the largest published data set and most comprehensively assessed programmes is lower gastro-intestinal (GI) surgery.

ERAS in specialties such as Lower GI[3], Orthopaedic[4], Thoracic[5] and Urological[6] surgery, increasingly are considered to be the standard of care. To date only the potential for enhanced recovery to be extrapolated to the use of patient's with head and neck cancer has been highlighted[7]. The department of health identified extrapolation of ERAS to the field of oncology as a strategic pillar to improve cancer outcomes.

Traditional ERAS applied to surgical patients focuses on the preoperative, perioperative and postoperative rehabilitation around a discrete surgical procedure. The primary outcome measured is that of median length of stay. Outcome measures in the oncological setting are not only treatment related morbidity and mortality but also confounded by the natural history of the disease, prolonged rehabilitation and surveillance.

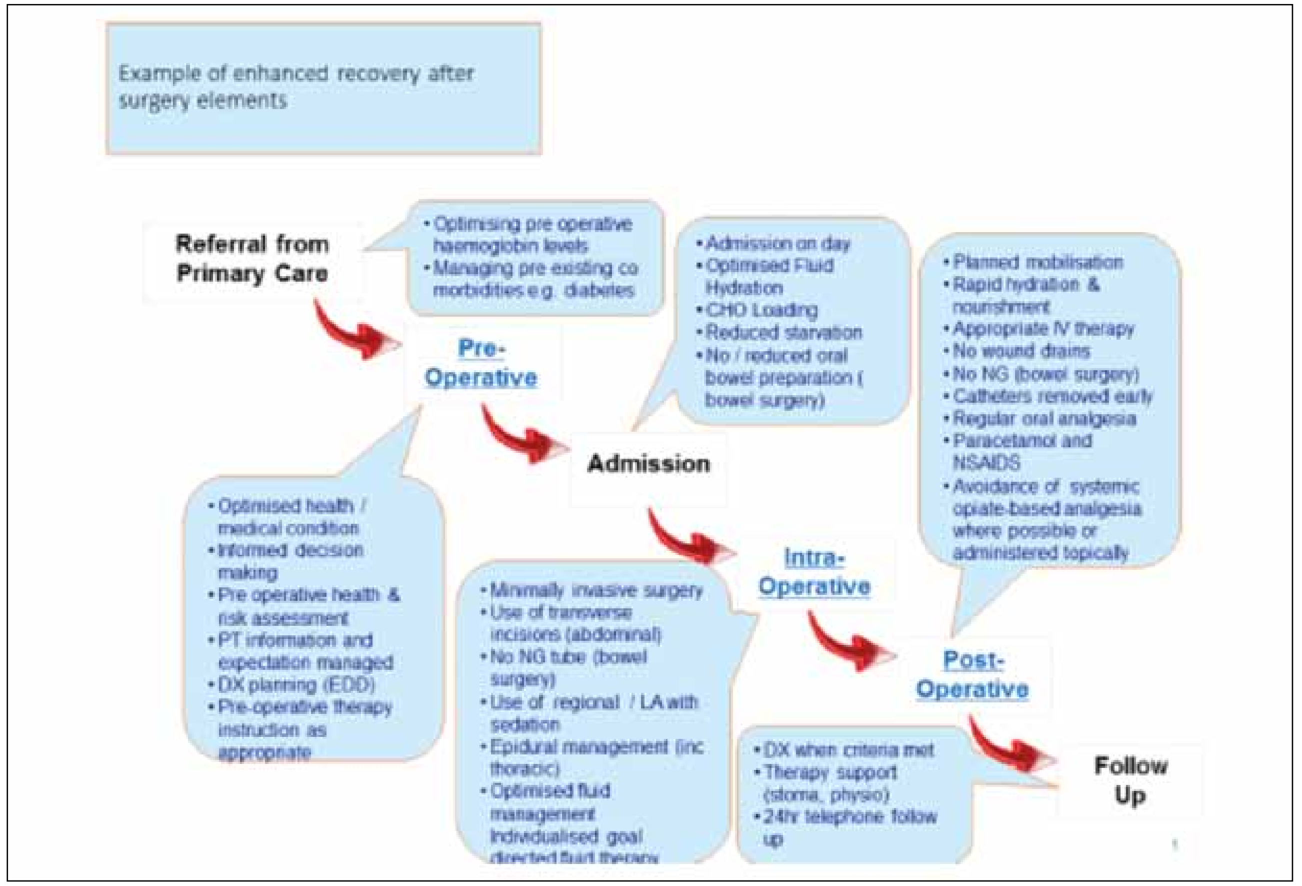

Figure 1: *Traditional ERAS interventions*

In order to improve outcomes in the oncological setting, a subtle change of approach in designing an ERP is required. The interventions most likely to improve traditional oncological outcomes lie outside the perioperative setting. Each patient needs to be fully engaged throughout their entire therapeutic journey with interventions considered from the point of initial referral, through treatment to discharge from service considered. The scope of this article is to describe the rationale for development of a comprehensive ERP for all head and neck cancer patients and map out the program for its adaptation to local use.

Developing an ERP in Head and Neck Cancer
Starting in 2010 our unit developed a comprehensive ERP for patients referred for screening for head and neck cancer through treatment and on to the point of discharge from care after 5 years of surveillance. We set out to design an ERP that would integrate the functions of the multidisciplinary head and neck team, facilitate team working and place the patient at the centre of their care[2].

The overall picture is a multi faceted approach to improve outcomes via a series of smaller interventions, which optimise the patient's condition before, during and after treatment. Integration of these interventions into a care pathway ensures co-ordinated systematic delivery so patients have the best possible care and experience optimal post-operative rehabilitation.

An ERP has traditionally been an amalgamation of assessments and interventions in the 3 main phases of care (figure 1). The pre-operative phase, including surgical and anaesthetic assessment, counselling, nutrition[14] and pre-treatment. An intra-operative phase focusing on standardised anaesthesia protocols, haemostasis and cardiac output monitoring and post-operative early drain and line removal, mobilisation, analgesia, nutrition and post-operative follow-up.

An ERP a steering group with representatives from all teams involved in the patient's pathway through referral to rehabilitation and follow-up was formed. Representation from all surgical teams (ENT, OMFS and Plastic Surgery), Oncology, Anaesthetics, H&N Nursing, Speech and Language Therapy, Dietetics, Physiotherapy, the community head and neck team and the Directorate

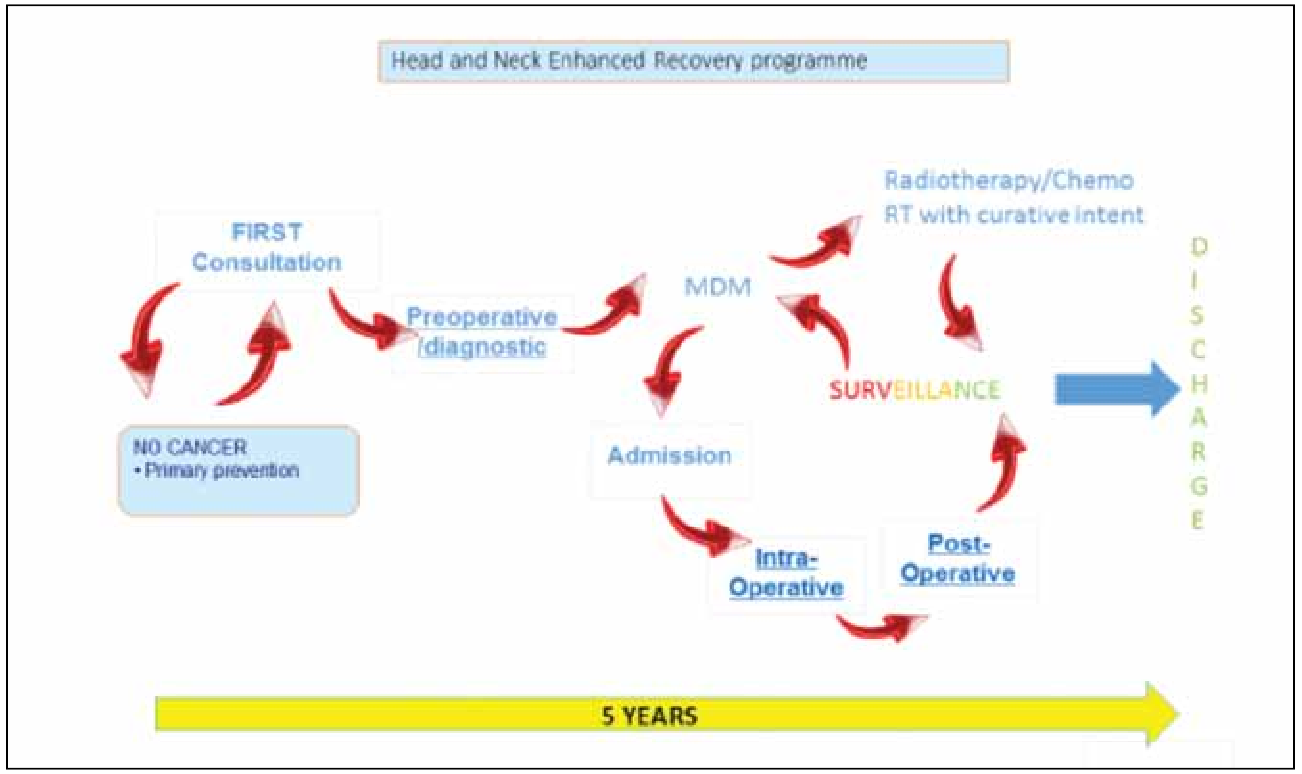

Figure 2: *Potential patient journeys for patient referred via the head and neck cancer 2-week wait pathway.*

Service manager. The head and neck cancer patient differs from the classical ERAS pathway (Figure 2).

Potential interventions to be considered when extrapolating enhanced recovery after surgery to an ERP for head and neck cancer fall into the following categories: Direct extrapolation from established ERAS methodology without modification: Direct extrapolation from established ERAS methodology with modification: Head and neck specific interventions: Oncology specific interventions.

Key points of enhancement

Pre-operative

- Health promotion and prevention - Engaging patient expectations with better interactive information
- Optimisation of general and pre-assessment clinics to fit the needs of head & neck oncological patients.
- Early supportive care input in particular physiological optimisation and nutrition pre and post operatively
- Running a Pre-treatment clinic with more time allocated to patients undergoing major resection, for counselling by allied health professionals.
- Admission on the day of surgery unless contraindicated.
- Pre-operative carbohydrate loading
- Co-ordinated management of difficult airways throughout the pathway
- Antibiotic prophylaxis

Peri-operative

- Defining perioperative protocols for resection (anaesthesia, blood transfusion, fluid balance).
- Defining perioperative protocols to optimise reconstructive conditions (patient temperature, fluid balance, haemodynamic state).

Post-operative

- Post-operative airway alerts and plans
- Post-operative flap monitoring protocols
- Early feeding (oral or enteral)
- Dynamic Airway assessment to speed up decannulation
- Integrated care pathways co-ordinated post treatment surveillance
- Repeat smoking cessation interventions for patients who continue to smoke.

Early detection and intervention for osteoradionecrosis.

These interventions were mapped to the pathway from referral to discharge after five years of post-treatment surveillance and became the template for the ERP. A 5-year implementation plan made was set, with early, intermediate and long-term objectives.

Each intervention was allocated to a work stream with a designated team and lead member to ensure accountability. The steering group met 6 weekly for regular progress reports with an annual open meeting as a forum for open discussion and new ideas, a progress report was given at each head and neck audit. Protocols established as ERAS interventions requiring modification were assessed utilising the trust governance structure before being trialled and refined by continuous PDSA cycles.

The PDSA Cycle[8] is a quality improvement tool used commonly in healthcare systems as a simple way of outlining short-term goals with the aim of continuously improving outcomes by revaluating and refining interventions. Through this process valuable learning and knowledge facilitates continual improvement of a product or process. (Figure 3).

Implementation of ERP for head and neck cancer patients.

Implementation of traditional ERAS measures has been shown in other specialties to improve outcome[9] by optimising the patients physiological and biochemical status and reducing the stress of major surgery. The most statistically robust improvement in outcome is a reduced length of stay by one postoperative day (0.5-3.5) without increased complication or readmission rates[10,15].

Figure 3: *Example of a PDSA Cycle.*

The focus of ERAS is on optimising and then feeding malnourished patients[11], a common characteristic of patients with both head and neck cancer and benign colorectal disease, the sub-speciality in which ERAS was pioneered. One would expect translation of existing interventions common to ERAS as previously described would yield similar improved outcomes. The department of health however have raised the bar for ERAS in oncological sub-specialities with an agenda to chase the golden chalice of improving the quality of care and oncological outcomes at decreased cost.

Challenges and opportunities for ERP in Head and Neck

There are a number of challenges to be faced in extrapolating ERAS to Head & Neck cancer care. However in contrast to conventional programmes for benign disease, there are opportunities for interventions with strong evidence base and potential for significant impact in isolation.

Interventions with a strong evidence base and potential for significant impact in isolation

Smoking and alcohol consumption

Primary prevention is one such opportunity, 74% of UADTSCC are associated with smoking and drinking or smoking alone, opportunity. Fully engaging patients in smoking cessation when they are referred by their GP using the two week wait referral system for head and neck cancer with a relevant and personal message to which most are receptive (a teachable moment), delivers a significant change in their attitude to smoking even when they do not have cancer[12].

Airway management.

The 4th National Audit project of the Royal College of Anaesthetists assessed the major complications of airway management, more than half (72/133) of the reported events involved a disease process of the head and neck, the majority of which (42/72) were related to tumour diagnosis or resection. A panel of expert reviewers described the plan for airway management as only good in 16% of cases. Unplanned use of a surgical airway was one of the events selected to be reported which, although saving lives in the acute setting is also described as an intervention likely to impact head and neck patient outcome adversely[13].

Pre-treatment optimisation and surveillance.

Surgery is only one possible treatment modality it may be offered alone, in combination with other modalities, reserved for salvage treatment or not offered at all. Each different sub-site has a bespoke optimal treatment packages dependent on its precise TNM stage. The exact combination and timing of different treatment modalities balance the patient's fitness for treatment; treatment related morbidity and subsequent impact on quality of life against optimal survival.

For patients with cancer addressing modifiable risk factors (smoking and alcohol consumption) is key, not only to address treatment related morbidity and mortality but also their capacity to impact patients after treatment, predisposing to recurrence or the development of a second primary cancer.

After treatment completion patients return for regular review to monitor for local or regional recurrence or a second primary cancer. Prompt detection may allow surgical salvage treatment with curative intent. This surgery carries a high risk of complications[9], treatment related morbidity and mortality. It usually involves radical resection of the recurrent cancer and microvascular reconstruction with prolonged hospitalisation. Outcomes for salvage surgery are generally poor with high rates of complications, early recurrence and low 5-year survival rates in some primary sites[10].

A motivated patient who addresses their risk factors optimises their chance of avoiding the expense, morbidity and mortality associated with salvage surgery (figure 4).

Data collection, Outcome reporting and Research.

There are lessons to be learnt from sub-specialities with long established ERAS programmes where spontaneous evolution at multiple institutions has resulted in a lack of standardisation and clarity to the fidelity of similar interventions between those institutions and how to put them in context.

Experience elsewhere has shown this there is little value in publishing outcomes from single institutions but lies in reporting how enhanced recovery programmes are implemented, resourced and experienced in the NHS setting[11]. By defining the interventions that constitute an enhanced recovery programme and the fidelity of institutional compliance with each intervention across large cancer networks one can benchmark the quality of the enhanced recovery programme in each institution against a gold standard and reduce variability of programmes between institutions through monitoring institutional outcomes against those of the wider network.

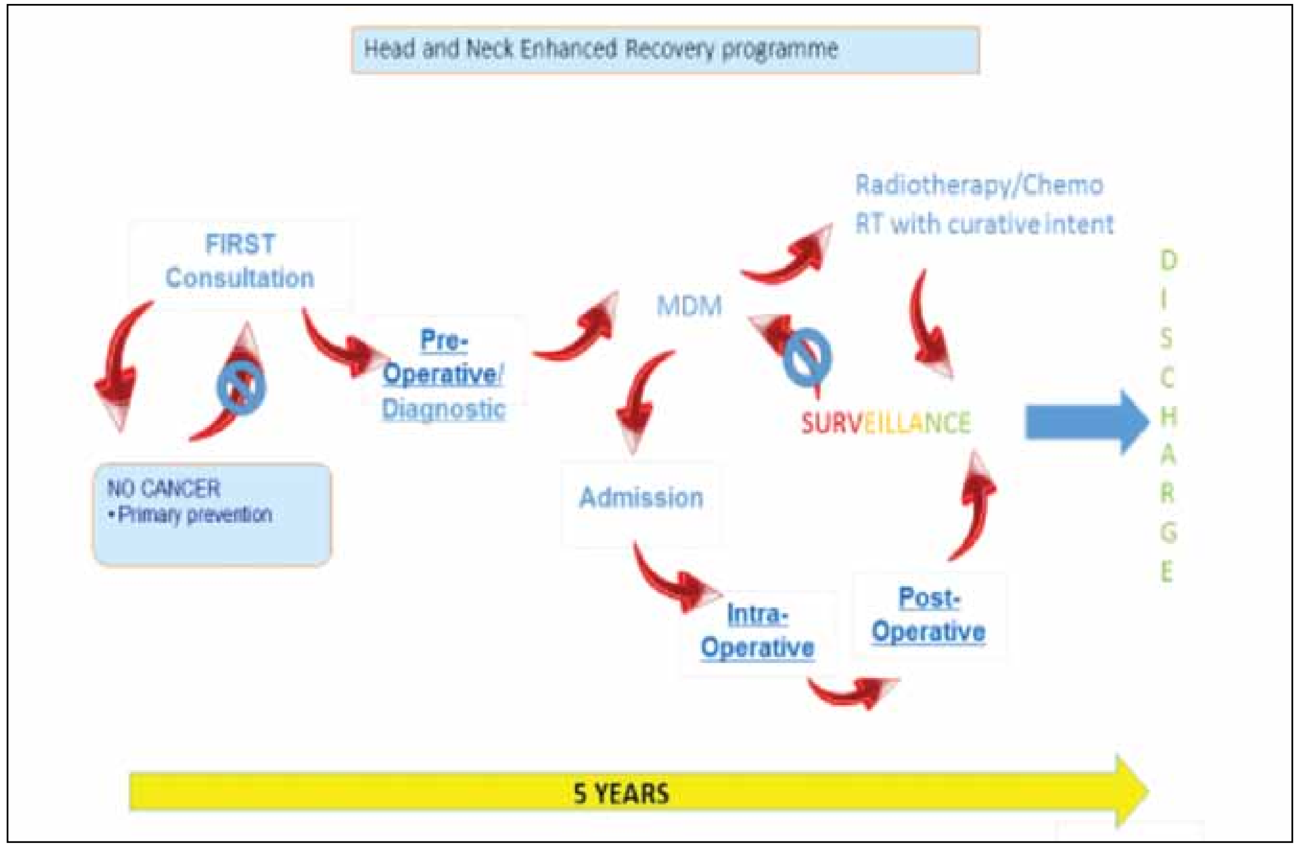

Figure 4: *Impact of addressing risk factors as a key intervention for a bespoke ERP for Head and Neck cancer patients.*

Early collaboration is required between centres to understand the detail of the programmes being introduced and how they compare.

Conclusions

ERP ensures patients are in optimal condition for treatment, have the best possible care during the operation and experience optimal post-operative rehabilitation. Key to this process is to involve the patients in the delivery of their care and rehabilitation as well as facilitating patient led decision-making. Bespoke ERP's for head and neck cancer patients, which include established ERAS, adapted and oncology specific interventions can be formulated and introduced in a stepwise fashion. Systematic introduction across wider networks in addition to reducing the average length of stay for patients may allow oncology specific outcomes such as treatment related morbidity and mortality to be improved in addition to reducing length of stay.

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11th Annual National ENT Masterclass®, 2015 Trainees' Gold & Silver Medal

A pilot study of evaluating the relationship between extra capsular spread and bone marrow micro metastases in head and neck squamous cell carcinoma

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Introduction:
The survival of patients with head and neck squamous cell carcinoma (HNSCC) is catastrophically affected by the presence of extracapsular spread in cervical metastases. Despite the appearance of adequately treated disease recurrence and metastases occur. Disseminated tumour cells, such as bone marrow micrometastases (BMM) may be the cause for this.

This study aimed to determine whether BMM could be identified by immunocytochemical methods and if there was any correlation, in this small group, with the presence or absence of extracapsular spread.

Methods:
After obtaining ethical approval, patients diagnosed with primary T^2-T^4 HNSCC and planned for primary surgical treatment of their disease were recruited. All patients underwent bone marrow aspiration whilst under general anaesthetic. The bone marrow specimens underwent immunomagnetic separation with MACS CD^{45} microbeads and subsequent immunostaining with Rabbit antimouse Ig, Streptavidin AB complex and Fast Red TR/Naphthol AS dye.

Results:
Fourteen patients were included in the study (10 male, 4 female). All patients underwent tumour resection and neck dissection as primary treatment. Four patients had evidence of BMM. We found a strongly suggestive correlation between nodal extracapsular spread (ECS) and BMM. All 4 patients with BMM also had nodal ECS. Only 1 patient had nodal ECS without the presence of BMM.

Conclusions:
The correlation between BMM and ECS in this pilot study suggests that BMM could be of significance. Further studies with larger numbers of patients are needed to reveal the potential impact of BMM and its association with ECS.

A qualitative study of outcomes following intervention for glue ear in children

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Background
Glue ear is a common childhood condition causing conductive hearing loss, which can have implications for the child's social and educational development. A Cochrane review[1] providing level 1a evidence tells us that the effect of grommets on hearing appears small and diminishes after 6-9 months, and that no effect was found on other child outcomes, data on these being sparse.

Aim
The aim of this study was to gather qualitative data regarding parents' perceptions of outcomes following their child's treatment for glue ear, in order to explore outcomes beyond the small improvement in hearing.

Methods:
Open-ended questionnaires were used to gather qualitative data from parents 3-6 months after their child's intervention for glue ear, (100 had grommets, 50 had hearing aids) regarding the effects they felt the intervention had had on their child. Inclusion and exclusion criteria matched the TARGET study.

Results:
Of children who had grommets, 100% of parents reported improvement in hearing, 4% reported one or more negative outcomes, and each parent reported an average of 4.2 additional positive outcomes. Of children who had hearing aids, 81% of parents reported improvement in hearing, 29% reported one or more negative outcomes, and each parent reported an average of 1.7 additional positive outcomes.

Discussion and Conclusion:
This qualitative study demonstrates that parents perceive many more positive outcomes from grommet insertion than merely hearing improvement. Children's social and educational development is a complex and emotive issue, and this study provides additional support for appropriate intervention in children with glue ear.

This work took place at Sheffield Children's Hospital; there were no additional authors and the presenting author agrees copyright permission and the contents of the paper for submission.

Reference:
1 Browning GG, Rovers MM, Williamson I, Lous J, Burton MJ. Grommets (ventilation tubes) for hearing loss associated with otitis media with effusion in children. Cochrane Database of Systematic Reviews 2010, Issue 10. Art. No.: CD001801. DOI: 10.1002/14651858.CD001801.pub3.

Pulse Oximetry in Paediatric Obstructive Sleep Apnoea -is it used appropriately?

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Objectives:
We assessed the use of pulse oximetry testing at our hospital in children with suspected OSA.

Methods:
A retrospective review was carried out in patients who underwent pulse oximetry testing between April 2013 and October 2013. Primary outcomes measures included; 'positive' pulse oximetry results, defined as McGill Oximetry Score 2-4

Results
Thirty-seven test results usable for analysis included 21 pre and 16 post-operative tests. Only 4 patients had a 'positive' test. There was a significant difference between pre and post-operative QOL outcome scores in the surgical group ($p<0.0001$).

Conclusion:
Pre-operative pulse oximetry should be used as a guide to help triage patients who require specialist paediatric services, such as Paediatric Intensive Care. The use of pulse oximetry, particularly in the post-operative setting, is unlikely to change the management of patients, and can create unnecessary financial cost to NHS Hospital Trusts.

Institution where study took place:
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HPV 16 E7 seropositivity in Head and Neck Squamous Cell Carcinoma compared to healthy controls

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Background:
It has already been established that infection with Human Papilloma Virus (HPV) 16 confers better outcomes and survival rates in those who have HPV positive Head and Neck squamous cell cancer (HNSCC). The HPV viral oncoproteins E6 and E7, have been implicated in the pathogenesis of tumourigenesis. Although it has been demonstrated that seropositivity to E6 and E7 in HPV positive HNSCC confers much better survival rates, little information is available which compares serum antibody titres to those in healthy controls. The aim therefore was to compare serum E7 antibody levels in both HPV positive HNSCC patients and healthy controls.

Methods:
The presence of HPV16 was determined in patients with established HNSCC (n=85) using p16 immunohisto-chemistry (CinTec®). Patients and healthy controls (n=25) were also tested for seropositivity to HPV-16 E7 with an ELISA developed in house.

Results:
Of the patients tested 22/85 were found to be p16 positive. No significant difference in E7 antibody level was observed amongst the HPV positive and negative patients and notably not all HPV positive patients mounted an antibody response to HPV 16 E7. Interestingly almost half of the healthy subjects also displayed an antibody response to E7 and no significant difference between E7 antibody response in HPV positive HNSCC patients vs. normal healthy subjects was detected.

Conclusion
Although seropositivity has been shown to confer better outcomes in HPV positive HNSCC patients, the presence of a similar level of antibody response to E7 in healthy subjects suggests antibody titres against this antigen are not useful as a diagnostic tool.

Creating a texture analysis model to accurately predict lymphomatous lymph nodes using ultrasound images in children

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Introduction:
The gold standard for lymphoma diagnosis requires nodal tissue histopathology. An invasive sampling procedure is necessary. Ultrasound is non-invasive test which can be easily performed in children. Ultrasound characteristics of lymphomatous lymph nodes include a round shape, well-defined border, hypoechogenecity and absence of an echogenic hilus. Our aim was to create a texture analysis model using automated computer software to reliably distinguish lymphomatous nodes from benign ones using existing ultrasound images.

Methodology:
We obtained pre-operative ultrasound images of 22 children (11 lymphoma and 11 reactive nodes on post-operative histology) that had undergone lymph node excision for diagnostic purposes at Sheffield Children's Hospital (2000-2014). Quantitative texture analysis of the ultrasound images was performed using MaZda software. These patients' images acted as a training set for our model. The top 20 texture parameters to differentiate between the two groups were obtained. The features and their corresponding values were exported into b11, a partner statistical package of MaZda.

Results:
Linear discriminant analysis was performed in the b11 software using the top 20 texture parameters giving a 0% misclassification error between the two groups. The resultant most discriminant factor (MDF) values were exported into the statistical package GraphPad Prism. The sensitivity, specificity and ideal cut-off MDF values were calculated.

Discussion:
We have successfully created a working texture analysis model to differentiate lymphomatous lymph nodes from benign nodes. We now plan to prospectively test the model on routine ultrasound images of patients undergoing lymph node excision. If the model accurately predicts lymphoma, the test could be used in routine clinical practice.

Transnasal oesophagoscopy: is there a role in the Head & Neck clinic?

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Objective:
To evaluate the role of transnasal oesophagoscopy (TNO) in the Head & Neck clinic and associated patient perceptions.

Method:
Prospective study (n=78) over a 1-year period. TNO pick up rate of pathologies of the upper and lower aerodigestive tract was evaluated as well as patient tolerance of the procedure using validated outcome measure tools.

Results:
Seventy eight patients underwent TNO (49 males and 29 females). The commonest indications included reflux symptoms (28.9%), pharyngeal hypersensitivity (27.6%), suspicion of neoplasia (26.3%) and globus (17.1%). Positive findings were identified in 72.4% of cases subdivided in: gastro-oesophageal reflux (32.9%), laryngo-pharyngeal reflux (25.0%), malignancy (7.9%), and benign structural lesions (6.6%). Of the patients that subsequently went on to have other investigations (barium swallow, oesophago-gasto-duodenoscopy), the findings were the same in 95.3% of cases. Only 5.3% of patients undergoing TNO subsequently required referral to Gastroenterology whilst 9.2% required surgery, most in the form of panendoscopy to visualise the hypopharynx, an area still best assessed with rigid endoscopy under general anaesthesia. Most (97.4%) patients tolerated TNO very well with 94.7% reporting that they would have it again if necessary.

Conclusion:
TNO is a simple investigation that can be performed in the outpatient setting without the need for sedation. It also allows biopsies to be obtained and is generally well tolerated. Particular indications include globus, reflux symptoms and suspicion of structural lesions or neoplasia of the oesophagus. With TNO, the majority of patients can be diagnosed in the clinic without the need for further investigations or referrals.

Can transnasal flexible laryngo oesophagoscopy (TNFLO) replace barium swallow?

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Background/introduction:

Barium swallow is a well utilised investigation for a variety of upper gastrointestinal and ENT presenting complaints. Despite limited radiological indications, its use is widespread for symptoms ranging from dysphagia to cough and abdominal pain. The emergence and increasing popularity of TNFLO may reduce the need for radiological investigation as a first line, allowing direct endoscopic visualisation of the pathological area in clinic.

Aim:

To review the barium swallow requests for appropriateness and identify whether the pathology found could have been diagnosed by TNFLO in clinic.

Methods:

Radiology requests for one month were retrieved and reviewed. Barium swallow requests were reviewed for indication and clinical findings.

Results:

Forty seven swallows were requested in September 2014 in our hospital, by 6 different specialities. Seventeen complied with radiological request guidelines. Time from request to investigation was 28 days (range 0-48). All positive pathological findings could have been identified and diagnosed by TNFLO in an outpatient clinic. Despite a clinical delay of 31 and 40 days respectively, two mucosal abnormalities seen on swallow required further endoscopic examination at a later date.

Conclusion:

Barium swallow is often inappropriately requested. The exposure to radiation is not insignificant, and is equivalent to 8 months background radiation. TNFLO in clinic, by an appropriately trained clinician, could avoid radiation exposure, reduce delay in diagnosis and offers a safe and well tolerated alternative to diagnose a range of common ENT conditions.

A pathway for the treatment of laryngopharyngeal reflux using Restech Dx-pH catheters

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Introduction:

Laryngopharyngeal reflux (LPR) represents a common diagnosis in the Otolaryngology clinic. While treatment of the condition is straightforward, its diagnosis is not and often leads to circular consultations. Scoring systems are used to make an objective diagnosis, however these are often largely non-specific and for now the gold standard for diagnosis is 24-hour continuous pH measurement. An objective measure of pH in the pharynx can be obtained via the use of a Restech Dx-pH catheter. This study aims to quantify the therapeutic cost to the patient and the hospital and proposes a future treatment pathway.

Methods:

A total of 25 Restech catheters and two Dx-recorder units were provided for use. 25 patients with suspected diagnoses of LPR were selected.

Results:

12 (48%) patients were male. Of the 25 recruited patients. 13 (52 %) patients were found to have positive results for LPR.

An average of 3 consultations occured prior to referral for Restech pH catheters. For patients without LPR on Restech, an average of 3.2 consultations were used. For patients with Restech proven LPR an average of 4.2 consultations were used. An average of 204 days was noted between original GP referral and definitive diagnosis of LPR.

Conclusion:

LPR is an elusive entity in the Otolaryngology clinic. The Restech Dx-pH catheter currently offers potentially the most effective objective means of establishing a diagnosis of LPR. We demonstrate that there are often prolonged and unnecessary revisitations to the outpatient department. A pathway for use of the Restech device in routine patient care is offered.

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