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JOINT ESSENTIAL INFORMATION

Gaviscon Advance Peppermint Flavour Oral Suspension, Gaviscon Advance Aniseed Suspension, Gaviscon Advance Mint Chewable Tablets

Active substances: Gaviscon Advance Peppermint Flavour, Gaviscon Advance Aniseed Suspension: Each 10 ml contains sodium alginate 500 mg and potassium hydrogen carbonate 100 mg.

Gaviscon Advance Mint Chewable Tablets: Sodium alginate 500 mg and Potassium bicarbonate 100 mg.

Gaviscon Advance Mint Chewable Tablets: Sodium alginate and Potassium bicarbonate tablets are not suitable for patients with phenylketonuria.

Precautions and Warnings:

Chewable Tablets: For oral administration after being thoroughly chewed.

Adults and children 12 years and over: One to two tablets after meals and at bedtime. Children under 12 years: Should be given only on medical advice. Ideally, no dose modification is required for the age groups.

Gaviscon Advance Peppermint Flavour Oral Suspension: Each 5 ml dose contains sodium alginate 500.0 mg and potassium hydrogen carbonate 100.0 mg.

Each 10 ml dose contains 200 mg (2.0 mmol) of calcium carbonate. This product should not be given to patients with phenylketonuria.

Side-Effects: Very rarely (<1/10,000) patients may develop allergic manifestations such as urticaria or bronchospasm, anaphylactic or anaphylactoid reactions.

Gaviscon Advance Mint Chewable Tablets: 60 Tablets – £3.07

Also Available:

Gaviscon Advance Peppermint Suspension (sodium alginate, potassium hydrogen carbonate) and Gaviscon Advance Mint Chewable Tablets (sodium alginate, potassium bicarbonate).

NHS List Price:

Gaviscon Advance Peppermint Flavour Oral Suspension: 250ml – £2.56, 500ml – £5.12

Gaviscon Advance Aniseed Suspension: 250ml – £2.56, 500ml – £5.12

Date of preparation: June 2013

UK/G-NHS/0613/0027

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Welcome message
Shahed Quraishi
The Benefits of Attending Academic Meetings – Reasoning and some Personal Comments!
Patrick J Bradley
Children with snoring: evaluation and management
Nigel KF Koo Ng MRCS, Haytham Kubba FRCS
Considerations for tympanic membrane repair in children
A S Takhar MRCS, DOHNS, G Lloyd MRCS, DOHNS, D K Selvadurai FRCS.
Cholesteatoma in children: management strategies
Andrew T Harris FRCS, Professor Chris H Raine Ch.M., FRCS.
ENT issues in children with cleft palate
Shueh Lim MRCS, David Wynne FRCS.
The current management of acute sinonasal infection in children
A Taghi FRCS, R Kuchai FRCS, H Saleh FRCS.
Iatrogenic facial nerve paralysis in mastoid surgery
Liam Flood FRCS, Maurice Hawthorne FRCS
Intratympanic pharmacology for dizzy patients
Glen J. Watson FRCS, ORL-HNS Richard M. Irving MD FRCS, ORL-HNS
Stenosing chronic otitis externa
Isobel Fitzgerald O’Connor DO-HNS, MRCS and Ian Bottrill FRCS
Current opinion on Vestibular Migraine
O Judd FRCS, A R Banerjee FRCS
Pathology and management of transitional cell papilloma of the sinonasal cleft
Sonia Kumar MRCS, Derek Skinner FRCS
Balloon sinuplasty
Hiba Al-Reefy, Alison Carter, Claire Hopkins FRCS
Nasal septal perforation: causes and management options
Andrew C. Swift FRCS, Samuel C. Leong MPhil, MRCS, DOHNS.
The pathology and management of antrochoanal polyps
Natasha Choudhury FRCS, Hesham A. Saleh FRCS.
The principles of upper eyelid blepharoplasty
Naresh Joshi FRCOphth, Maeve O’Doherty FRCS
Squamous cell carcinoma of the temporal bone
Marc-Elie Nader, Randal S. Weber, Paul W. Gidley.
Minor salivary gland neoplasms
Christopher Goh FRCS, Mahalakshmi Rangabashyam, Tan Tiong Yong

Paralytic dysphonia – modern management strategies
Declan Costello, FRCS (ORL-HNS)

Nerve monitoring in thyroid and salivary gland surgery
Helen Atkinson, Sanjai Sood

Incidence, evaluation and management of synchronous primary malignant tumours of the head and neck
Kerrie McAllister MRCS, Ken MacKenzie FRCS

Assessment and management of adult laryngotracheal stenosis
Guri Sandhu MD, FRCS, FRCS (ORL-HNS)

What is the future of targeted therapy in head and neck cancer?
Steffen Wagner, Jens Peter Klussmann, Claus Wittekindt.

Advances in the surgical management of hyperparathyroidism
Michael C. Singer and Gregory W. Randolph

Retrosternal goitre: contemporary challenges and controversies
Navin Rudolph FRACS, Barney Harrison FRCS

Changing practice in the management of advanced hypopharyngeal cancer
Giannis Thrasyvoulou MD, DOHNS, Liam Masterson MRCS, DOHNS,
Carsten Palme FRACS, Faruque Riffat FRACS.

Transoral Robotic Surgery (TORS): An overview of the literature, current national guidelines and the clinical applications in oropharyngeal surgery

Evaluation and management of cervical nodal disease after chemoradiotherapy in head & neck cancers
Mumtaz J Khan, MD, FACS


Disclaimer: The individual authors have responsibility for the integrity of the content of the manuscripts.
Welcome to Volume 6 Issue 1 of Journal of ENT Masterclass 2013

The ENT Masterclass® shall be celebrating its tenth anniversary at the January 2014 course at the Royal College of Surgeons', London. The last decade has seen this training platform blossom from a single 3-day course at Doncaster, England into a substantive series of free educational resources. The focal point of all our activities is our website: www.entmasterclass.com

Over the years, hundreds of surgical trainees, consultants, nurse practitioners and allied workers have benefited from over £1.2 million worth of free educational resources. The delegates at the last few courses were from as far away as Australia and South Africa as well as from a number of European and Asian countries. Locally the demand has been tremendous and though we increased the delegate numbers by 50% to over 600 annually, we still have a large waiting list. This has been tackled to the benefit of the local and distant trainees by introducing free live Webcasts: http://www.entmasterclass.com/webcast.htm for later/repeat viewing.

Moving our flagship 3-day, 'National ENT Masterclass' to the Royal College of Surgeons in 2012 has been very well received both in UK and in Europe. It certainly has helped with the travelling plans for the delegates but has been a costly challenge for the organisers.

The other courses are themed and are held at Doncaster Royal Infirmary, England on Thyroid & Salivary Glands, ENT Emergencies, ENT Radiology, ENT Nursing and Tracheostomy care. In 2008, the free Annual Journal of ENT Masterclass was launched in full colour with approx 126 pages. The popular Cyber textbook of ENT Surgery was launched in 2011 and is the most popular part of our website: http://www.entmasterclass.com/cybertextbook.htm This consists of over 160 surgical videos on common Head & Neck procedures from Neck dissections to rhinoplasties to mastoidectomies. To engage the senior trainees, in 2011 an ENT Masterclass Registrar’s Gold medal was introduced for the best paper presented from a final shortlist of 8 papers. This has since become a popular annual event for the trainees.

All this has been happening due the generous support of the faculty who give their own time and resources to this platform. All of them pay for their own travel and accommodation so allowing us to keep the costs down. The support of the Royal College of Surgeons, ENT-UK and Doncaster & Bassetlaw NHS Foundation Trust deserves special mention.

I would personally like to thank the tremendous contribution of Prof Patrick Bradley who has given his precious time and effort to the ‘cause’ and has always been a telephone call away to help the ENT Masterclass team. Working as the Chairman of the Editorial Board he has successfully delivered six high quality publications, with contributions invited from all corners of the world. The current Editorial Board has been reorganised with section heads and a more international profile. His advice and support has been much appreciated by the delegates and the Masterclass team. Currently we have over 60 members in faculty and last year we were fortunate to include the first International volunteer faculty member, Prof Oliver Kaschke from Berlin who shall this year be joined by Prof Mumtaz Khan from Cleveland Clinic USA.

Perhaps our most ambitious venture is going to be the planned free ‘ENT Masterclass Australasia’. Last year we were approached by Australian ENT surgeons for a ‘franchise’ for down under! The plan is to cater for Australia, New Zealand, Singapore, Malaysia and other South East Asian states by having an Annual Masterclass in Sydney. The first one is scheduled for summer 2014, .......watch this space.

The survival of this platform depends on the goodwill and support of all involved and I would like to invite you to visit our Guest Page on the website and give us your feedback and suggestions: http://www.entmasterclass.com/guestbook.htm

Mr M Shahed Quraishi, FRCS, FRCS (ORL, H&N)
Editor, Journal of ENT Masterclass.
10th Annual National ENT Masterclass®
in conjunction with ENT-UK

Venue: Royal College of Surgeons, London
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- 8th ENT Nursing Masterclass® 24th October 2014
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Hon Clinical Senior Lecturer in Surgical Oncology
Doncaster & Bassetlaw NHS Foundation Trust

Tel: 01302 647231  E-mail: secretary@entmasterclass.com  www.entmasterclass.com

These courses are sponsored by the Faculty Members with Institutional support
The Benefits of Attending Academic Meetings – Reasoning and some Personal Comments!

Patrick J Bradley, Nottingham

Description of academic meetings:
An academic conference, meetings or symposium is a gathering of researchers (not necessarily academics) as well as clinicians to present and discuss their work. Conferences are usually composed of various presentations, most of which are short and concise, and may be grouped together followed by discussion or questions and answers. Included within this conference plan may include keynote lectures, lasting longer, on a recently clinical practice event, or a new discovery. Many conferences include panel discussions, round tables on various issues and workshops. At some conferences, usually national or international, commonly lasting 2 days or more, frequently there are social or entertainment activities for partners as well as delegates, such as tours and receptions included.

Categories of academic meetings:
Academic conferences generally fall into three categories:

- The themed conference, small in size, generally short, a day or two, around a particular topic

- The general conference, a conference with a wider focus, with sessions on a wide variety of topics, organised nationally or international by learned societies, and are held annually or at regular intervals every two - four years

- The professional conference, large conferences not limited to academics but including sessions on academically related issues.

Meetings can also be described in descending order of utility and frequency for doctors: informational, decision making, creative and motivational.

Introduction of revalidation in the UK:
The introduction of ‘revalidation of doctors’ in the UK became live December 2012, and the initial process aims at completing evaluation of all doctors currently practicing by April 2016. Documents by the General Medical Council (GMC), have tabulate the main areas for which supporting evidence must be supplied – ‘Good medical practice’ and ‘Continuing professional development’. This information is clearly available on the GMC website: http://wwwgmc.uk.orh/static/documents/content/Meeting_our_requirements_in_the_first_cycle.pdf

In order to assist, the Academy of Royal Colleges have provided generic information for all domains of appraisal and individual colleges have provided specific documents for their areas if practice. This information can be found using the associated link to the Academy website: http://www.aomrc.org.uk/revalidation/revalifdation-publications-and -documents/specialty-guidance.html

In addition, ENT-UK has produced a specialty-specific recommendation, which identifies how practitioners in differing subspecialties could provide relevant supporting evidence https://entuk.org/docs/members/cpd/criteria_standards_evidence_guidance_ent_surgeons

Revalidation for ENT doctors:
ENT-UK has produced a specialty-specific recommendation, which identifies how practitioners in differing subspecialties could provide relevant supporting evidence https://entuk.org/docs/members/cpd/criteria_standards_evidence_guidance_ent_surgeons

ENT Surgeons as defined by ENT-UK document above “are specialists who have undertaken additional training and assessment, where appropriate, in order to offer effective, informed and up-to-date care to patients through surgical interventions within the area of the head & neck. They ensured that their knowledge of surgical procedures is maintained on a regular basis by a variety of measures, including regular evaluation of patient safety incidents. Their practice is multi-disciplinary using the knowledge and skills of other professionals groups to enhance and inform their work. They are committed to learning from a variety of sources. They recognise that good surgical practice requires constant review and ensure that their regular Continuing Professional Development (CPD) activities focus of the generality of ENT as well as on their own area of subspecialisation. They record their own career progression and CPD portfolio which reflects their professional practice.”
Listed are examples (which are representative only) of how CPD needs may be met these may be collected a clinical or non-clinical – below are some of those examples relevant to this article include:

- Attendance at annual general meetings of BAO-HNS (or equivalent body at home or abroad)
- Attendance at sub-specialty professional surgical meetings (BAPO, BAHNO etc)
- Attendance at practical skills, revision workshops; temporal bone, cadaveric dissection – head and neck surgery, sinus surgery, skin flaps etc
- Attendance at critical appraisal of literature or equivalent course
- Regular review of a relevant Journal (Clin Otolaryngol, JLO) or an equivalent foreign journal / sub-specialty journal
- On line / distance learning
- Training for educational supervision, training for management or academic training
- An ENT surgeon should ensure that they have undergone a period of appropriate training before undertaking a new procedure on a patient (where that procedure has been shown to be of value).

At each appraisal meeting, a description of CPD undertaken each year should be provided including:

- Its relevance to your individual professional work
- Its relevance to your personal development plan
- Reflection and conformation of good practice or new learning / practice change where appropriate

Normally achievement of at least 50 credits per year of the revalidation cycle is expected and at least 250 credits over a 5 year revalidation cycle. The CPD should be recorded against categories: clinical, academic, professional (including management) and context: internal, external and personal. Each surgeon will have different balance of activities to reflect their role but should show some diversity in topic and the types of activity.

Some of the drawbacks include:

- Time away from work
- Missing “loved ones”
- Extra work pressure when one gets home
- The exhaustion or “jet-lag” - depending on where the meeting has been held!
- The expense!

My advice:

Should you plan to go to a meeting, have some real and simple target objective for the selection of your planned choice of meeting! Make travel and accommodation plans well in advance! Naturally seek study leave and any financial support! It’s usually best to attend with a colleague, who is a friend with similar academic and social interests – reduces the boredom and frequent loneliness! Obtain the programme as far in advance as it’s possible, then study the programme and mark out what sessions and topics to attend that will achieve your objective! Mark other topics / sessions that are desirable
but not essential! Stay near the conference centre – as commuting long distances becomes a chore either early or late in the day!

Do not necessarily stay in the most expensive hotel – but if funds allow it certainly makes the stay more relaxed and enjoyable! Should funds allow stay at the conference hotel – this will allow for possible meeting of friends and new acquaintances! More recently when attending and one finds colleagues are also in attendance – arrange and communicate with others delegates, that you as a group will meet every evening, early 17.00 – 18.00 hrs, at a fixed social location to discuss the days’ proceedings – this I have found encourages greater friendships! Most conferences after 2 days tend to “drag on” – and there is a tendency to not attend with the same enthusiasm that one had initially, either the content has become less of an interest, bored, tiredness, jet-lag, or just “time to go home”!

During your career your reasons for attending meetings change – in your early career you just want to see, hear and maybe meet some of the authors that have impressed you during your reading or attempts at composing your obligatory publications! Mind you some of these “superstars” do not always impress as much when seen in the flesh!

Do not be shy when at meeting – if there is a presenter or identifiable author whom you would like to speak with – approach them when they are alone, seems to be looking about, maybe even seeking somebody they know, in summary they too are usually “bored” – go and introduce yourself! They are just as likely to be delighted to meet a “new person”! When introducing yourself, naturally start with name and status, with whom you work with/for or maybe you think that they are likely to know with whom you work locally or have worked for! Do not be surprised if they do not “instantly” know your local hero! A suggestion: “do not go on about how good/famous your mentor or “local hero” is, as they may not be known to them and by persisting will add to their embarrassment! By then they will have entered into conversation anyway! I would suggest if you are seeking to be remembered – an important question, seeking a position – a fellowship or even a short visit, then get some printed visiting cards with your name, qualifications, hospital address (home address they will not require!) with an e-mail and telephone number! If things work out they will exchange their card for yours – then should time allow write onto their card what you want them to do for you. When you get home send them a polite e-mail thanking them for their time, and remind them of what you discussed and what arrangements were thought to have been agreed! Add in your CV to support your planned request? Then wait! If things look good they will respond within 7 days – if no response after 4 weeks then things may not look so good? Try again or seek another position or establishment! Offering to visit for a few days if you are seeking a fellowship for 6 – 12 months is always a good move and is usually appreciated! Yes it cost money but a good investment for a better and likely more lucrative position!

One of the better ways to get noticed is to “present a paper” – these are usually peer reviewed and the process takes place many months prior to the date of the meeting. Ask your current boss, or if you are smart (well we all are!) you can see trends within the site specific journals on topics that seem to rotate every 4 – 6 years and repeats during your life-time! If you can spot one such topic and submit at the correct time then bingo! Otherwise hope that your boss knows somebody that is secretary or president! But generally if the topic is summarised and submitted on time then it’s likely to be accepted! Remember that some conferences and societies require that a manuscript of your presentation is presented prior to your presentation! I have seen a young trainee “publically embarrassed and not allowed to present” for not having his manuscript with him! And banned for 5 years of submitting again!

Another way is to get your boss and yourself to submit an instructional course” on his favourite topic – one in which there is adequate data and pictures to support whatever argument supports the practice, and the results! In the end a Plenary Session or a Keynote speech is a high accolade! Best is to be a Society Guest Lecturer or to be an Eponymous (Named after an important person) Lecturer – once or twice in a life-time is terrifying and usually an enormous honour! Occasionally the organisation will “cover the natural expenses incurred”! Much less frequently now-a-days than previously! Do not expect much when asked and seldom will the invitation be enhanced by demanding “appearance / performance fees”!

After a number of years as a consultant, and attending the same meeting on an annual basis, these sessions and meeting of friends becomes an event looked forward to! There is a need to “get a break” from work and going to some meetings become greater fun, more restful, than educational! But in the early years going to meetings needs to be worked upon!

Recommendation:

“Invest in your future when young, job satisfaction and rewards are there for the asking, it is better to achieve ambitions early than to regret your dissatisfaction about your eventual achieved status for the rest of your working life!”
Children with snoring: evaluation and management

Nigel KF Koo Ng MRCS, Haytham Kubba FRCS

Abstract
Snoring is a common problem affecting 12% of children in the UK. There is a continuum of disease ranging from simple snoring to obstructive sleep apnoea (OSA), all of which come under the umbrella term of sleep related breathing disorders (SRBD). OSA is a serious condition and identifying those children who have OSA from those who just have simple snoring is key. Delayed diagnosis of OSA has significant far reaching and potentially life-threatening consequences and therefore correctly identifying and appropriately treating patients with the condition is important. However, there remain many unanswered questions and as a result there is a wide variation in practice. Further research is needed to optimise the management of children with SRBD.

Key words
Snoring, obstructive sleep apnoea, sleep-disordered breathing, adenotonsillectomy.

Introduction
Snoring is a common problem affecting 12% of children in the UK1. There is a continuum of disease ranging from simple snoring to obstructive sleep apnoea (OSA), all of which come under the umbrella term of sleep related breathing disorders (SRBD). OSA is a serious condition with a prevalence of 1.2 to 5.7%2 and identifying those children who have OSA from those who just have simple snoring is key issue. Delay in diagnosis can result in significant morbidity including hypertension, cor pulmonale, pulmonary oedema, failure to thrive, neurobehavioural problems and poor academic performance.

OSA is defined as a disorder of breathing during sleep, characterised by prolonged partial upper airway obstruction and/or intermittent complete obstruction that disrupts normal ventilation during sleep and normal sleep patterns3. Upper airway obstruction can cause episodes of apnoea, hypopnoea and increased work of breathing as part of upper airway resistance syndrome. Simple snoring, on the other hand, is defined as snoring without obstructive apnoea, frequent arousals from sleep or gas exchange abnormalities4. Despite these formal definitions, differentiating OSA from simple snoring in clinical practice is not always straightforward. Although guidelines have been published in recent years, the diagnostic criteria are arbitrarily defined and the condition is still not fully understood.

In children, OSA has different clinical features and is managed differently from adults5. Risk factors for SRBD in children include adenotonsillar hypertrophy, obesity, craniofacial abnormalities and neuromuscular disorders. Physiological hypertrophy of the adenoids and tonsils occurs mainly between the approximate ages of 18 months and 6 years and is the most common cause of SRBD in children. In 80% of children with SRBD, adenotonsillectomy is an effective treatment6. However, not all children with adenotonsillar hypertrophy have OSA and this is thought to be due to differences in pharyngeal muscle tone and anatomy between patients7. In the vast majority of cases, OSA occurs in otherwise healthy children although there are certain groups of patients such as those with Down’s syndrome, micrognathia and craniofacial syndromes who have a much higher incidence of OSA.

Assessment of the snoring child:
An accurate assessment of the snoring child is essential in order to provide appropriate treatment to those children with OSA, to identify higher risk patients more likely to develop complications from treatment and to avoid unnecessary treatment in those without OSA8.

Although clinical history is a sensitive screening tool for OSA, it has a low specificity and does not correlate well to severity9. In clinical practice however, the most useful predictor of OSA is a history of heavy snoring with disturbed sleep, respiratory pauses and snort arousals10. Loudness of snoring does not correlate with the degree of OSA8. Specific points to cover in the history include:
Features of OSA – this can be divided into night time and daytime features.

• Night-time features which suggest a diagnosis of OSA include snoring with gasps, snorts, apnoeas, increased work of breathing, restless sleep and unusual sleep positions, for example with an extended neck position in an effort to improve the airway. There may be associated night terrors and secondary enuresis.

• Day-time features can be very non-specific such as hyperactivity, behavioural problems, poor concentration and learning difficulties with poor academic performance. In contrast to adults, daytime tiredness is not usually a predominant feature in children with OSA as children return much more quickly to the refreshing, deep levels of sleep (stages 3 and 4 slow wave sleep) after each arousal.

• Co-morbidities: Children with certain conditions such as Down’s Syndrome, Neuromuscular Disease, Craniofacial abnormalities, Achondroplasia, Mucopolysaccharidosis and Prader-Willi syndrome have a much higher incidence of OSA and it is also more likely to be severe. Previous cleft palate repair should be noted as these children are at greater risk of velopharyngeal insufficiency if they undergo adenoidectomy.

• Other ENT co-morbidities: The presence of other ENT conditions such as otitis media with effusion, recurrent acute otitis media and recurrent tonsillitis may influence the decision to proceed with surgery.

In addition to a full ENT examination, specific areas to cover in the examination include:

• General examination: Obesity is less common in children than in adults as a cause of OSA but it is becoming an increasing problem. In severe OSA, there may be failure to thrive and serious cardiopulmonary complications such as pulmonary hypertension, pulmonary oedema and cor pulmonale. Craniofacial abnormalities (e.g. retrognathia and midface hypoplasia) should be noted.

• Examination of the nose: In the clinic, this is usually performed using an otoscope or headlight and it may occasionally be possible to visualise the adenoids directly through the nose. However, this is uncommon and direct visualisation by nasendoscopy is often not tolerated, nor practical in clinic. There may be evidence of rhinitis secondary to adenoidal hypertrophy, with hypertrophy of the turbinates and thick nasal secretions. Adenoid hypertrophy is more likely to be the cause of nasal symptoms in pre-school age children rather than allergic rhinitis, whereas the opposite is true in school age children. There may be a septal deviation or other rarer abnormalities such as nasal polyps (suggestive of cystic fibrosis), tumour or choanal stenosis.

• Assessment of nasal airflow: This can be performed by looking for misting on a cold metal spatula. The presence of mouth breathing and quality of voice (in particular hyponasality) can further suggest nasal obstruction from adenoidal hypertrophy.

• Examination of the oral cavity/oropharynx: An assessment of the size of the tonsils should be made and any abnormality of the palate and uvula should be noted.

Investigations:

Polysomnography (PSG) is considered the gold standard for diagnosing OSA (Figures 1a and 1b). It provides a measure on numerous parameters including the number of apnoeas and hypopnoeas, which added together, provides the apnoea-hypopnoea index (total number of apnoeas and hypopnoeas per hour of sleep). PSG can be used to determine whether these episodes are obstructive or central in origin and also assess severity. One of the difficulties in managing OSA, however, is that it is arbitrarily defined and even within studies, there is variation in the interpretation of PSG results (for example the AHI criteria used for diagnosis and treatment of OSA). Adult criteria cannot be used in children.

The American Academy of Pediatrics guidelines recommends that PSG should be performed in all children with snoring and symptoms/signs of OSA. If PSG is not available then alternative tests include overnight pulse oximetry, nocturnal video recording, daytime nap polysomnography or ambulatory polysomnography. PSG is an inpatient investigation and in the UK there are insufficient resources to perform PSG in all children with suspected OSA at present.

Overnight pulse oximetry is much more readily available and can be performed at home but only provides information on heart rate and oxygen saturations. As not all apnoeas result in a drop in oxygen saturations, a normal study is not able to exclude OSA. The positive predictive value of overnight pulse oximetry for OSA however is very high being at least 97% whilst the negative predictive value is only 53%. It can therefore be used as a screening tool for PSG or surgery. However, there is wide variation in the utilisation of respiratory investigations across the UK. Some clinicians perform respiratory investigations in all patients whilst others may reserve investigations only for selected cases or perform none at all.
If there is clinical suspicion of OSA despite a normal oximetry study, some might consider referral for PSG whilst others might proceed straight to adenotonsillectomy (as OSA cannot be excluded on oximetry). Patients with suspected OSA and a positive overnight pulse oximetry result are highly likely to have OSA. They do not usually warrant further respiratory investigations and are likely to benefit from treatment. Further, the degree of abnormality on overnight oximetry can indicate severity of OSA. Some argue that as the severity of disease can be difficult to assess clinically, all children undergoing adenotonsillectomy for OSA should have pre-operative oximetry to ascertain the need for an HDU/PICU bed.

Patients with a pre-operative oxygen saturation nadir of <80% or baseline hypoxaemia should not undergo adenotonsillectomy in a DGH and should be referred to a centre with HDU/PICU facilities.

In 2009, there was a UK working party consensus statement which recognised that the decision to operate in patients with suspected OSA was a clinical one, based on severity of symptoms and complications. In straightforward cases of healthy children older than 2 years old with adenotonsillar hypertrophy, it is not unreasonable to proceed directly to adenotonsillectomy. However, in children with severe OSA, significant co-morbidity or where the diagnosis is not clear, the UK working party consensus statement recommends that these patients must be referred for pre-operative paediatric respiratory investigations.

**Indications for paediatric respiratory investigations**

- Diagnosis of Obstructive Sleep Apnoea unclear or inconsistent
- Age <2 years
- Weight <15 kg
- Down’s syndrome
- Cerebral palsy
- Hypotonia or neuromuscular disorders
- Craniofacial anomalies
- Mucopolysaccharidosis
- Obesity [BMI (Body Mass Index) >2.5 SDS (Standard Deviation Scores) or >99th centile for age and gender]
- Significant co-morbidity such as congenital heart disease, chronic lung disease
- Residual symptoms after adenotonsillectomy

**Treatment:**

In most cases, OSA in children is secondary to adenotonsillar hypertrophy and there is no underlying medical co-morbidity. Adenotonsillectomy is the most appropriate treatment in these cases and is effective in the majority of children. Many studies have shown an improvement in the symptoms and sequelae of OSA.

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**Figure 1a: PSG: Normal**
following adenotonsilllectomy including improvements in obstructive symptoms, growth, behaviour, academic performance, enuresis, the majority of cardiovascular complications and quality of life9.

Adenoidectomy alone is usually inadequate to treat OSA9. However, in children younger than 18 months where there may not be any significant tonsillar hypertrophy, adenoidectomy alone may relieve symptoms whilst avoiding the potential complications of tonsillectomy10. Over the next 2 to 3 years about 25% of these patients will subsequently need tonsillectomy.

In addition to the usual risks of adenotonsilllectomy including significant bleeding and pain, there may be respiratory complications following adenotonsilllectomy in patients with OSA. Post-operatively, there may be breathing difficulties and hypoventilation which may require additional oxygen and ventilator support. Some studies from North America have reported respiratory complications to be as high as 20-25%15-17, although these have involved patients with significant co-morbidities and with the diagnosis of OSA made on PSG6. This high complication rate has raised concerns about whether adenotonsilllectomy is safe to perform in district general hospitals. However, other studies involving patients with less co-morbidity and where the decision to operate was made on clinical grounds, have reported much lower levels of respiratory complications of 1.3% to 2.3%18,19. This is more likely to be the situation in the DGH setting and The UK working party consensus statement concluded that for the majority of children with SRBD, adenotonsilllectomy can be safely performed in a DGH. It also highlighted which patients are at higher risk of developing respiratory complications such as those with underlying syndromes, the very young or those with severe OSA. In these patients, adenotonsilllectomy should not be performed in a DGH, as there needs to be immediate access to an HDU/PICU.

**Children at risk from respiratory complications unsuitable for District General Hospital adenotonsilllectomy**6

- Age <2 years
- Weight <15 kg
- Failure to thrive (weight <5th centile for age)
- Obesity (BMI (Body Mass Index) >2.5 SDS (Standard Deviation Scores) or >99th centile for age and gender)
- Severe cerebral palsy
- Hypotonia or neuromuscular disorders (moderately severely or severely affected)
- Significant craniofacial anomalies
- Mucopolysaccharidosis and syndromes associated with difficult airway

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*Figure 1b: PSG: Obstructive sleep apnoea*
• Significant co-morbidity (e.g. congenital heart disease, chronic lung disease. ASA 3 or above)
• ECG or echocardiographic abnormalities
• Severe Obstructive Sleep Apnoea (described by polysomnographic indices including Obstructive Index >10, Respiratory Disturbance Index >40, and Oxygen saturation nadir <80%)

Obese patients with OSA and adenotonsillar hypertrophy can also benefit from adenotonsillectomy, although the benefit may be less than in healthy children. These children should also be recommended weight loss but as this is not instant, adenotonsillectomy should be undertaken in the meantime. High risk patients with OSA such as those with Down’s syndrome, Mucopolysaccharidosis and Achondroplasia may also benefit from adenotonsillectomy9.

Topical nasal steroids have been shown to reduce the number of apnoeas in patients with OSA over a period of 6 weeks20 and leukotriene antagonists (with or without nasal steroid) may also be of benefit21,22. The Royal College of Paediatric and Child Health recommends that in mild OSA or persistent abnormalities after adenotonsillectomy, nasal steroids and/or leukotriene receptor antagonists may be considered9.

In patients with OSA without adenotonsillar hypertrophy, The American Academy of Pediatrics recommends that other treatments such as non-invasive ventilation (NIV) should be considered2. However, assessment of the true size of the tonsils, particularly in the clinic, is very subjective and surgery may still be appropriate. NIV can be an effective treatment although this can be difficult to administer in children9. It should, however, be offered in cases of significant OSA, when surgery is contraindicated, in certain conditions such as neuromuscular disorders or when adenotonsillectomy has failed9.

Although, the natural history of SRBD remains largely unknown, simple snoring is considered by most to be a benign disease that often resolves with time and does not require any treatment23. However, it has been reported that simple snoring without OSA may be associated with neurobehavioral effects in some children24. That said, most would not recommend surgical intervention in children with simple snoring alone.

Conclusion:
The evaluation and management of the snoring child is important to correctly identify and appropriately treat those patients with OSA. Delayed diagnosis of OSA has significant far reaching and potentially life-threatening consequences. OSA in children was not widely discussed 10 to 15 years ago and there are still many unanswered questions. As a result, there is a lack of consensus and a wide variation in practice. Further research is needed to optimise the management of children with SRBD.

References:
Considerations for tympanic membrane repair in children

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Abstract
Surgical repair of simple tympanic membrane perforations is by way of a myringoplasty (Type 1 tympanoplasty) and is a commonly performed procedure in adults and children with a reported success rates ranging between 25 - 94% in children and 60 - 99% in adults. The lower success rate in children has been a focus of much research and debate in otology and there is little consensus on the definitive factors that can influence success.

The purpose of this review is to explore the most recent literature and give surgeons an up to date understanding of the important considerations when managing the child with a persistent tympanic membrane perforation.

Key words
Paediatric, tympanoplasty, myringoplasty, tympanic membrane perforation.


Introduction
Surgical repair of simple tympanic membrane perforations by way of myringoplasty (type 1 tympanoplasty) is a commonly performed procedure in adults and children with success rates of 25 to 94% in children and 60 to 99% in adults. The lower success rate in children has been a focus of much research and debate in otology and there is little consensus on the definitive factors that can influence success.

One problem is that definitions of success and length of follow up vary greatly in the published literature. Some studies only report on the repaired intact tympanic membrane, whereas others consider on going middle ear disease, quality of life outcomes and hearing improvement. A number of possible factors that may influence success have been studied including age of patients, perforation characteristics, the presence of otorrhoea at the time of surgery, previous adenoidectomy and health of the contralateral ear. Factors such as surgical technique and seniority of operating surgeon have also been implicated.

There are also important pathophysiological differences to consider in children due to immaturity of local anatomy and immune systems including eustachian tube function, adenoidal hypertrophy and pneumatisation of mastoid air cells. These factors all contribute to the increased incidence of otitis media in children which may compromise post-operative healing or lead to re-perforation.

Age:
The appropriate age at which to perform tympanic membrane repair has long been debated and much of the literature presents varying standpoints. In 1990 Koch et al. published a series of 64 paediatric tympanoplasties and concluded that repair of tympanic membrane only be performed on children aged 8 years or older. Age is the only factor to have been shown by meta-analysis of 30 studies to have an affect on outcome, with success rates increasing every year up the age of 13, however 25 of the 30 studies included in the meta-analysis did not independently report differences in success with respect to age, this could be due to them having insufficient power individually. In this meta-analysis the only parameter measured for success was tympanic membrane closure.

Over the last few years many publications have not supported the association of age with poorer success rates. In 2006 Albera et al. published a series of 212 patients who underwent myringoplasty, their study included adults (n=183) and children younger than 18 (n=29), they found no significant differences in rates of tympanic membrane closure amongst different age groups and concluded it could be performed in younger children with success equal to that of adults.

In 2007 Yung et al. published a longitudinal study of 51 first primary myringoplasties in children whom were followed up at 12 months post – operatively. Patients were divided into two groups according to age 4-8 years & 9-13 years. Success was determined as having an intact tympanic membrane without effusion, atelectasis or otorrhoea and with stable or improved hearing. The overall one year success rate by their criteria was 63.0% with 54.5% of the younger age group and 68.8% of children aged between 9 to 13 years were deemed successful.
However this difference was not considered statistically significant leading the authors to conclude that age does not influence surgical outcomes. Another study by Kumar et al. utilised near identical outcome measures for success as Yung at 12 months post-operative and found a similar overall success rate of 67.3%. In this study of 98 myringoplasties they also divided children into a younger group (<8 years) and an older group (>8 years). They did find that myringoplasties in younger children were more likely to fail (p<0.0047) however the sample of younger children was much smaller (n=20) than the group of older children (n=78) which may have affected statistical significance. In a further series of 213 myringoplasties published by Charlett et al. they demonstrated an increased success rate in older children, especially over the age of 10 (p=0.003), however they only measured success in terms of intact tympanic membrane and absence of middle ear disease with no analysis of audiological outcomes.

Sckolnick et al. in Pittsburgh published another large retrospective study of outcomes in 2007. They followed up 777 children who had undergone myringoplasty with gelfoam, paper patch, or fat graft. The mean follow up was 5.6 months and overall rate of successful tympanic membrane closure was 87.3%. Analysis of age and outcome using a logistic regression model found with each 1-year increase of age there was a 9% decrease in the odds of success however a more complex non-linear relationship was identified using loess smoother. This demonstrated that success rate decreases for every 1 year from the age of 1 to 9 years however beyond this point the odds ratio of success increases for each one year of age up the age of 18. In this paper they also established that increased numbers of prior tympanostomy tubes negatively affected closure rates. Therefore children who still require tubes at older ages, culminating in a myringoplasty, would be more likely to be found in the older spectrum of their data analysis.

Most recently Friedman et al have published a series of 119 patients who all underwent cartilage tympanoplasty. The children were divided into three age groups: Group 1 (<7 years), Group 2 (7-10 years) and Group 3 (10-13 years). An algorithm whereby children over 4 years of age with a contralateral normal ear were considered suitable for tympanoplasty determined timing of surgery. If the contralateral ear was abnormal they were treated appropriately and tympanoplasty delayed until the age of 16 years. In this series there was a mean follow up of greater than 1.5 years. The success rate for tympanic membrane closure was 95% with a statistically significant improvement in the air bone gap (p<0.0001). There was no difference with outcomes between the different age groups studied suggesting age is not relevant to timing of surgery.

The author’s suggest their regimented timing algorithm may have had a positive impact on their outcomes compared to other studies.

The evaluation of the most recent literature and other recent review articles still fails to find consensus on whether younger age should be a contra-indication to surgery. Most studies use the age of 8 years as a cut off as this is believed to be the age the Eustachian tube matures and hence middle ear ventilation will confer better results. It appears from the evidence available that age cannot be definitively proven to alter surgical outcome and should not override other clinical and technical factors that need to be taken into account when considering timing of myringoplasty.

Perforation characteristics and otorrhoea:
A small perforation in an easily accessible location is traditionally easiest to close. Anterior perforations are technically more difficult to access and adequately place grafts in good contact with the tympanic membrane. Repairing a perforation of a non-inflamed drum is also easier as bleeding is less likely to obscure the surgical view. In children the ear canal is proportionally smaller than the tympanic membrane compared to adults; this can pose challenges when grafting adequate tissue from the tragus. Two other recent publication’s of case series of paediatric tympanoplasties found that in their series anterior perforations were more likely to fail.

Two recent studies of 40 patients and 777 patients respectively have found no difference in outcomes based upon location of perforation repaired whereas Albera’s series of 212 patients actually found posterior perforation repairs were more likely to fail. In some of these studies approach and technique varied depending upon the location of the perforation so these factors could account for variation in findings.

Some recent studies assessing outcomes relative to perforation size in adults and children have reported that repair of perforations greater than 50% have a significantly lower success rate. Contrary to this a number of other studies specifically assessing successful outcomes of myringoplasty in children reported no correlation between perforation size and outcome. Whilst there is contrasting evidence it is the author’s opinion that the appropriate choice of surgical approach and graft material for the size of perforation can maximise the chances of successful outcome.

Many surgeons have long seen the presence of otorrhoea as an unfavourable circumstance for placement of a graft thus advocating treatment with topical antibiotics and
water precautions to achieve a dry, clean ear before undergoing surgery\textsuperscript{10,17}. The series published by Albera et al. in 2006 where autologous or homologous temporalis fascia grafting was used analysed prognostic factors for successful tympanic membrane closure including ototrrhoea and found no difference in successful closure\textsuperscript{4}, they also proposed that closure of a defect can favour middle ear normalisation. In a retrospective review of 1000 cases Dornhoffer found that a wet ear does not lead to an increase in surgical failure when cartilage is used as the graft material\textsuperscript{18}. It is hypothesised that cartilage as graft material rigidly fixates and is less likely to medially migrate\textsuperscript{9}.

The contralateral ear and adenoidal status:
As with other considerations in paediatric tympanic membrane repair there is considerable variation in views regarding the status of the contralateral ear, in the late 1980’s it was hypothesised that good contralateral ear Eustachian tube function predicted good surgical outcome, while poor tubal function was not necessarily an indicator of poor outcome\textsuperscript{1}. More recent studies have gone further to suggest contralateral diseases is a marker of poor outcome\textsuperscript{1}. One study found that when the contralateral ear exhibited perforation or retraction there was significantly lower success rate with good hearing\textsuperscript{17} whereas Collins et al cited contralateral negative pressure, effusion and atelectasis but not contralateral perforations as risk factors for poor middle ear ventilation on the operated ear after surgery\textsuperscript{19}. Another study proposed that tympanometric volume was a positive predictive factor for intact membranes at follow up as low volumes corresponded to a poorly aerated or diseased middle ear which can cause higher failure rates\textsuperscript{16}. In other case series’ of 212 and 40 patients no correlation has been found between contralateral ear status and outcomes of paediatric tympanoplasty\textsuperscript{4,13}. One important consideration raised by a recent review paper regarding contralateral ear status discusses the potential risks of performing tympanoplasty on a patient with a contralateral atelectatic tympanic membrane as ‘successful’ closure may result in bilateral atelectasis with potential for worsening of overall hearing\textsuperscript{10}.

Adenoid hypertrophy is associated with otitis media, peaking at age 3 to 5 years and regressing between 7 and 10 years 20. Adenoidectomy has also been shown to relieve middle ear effusions in small children\textsuperscript{21}. In Charlett’s series of 213 myringoplasties a history of previous adenoidectomy was studied to assess it potential differences to outcomes. 37.1% of children in this study had undergone prior adenoidectomy and in this group 79.1% were found to have an intact tympanic membrane free of middle ear disease at follow up compared to 67.4% in the non-adenoidectomy group, when analysed with multivariate logistic regression analysis this was not found to be a statistically significant difference \( (p=0.157) \) although the authors do comment that if the study had included larger numbers there may have been a tendency towards a significant difference\textsuperscript{7}. In another series of 777 paediatric patients undergoing myringoplasty they found no difference in rates of intact tympanic membranes in patients with intact adenoids, previously removed adenoids or those undergoing adenoidectomy at the time of myringoplasty\textsuperscript{8}. It appears at present there is no recent evidence to support adenoidectomy as a positive indicator of success in paediatric tympanoplasty.

Surgical technique:
There are a number of factors to consider in the surgical repair of the tympanic membrane perforation, the choice of approach and graft material have long been a topic of debate. These factors are likely to be affected by the site and size of the perforation along with the individual surgeon’s experience, preference, training and local case load.

A number of studies looking at postauricular and transcanal approaches have failed to find any variation in success rates\textsuperscript{16,19} whereas Albera et al found that a postauricular approach and general anaesthesia were predictors of success\textsuperscript{4}. There appears to be little evidence supporting any particular approach in type 1 tympanoplasty when there isn’t any significant co-existing middle ear or special anatomical considerations.

A wide variety of techniques can be used to repair the defect but most commonly either an underlay or overlay technique of grafting is used. In two published series of children undergoing both techniques they did not find a significant difference in outcomes\textsuperscript{19,22} whereas in one other series they found that an overlay technique had an increased successful closure rate\textsuperscript{4}. Another recently published series of 1000 myringoplasties found slightly better results for the overlay technique but a higher incidence of minor post-operative complications\textsuperscript{23}. The importance of the graft is to provide a scaffold for the TM to regrow over and it is vital that it is in good contact with the entire rim of the perforation in order to be effective. The characteristics of the perforations, graft material and surgical approach are all variables that will affect the outcome and ability to provide a good scaffold, therefore different techniques may be more appropriate for individual cases.

The use of temporalis fascia as a graft material has been shown to have excellent results in large case series of children with closure rates of 85 – 100% and significant improvements in hearing\textsuperscript{24,25}. Over the last decade or so
there have been a number of publications comparing cartilage and temporalis fascia in adults and children and it is now gaining acceptance as an alternative to fascia. In 2010 a literature review by Nicholas et al. proposed cartilage grafting in children was both a safe and effective technique with comparable audiological outcomes and superior perforation closure rates than temporalis fascia. This review only found four studies of level three or four evidence from which it drew the conclusion. Of three randomised control trials published comparing cartilage and temporalis fascia, two found the outcomes equivalent and one found better outcomes with cartilage grafting. A comparative study also demonstrated higher successful closure rates and equal audiological outcomes to temporalis fascia. The most recently published series of 119 children aged 4-13 years undergoing underlay cartilage myringoplasty reported a success rate of 95% and a significant improvement in hearing (p<0.0001) however their high success rates may also be attributable to the use of a rigid selection criteria prior to undergoing surgery. Most of these studies are single centre studies and individual surgeons training and experience will undoubtedly be a factor in the appropriate choice of graft material to ensure the best results at a local level.

There are a number of potential drawbacks to cartilage. Firstly there are cosmetic considerations, if a rim of tragus is not left intact when harvesting tragal perichondrium there could be a resultant deformity. It is also felt that the opaque nature of cartilage restricts the otoscopic view of the middle ear and tympanometric assessment cannot be accurately performed due to its effect on tympanic membrane compliance.

There are numerous other materials that can be used for graft material including fat and synthetic materials, there have been a number of recent publications of paediatric series demonstrating good results. Firstly Skolnick et al. report a series of 777 myringoplasties where they compared gelofom, paper patch and fat graft. They reported a success rate of 90.8% for gelofom which was significantly higher (p=0.001) than the other methods used, average follow up in this series was only 5.6 months and they do not consider audiological outcomes. In this series there is also no discussion regarding perforation size and the majority (634) of the procedures were performed at the time of retained tympanostomy tube removal suggesting they were predominantly smaller perforations. The authors also comment that three different surgeons were performing the procedures with different graft use preferences which may have influenced outcome, in addition others propose that adjuncts such as gelatin sponge and hyaluronic acid may contribute to middle ear adhesions and impair tympanomastoid ventilation. There are also proponents of fat graft myringoplasty, Saliba et al published a series in which they compared underlay, overlay and hyaluronic acid fat graft. Underlay and overlay techniques were performed with either temporalis fascia or tragal cartilage. They reported success rates of 85.7% for underlay, 86.5% for overlay and 87.0% for fat graft. Audiological evaluation also demonstrated a significantly greater improvement in the fat graft patients compared to overlay or underlay technique. Interestingly the fat graft procedures were performed under local anaesthetic with fat being obtained from a 5mm incision below the mastoid tip. Their exclusion criteria included patients in whom the anterior rim of the perforation could not be visualised which may have lead to some selection bias.

Conclusion:
There are clearly a number of considerations that need to be taken into account when assessing and deciding on the management of children with tympanic membrane perforations. Impact upon quality of life and development should be considered, evidence using health related quality of life questionnaires has clearly demonstrated that surgery can have a positive impact upon quality of life. Factors such as hearing aid use and swimming should also be considered in the decision making process.

In order to maximise success of repair the timing of surgery should be carefully considered, from the most recent evidence it certainly does not seem unreasonable to consider surgery in children younger than 8 providing there is not significant evidence of eustachian tube dysfunction or obstructive adenoidal hypertrophy. Both temporalis fascia and cartilage grafts have proven high success rates and equal audiological outcomes. Cartilage grafts may have some additional benefits for younger children given its likely resistance to re-retraction in the presence of persisting negative middle ear pressure. In children with cleft palate it is important to consider that Eustachian tube dysfunction persists longer through childhood and in Down syndrome anatomical challenges such as ear canal stenosis will have implications for surgery.

Overall, a comprehensive assessment of the child, careful timing of surgery and selection of appropriate surgical technique can provide excellent results both in terms of successful closure and improvement in hearing.

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Cholesteatoma in children: management strategies

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Abstract
Cholesteatoma is squamous epithelium and keratinocytes within the middle ear cleft and mastoid cavity. In childhood this can be a very aggressive disease causing erosion of the ossicles with concurrent otorrhoea and hearing loss. The aetio-pathogenesis of this condition is somewhat debated with congenital and acquired causes being purported. Management is surgical, the aim being to clear the disease, with a resultant ‘safe’, ‘dry’ ear. The two basic surgical techniques are the canal wall up and the canal wall down procedures. Once clearance of the cholesteatoma has been achieved reconstruction of the ossicular chain, if necessary, can be performed as a primary or a secondary procedure to attempt to improve hearing.

Key words
Paediatric, cholesteatoma, mastoid, canal wall up, canal wall down, Ossiculoplasty.


Introduction

Definition of Cholesteatoma
Cholesteatoma is squamous epithelium and keratinocytes within the middle ear. Essentially ‘skin in the wrong place!’ Cholesteatoma is a three-dimensional epithelial lined structure with an outer sac, termed matrix, and a keratinous inner layer. The matrix has a layer of sub-epithelial connective tissue and an inner layer of keratinizing squamous epithelium. The content of the sac is acellular keratin debris. The term cholesteatoma being a misnomer as it neither contains cholesterol nor is a tumour.

Paediatric cholesteatoma is generally deemed more aggressive disease than that of adulthood. There is usually an advanced stage of disease at presentation, a greater incidence of ossicular chain erosion and a higher recurrence rate after primary treatment.

The presence of cholesteatoma generally leads to continued malodourous ear infections; it is also a locally destructive lesion with the ability to erode bone through production of proteolytic enzymes, hence hearing can be affected, with destruction of the ossicles, and inner ear damage. Ear discharge and hearing loss are the two main modes of presentation of a child with cholesteatoma. Otoscopy (Picture 1) showing a cholesteatoma in a retraction pocket may be the ‘tip of the iceberg’.

Balance symptoms can ensue with erosion into the labyrinth. The course of the facial nerve through the middle ear makes it at risk from this destructive lesion with ensuing paralysis of the muscles of facial expression; ultimately erosion into the cranial vault can occur leading to intra-cranial complications. These are generally rare as first presentations in developed nations.

Picture 1: Left ear with postero- superior retraction pocket with cholesteatoma
Aetiology of Cholesteotoma

This paper is essentially concerned with the management of cholesteotoma in childhood. It is beyond the remit to discuss in detail evidence for and against aetio-pathogenesis of cholesteotoma but for completeness an overview of current theories will be described below. There are two main categories for the aetiology of cholesteotoma congenital versus acquired.

Congenital versus acquired

The patient having no previous history of ear symptoms such as otorrhoea, no history of otological surgery, no perforation of the tympanic membrane (TM) and a normal looking pars tensa and flaccida, with a pearly white mass medial to the tympanic membrane clinically defines congenital cholesteotoma. The question of how this got there is of some debate. Keratin cysts are thought to arise from a developmental abnormality, such as epidermal cysts, invagination of squamous epithelium from the developing ear canal, or possible ingestion of squamous elements in the amniotic fluid. Congenital cholesteotoma suggests a childhood presentation although this is not necessarily the case, patients may present in their fourth or fifth decade of life.

Acquired cholesteotoma is thought to occur through a number of aetiologies, a progressive retraction of the pars flaccida or tensa through Eustachian tube dysfunction, leading to a diverticulum. Keratin accumulates in the diverticulum, as normal migration is lost. The pars flaccida having less fibrous support is the ‘weakest’ area and thus is more prone to such invagination in negative middle ear states.

Migration of squamous epithelium through a TM defect is another proposed mechanism of cholesteotoma formation. The initial insult may be an episode of acute otitis media in which there was a perforation of the TM, or an iatrogenic cause such as grommet insertion and on extrusion the perforation fails to heal.

Another proposed mechanism is proliferation of the basal layers of the keratinizing epithelium of the pars flaccida. This is where the cells of outer keratin layer essentially ‘grow’ through damaged areas in the basal lamina. This is one theory on how cholesteotoma can form behind an intact TM. There is thought to be expression of various cytokines and adhesion molecules for this to occur, which may be initiated by inflammation, and infection within the middle ear cleft.

It has been purported that the simple squamous or cuboidal epithelium of the middle ear could undergo metaplasia if chronically inflamed. The transformation is to keratinizing epithelium thus giving the desquamated debris and keratin.

A final theory is implantation, for example at the time of surgery where keratinizing epithelium is introduced into the middle ear.

The vast majority (approximately 65 to 70%) of cholesteotoma in childhood are acquired.

Epidemiology

Cholesteotoma tends to affect between 0.5 and 2 children per 10,000 in most European studies with boys affected more than girls. Peak presentation occurs in the teenage years. As mentioned previously there is a difference between childhood and adult forms of the disease. Children by enlarge have greater spread within the middle ear cavity, with involvement the Eustachian tube.

Management

Pre-operative assessment

The ‘work-up’ for children will involve examination and audiological assessment in the outpatient clinic. Younger children may not tolerate aural toilet with micro-suction in the outpatient setting so an examination under anaesthetic (EUA) may be required. A computer tomography (CT) scan may be a useful adjunct as it can aid in identification of boney erosion, size and aeration of the mastoid cavity, status of the ossicular chain, course of the facial nerve and boney dehiscence, together with the integrity of the tegmen. A CT scan will have a high sensitivity for an abnormality (potentially cholesteotoma) but a low specificity, i.e. whether cholesteotoma, granulation tissue or fluid it is actually highlighting. Children over the age of 5 years generally do not need a general anaesthetic. We do not routinely use MRI scanning.

Surgical principles

Essentially the management of cholesteotoma is surgical. Surgery is to eradicate the disease and thus manage its potential complications. Medical therapy in the form of topical antibiotics and steroids, along with occasional oral antibiotics may have been used to treat a super-imposed infection but this will not clear the underlying disease.

Surgical options for treatment broadly falls into two categories; canal wall up (CWU) versus canal wall down (CWD) procedures. The role of treatment is to eradicate disease with subsequent conversion of a ‘wet’ ear to a ‘dry’ ‘safe’ one. With this over-riding aim as a focus, one can then consider hearing restoration techniques, which may be performed at the time of primary surgery, or at a later stage.
Another way of looking at surgery for cholesteotoma is to perform an anatomical dissection, which incorporates the disease removal versus an operation based solely on the disease removal, thus limited anatomical dissection. It is paramount that if surgery is to be successful the surgeon is armed with multiple techniques and adaptive to the findings. This article will attempt to explain various surgical procedures and produce an algorithm for paediatric cholesteotoma management.

Operative management

In all cases, preparation involves the use of facial nerve monitoring. It is, however, acknowledged that it might not reduce the incidence of operative palsy; monitoring is not a replacement to surgical knowledge and skill. Understanding of potential congenital anomalies regarding the course of the facial nerve is necessary.

The various approaches to mastoid and middle ear are well known. In children it would be our preference to perform a post-aural incision as it gives good exposure, easy harvesting of temporalis fascia and cartilage. A post auricular incision lends itself to subcuticular suturing, this obviously being advantageous in a child. It also reduces the problems associated with wound care sometimes encountered in end-aural or permeatal approaches - ultimately exposure of the disease is essential.

The superficial nature of the facial nerve in the young child must be kept in mind. To avoid unintentional injury, a post-auricular incision should be modified to avoid cutting near the junction of the tympanic ring and mastoid tip, and placing a finger over the area and incising more posteriorly if necessary should protect this area.

Canal wall up procedure combined with posterior tympanotomy can give excellent exposure to most of the middle ear cleft.

A simplified overview of the procedure will be given. Firstly, microscopic examination is undertaken to assess the areas or normality and demarcate the abnormality and if possible the status of the ossicular chain. A post-auricular incision is then made followed by dissection through to the bloodless plain just lateral to temporalis fascia heading towards the ear canal. Once the skin of the posterior canal wall is reached an incision is made along the inferior border of the temporalis fascia down to bone. A further incision is made counter to this to the mastoid tip. The periosteum can then be elevated exposing the mastoid bone with the key landmarks of the temporal line, and McEwen’s triangle. The posterior canal wall skin is elevated along with the TM to give trans-canal access to the middle ear. The cortical mastoidectomy can be performed keeping the posterior canal wall intact. The mastoidectomy needs to reach the tegmen tympani superiorly, the sigmoid sinus, the sino-duro angle and the posterior canal wall anteriorly (Picture 2).

By this stage the state of the ossicular chain and to a certain degree the extent of the disease is known. The cortical mastoidectomy can be extended to the root of the zygoma to gain access to the anterior epitympanum.

The surgical algorithm’s [fig 1 and fig 2] are used dependent on the state of the ossicular chain.

Where possible, if the ossicular chain is intact and the disease is lateral, and safely removable, then the ossicles can be retained. However, if the disease is medial it may be necessary to remove the ossicles and perform ossiculoplasty.

**Figure 1.** An algorithm for the surgical management of cholesteotoma if the ossicles are intact, depending on disease being lateral or medial to the ossicles, and ossiculoplasty may be needed.
be left in-situ without being dis-articulated. Care must be taken when drilling not to touch the ossicular chain as this could result in a sensorineural hearing loss. Disarticulation of the incudo-stapedial joint should be considered. In cases where the ossicles have to be sacrificed to gain access then the management is similar to the second scenario Fig 2. The first stage would be removal of the incus or its remnant, the next stage, when necessary is the removal of the malleus head. This also gives good access for removal of disease in the anterior epitympanum, and hence ventilation to the epitympanum and hence mastoid. Access to the middle ear through a posterior tympanotomy, allows access to the sinus tympani by both trans-mastoid and transcannal approaches. When the disease is deemed to be too extensive for a canal wall up procedure and clearance would be compromised then the posterior canal wall can be taken down.

**Ossicular issues**

The management of the transformer mechanism can be addressed at the time of initial surgery or in cases of ‘second look’. The basic principle of ossiculoplasty is to re-establish a connection between an intact TM and the foot-plate in the oval window. The most common place of ossicular erosion is the incudo-stapedal joint and lenticular process of the incus (80%). This can give up to a 60 decibel hearing loss meaning it is highly important especially in the paediatric population to try and correct. In cases where the incus has been eroded and there is no continuity with the stapes supra-structure, the author’s preference is to remove the incus remnant and head of the malleus and rotate handle of the malleus still connected by the tendon tympani, over the stapes (picture 3) and stabilized with small fascial patch. Other options are refashioning the incus to connect to the malleus or act as a PORP. Equally various prosthesis are available that can give reasonable long term results.

**Reconstruction issues**

The tympanic membrane can be reconstructed with fascia or cartilage or in combination (picture 4). It is important to reconstruct the attic and posterior canal walls with cartilage / bone pate, thus blocking the attic hopefully preventing retraction and recurrent disease. Development of a deep retraction pocket post surgery is potential for

**Picture 2:** An algorithm for the surgical management of cholesteatoma if the long process of the incus has been eroded and ossicular reconstruction is needed.

**Figure 2:**

**Picture 3:** The handle of the malleus has been rotated and placed directly onto the stapes.

**Picture 4:** Demonstrating the reconstruction with cartilage in place of the tympanic membrane and this can be covered with a fascial graft.
re-accumulation of keratin. The use of cartilage grafting + / – temporalis fascia for reconstruction of the tympanic membrane affords greater protection to this occurring than the use of fascia alone especially when the eustachian tubal function is poor.

Surgically disease in the anterior epitympanum and the lower sinus tympani would make recurrence rate higher in CWU procedures and thus CWD be considered\textsuperscript{10}. Certainly in those cases where the disease has been staged involving these areas a second look is always planned.

It is generally less desirable in children to have an open cavity. So when a CWD is performed primary reconstruction is attempted. The walls are either reconstructed using conchal or tragal cartilage or the volume of the cavity is reduced. Such obliteration is by harvested bone pate, which is covered by cartilage/fascia, temporalis muscle can be used. Foreign compounds such as hydroxyapatite can also be used to fill the cavity\textsuperscript{11} although they are rarely used in the authors practice.

Learning points

- Cholesteatoma can be an aggressive disease in childhood and surgery is the only method of clearance
- A canal wall up procedure is preferred in children as it prevents the formation of an open mastoid cavity
- A post-auricular incision allows good access and graft harvesting, being mindful in a young child not to extend too inferiorly for risk of facial nerve injury.
- A posterior tympanotomy allows facial recess clearance and access to the sinus tympani, an endoscope is a useful adjunct if there is doubt regarding disease clearance
- Reconstruction of the ossicular chain can be with autologous or prosthetic implants, being covered with cartilage and a fascial graft

Conclusion

Paediatric cholesteatoma can be an aggressive disease, causing much morbidity but rarely leading to life threatening complications. The management of this condition is primarily surgical with disease removal and ossicular chain reconstruction when necessary. Surgery for disease clearance falls into two main categories: CWU versus CWD procedures. In children the aim would be to try and keep the posterior canal wall intact to prevent the formation of a mastoid cavity, giving the possible problems of persistent discharge and needing regular aural toilet. Ultimately the type of operation chosen will depend on disease, patient factors and the surgeon’s preference.

References:

ENT issues in children with cleft palate

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Abstract
Children with cleft palate can present with multiple issues including hearing impairment, airway obstruction and difficulties with feeding. The involvement of an otolaryngologist in the multidisciplinary cleft team is essential to optimise the child's care.

Key words
Cleft palate, airway obstruction, feeding, hearing impairment.


Introduction
Cleft palate is the most common congenital craniofacial abnormality caused by abnormal facial development during gestation. Approximately 1 in 700 children born have a cleft lip, palate or both. This condition usually presents as an isolated anomaly but may be associated with other syndromes and associations (e.g. Stickler’s syndrome). The diagnosis of an orofacial cleft has significant implications for the child’s care. The current standard of care consists of a multidisciplinary cleft team which includes cleft surgeons (usually from maxillofacial or plastic surgery in the UK), an otolaryngologist, a craniofacial surgeon, a geneticist, an audiologist, specialist nurses, speech and language therapists, psychologists, orthodontists and dentists. The role of the cleft team is to provide a coordinated approach to the provision of the child’s care.

Epidemiology:
There are racial differences in the incidence of cleft lip and palate. Native Americans have the highest rate (3.7/1000 live births) compared to Afro-Caribbean (0.3/1000 births). Cleft lip and palate occurs about twice as often in males compared to females. However, isolated cleft palates are found more frequently in girls. Children born with cleft palate are more likely to have an associated syndrome than those who also have cleft lip.

Having a child with a cleft raises the recurrence risk for future pregnancies. The risk of a further child with cleft is reported between 2-5%. This risk increases to 10% if there is more than one person in the immediate family with cleft. Unaffected siblings of an individual with cleft have a 1% risk of having a baby with cleft. If a syndrome is associated, the risk of recurrence within the family could be as high as 50% if autosomal dominant. Genetic evaluation and counseling can provide information on specific recurrence risk for the family.

Risk Factors:
50-60% of cleft palate occurs on isolation. This is thought to result from the interaction between genes and the environment. Fogh-Anderson has reported on the role of genetic factors in the aetiology of cleft palate and lips. Most of the genetic studies carried out are based on segregation, allelic association and linkage analyses. Proposed aetiologies include single gene disorders, chromosomal disorders and polygenic interactions. Genetic factors contributing to cleft palate formation have been identified in most of the syndromes. Currently, there are more than 400 syndromes associated with clefting (Table 1). Cleft lip and palate and cleft palate alone are the most common syndromic cleft subtypes.

<table>
<thead>
<tr>
<th>Table 1. Common syndromes associated with cleft palate</th>
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<tbody>
<tr>
<td>Pierre Robin Syndrome</td>
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<tr>
<td>Velo-cardiofacial Syndrome</td>
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<tr>
<td>Goldenhar Syndrome</td>
</tr>
<tr>
<td>Stickler Syndrome</td>
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<tr>
<td>Treacher Collins Syndrome</td>
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<td>Van Der Woude Syndrome</td>
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Cleft lip alone is rarely syndromic. Environment factors such as maternal consumption of alcohol in the first trimester, smoking and anticonvulsants have been shown to increase the risk of facial cleft. Other factors such as seasonal conception, caffeine intake, organic solvent, nitrate compound exposure, maternal zinc level and pesticide exposure have also been studied (Table 2). The role of folic acid remains controversial. One study showed no significant reduction in the incidence with
additional folic acid in maternal diet\(^5\), another study showed a decrease in cleft lip in a folic acid treated population\(^6\).

**Diagnosis:**
Traditionally, the diagnosis of cleft lip and palate is made on clinical examination at birth. One exception is submucous cleft palate which is often diagnosed late when speech problem occurs in the form of velopharyngeal insufficiency (VPI). Early identification and treatment is vital before cleft type speech articulation becomes permanent. Recent advances in prenatal diagnosis such as the use of 3D and 4D ultrasound for evaluation of fetal face anomalies have allowed obstetrician to perform screening and offer antenatal counseling. Cleft lip can be accurately diagnosed as early as 13-16 weeks. Isolated cleft palate remains more difficult to be detected prenatally as it is dependent on the child’s mouth being open at the time of the ultrasound scan.

**Problems for the Neonate with a Cleft Palate**

**Airway:**
Neonates with cleft palate often have problems with feeding and airway management. Pierre Robin sequence, consisting of micrognathia, glossoptosis and cleft palate, is the most common craniofacial abnormality associated with airway problems. The small mandible results in displacement of tongue, which obstructs fusion of the posterior palatal shelves. This position of the tongue into the palate is thought to explain the ‘V’ shape in typical cleft palate versus the ‘U’ shape in Pierre Robin cleft palate. Respiratory compromise is often due to glossoptosis associated with micrognathia causing upper airway obstruction.

Treatment of airway obstruction in Pierre Robin Syndromic children are many and varied. A simple adjunct such as using a nasopharyngeal tube may be sufficient to improve the child’s breathing. This can either be premade or bespoke nasopharyngeal airway. A correctly placed nasopharyngeal airway will lie just above the epiglottis. This position can be confirmed by nasal endoscopy or X-ray.

In severe obstruction, a tracheostomy may be required. In the neonatal period, airway obstruction may be present from birth or progress over the first few months of life. It is recommended that cleft palate patients undergo some form of sleep study by 8-12 weeks of age\(^7\). The minimal study should be a TOSCA (continuous transcutaneous monitoring of oxygen and carbon dioxide saturations). These children are at increased risk of developing obstructive sleep apnoea, either immediately after cleft palate repair, or later in childhood as a new problem. Depending on the aetiology and extent of the upper airway obstruction, various management strategies may be involved (Table 3).

**Hearing:**
Children with cleft palate are more susceptible to middle ear disease and hearing loss. This is due to Eustachian tube dysfunction secondary to the malrotation of the palatal musculature.

All cleft children will have their hearing tested at birth as part of the universal neonatal hearing screening programme. The recommendation from the cleft and craniofacial review body are cleft children should receive regular hearing assessment. Often this would be at birth, at 6 months, at 1, 2, 3, 4, 9, 10, and 15 years of age and then at any other time as deemed appropriate by family or carers.

Chronic middle ear disease is also more frequent in these children, with cholesteatoma incidence thought to be as high as 10%. The risk for sensorineural hearing loss is identical to the normal population for children with non-syndromic cleft but is significantly higher in those with a syndrome, such as Stickler’s or velo-cardio-facial syndrome (22q11.2 deletion).

There are no consistent results from worldwide literature on the prevalence of otitis media with effusion. Management of this condition varies with different healthcare provider. In the UK, the Management of Otitis Media With Effusion In Children With Cleft Palate (MOMENT) trial is underway to identify the best treatment.
Current treatment options include hearing aids or ventilation tubes. Recent NICE guidelines suggest ventilation tubes should be offered as first line treatment in cleft children with otitis media with effusion\(^8\). Insertion of ventilation tubes at primary closure of the cleft palate should only be performed after careful otological and audiological assessment and is no longer considered routine.

**Feeding:**
The difficulty arising from feeding a baby with cleft palate is due to the baby’s inability to generate an adequate negative pressure. Due to the cleft between the mouth and nose, it is often difficult for the baby to maintain a seal. As a result, babies with cleft palate often struggle to breast feed. Most techniques to feed babies with cleft palate involve overcoming or supplementing the oral phase of swallowing, such as a Haberman feeding bottle or higher calorie feeds. Nasogastic ‘top ups’ may also be used. Gastrostomy is only used as a last resort in children whose feeding difficulty result from airway obstruction.

**Surgery:**
Operative procedures are often categorized into primary and secondary procedures. Primary procedures including repair of cleft lip and palate deformity are usually performed before 12 months of age. Secondary procedures are aimed at improving speech and facial appearance. These include pharyngoplasty, soft palate revision surgery and palatal fistula repair (Table 4). The timing of surgery for secondary procedures varies except for soft palate revision which occurs before the age of 3 to improve speech outcomes.

**Hard and soft palate repair:**
The exact timing and approach to hard palate repair remains controversial. A number of methods have been described including transposition of bipedicled or axial mucoperiosteal flaps that are based on the greater palatine vessels. Other described methods include the use of vomerine inferiorly or superiorly based mucoperichonial flaps. These flaps can be utilised either as part of single layer or more anatomical double layer repair. Hard palate repair can be performed at the time of primary lip repair, as part of a second procedure that follows on from a combined lip and posterior palate repair or as part of a single stage complete repair of the lip and palate.

At the centre of the debate around timing and approach to hard palate closure is the compromise between achieving a robust repair without the development of fistulas versus utilizing a technique that has minimal effect on the potential for mid face growth in both the anterior and transverse planes. Over the last 15 years following the publication of the Eurocleft study results, the UK cleft community has increasingly adopted the ‘Oslo’ protocol for repair of unilateral complete clefts. This protocol involves repair of the lip along with the anterior palate (utilizing a superiorly based vomerine mucoperichondrial single layer turnover flap) between 3 and 5 months of age with subsequent soft palate closure before the age of 12 months. However questions regarding this approach have been raised following the recent first oral presentation of the ScandCleft trial results. (12th international Cleft Congress)

The ScandCleft trial involves multiple parallel trials comparing a common arm of Lip and soft palate repair at 3-4 months followed by hard palate closure at 12 months with a delayed hard palate closure at 3 years, complete hard and soft palate at 12 months and the ‘Oslo’ protocol. The primary end points of the trials were speech and midfacial growth. The only significant findings reported to date indicate that delayed (at 3 years) hard palate closure is associated with increased articulation errors while early hard palate closure (at 3-4 months utilizing a vomerine flap) is associated with increase rates of transverse growth restriction (lesser segment malocclusion/cross bites) It is postulated that the healing of the vomerine flap donor area by secondary intention is the major determinant of the lesser segment issues.

In the UK, soft palate surgery is usually performed between 6 to 12 months of age. Most common technique include intravelar veloplasty (midline repair) and Furlow repair (Z plasty)\(^9\).

**Pharyngoplasty:**
When a child has symptoms of velopharyngeal inadequacy with or without cleft type speech characteristics, a palatal re-repair or lengthening procedure is considered prior to a pharyngoplasty in the first instance. If a pharyngoplasty is performed, then this may be done to augment the posterior wall or increase the sphincter tone constrictor of the pharynx. Common types of pharyngoplasty used include the Orticochea (dynamic sphincter) and Hynes (posterior pharyngeal wall).
Conclusion:
Clefts palate is a common congenital birth anomaly. Children with cleft palate present with a wide range of ENT issues. A multidisciplinary team approach is required to provide a coordinated approach to the child’s care.

Acknowledgement
We would like to thank Mr. Craig Russell, United Kingdom Interface Fellow In Cleft Surgery and Specialist Registrar In Plastic and Reconstructive Surgery for his kind contribution to this article.

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The current management of acute sinonasal infection in children

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Abstract
In children, acute bacterial rhinosinusitis (ABRS) is a common health problem, which has increased in prevalence and incidence, and although rare, it causes significant symptoms that can affect the quality of life and carries potential for a serious and life threatening complications. Bacterial rhinosinusitis usually follows a viral infection or allergic rhinitis. Early diagnosis and prompt effective antibacterial therapy is essential to shorten the duration of infection, hence severity of the illness. It also prevents the spread of the infection to the orbit or the cranium. Since signs and symptoms are overlapping, an accurate diagnosis poses a clinical challenge.

Infection with Streptococcus pneumoniae accounts for the majority of infections. The proper choice of antibiotic therapy depends on the likely pathogens, taking into consideration the anti-microbial resistance. ABRS has a potential to develop serious sequelae, thus vigilance among clinical staff is very important and multidisciplinary team approach is a prerequisite.

Key words
Rhinosinusitis, orbital complications, paediatric.


Introduction
Acute rhinosinusitis (ARS) in children (up to 15 years old) is defined as the sudden onset of two or more of the symptoms: discoloured nasal discharge, nasal blockage/obstruction/congestion and cough at daytime and nighttime for less than 12 weeks. Symptoms free intervals may exist if the problem is recurrent. Post-viral ARS is defined as an increase of symptoms after 5 days or persistent symptoms after 10 days. While acute bacterial rhinosinusitis (ABRS) is defined as the presence of at least 3 of the following symptoms or signs: discoloured discharge (with unilateral predominance) and purulent secretion in the nasal cavity, severe local pain (with unilateral predominance), fever (>38. C), elevated ESR/CRP and double sickening (i.e. a deterioration after an initial milder phase of illness)1.

Bacteriology:
The most common bacteria recovered from paediatric patients with ABRS are S. pneumoniae, H. influenzae, M. catarrhalis, S. pyogenes, S. viridans and in 8% the isolated bacteria are anaerobes. It’s polymicrobial in 30% of the cases1–7. The early phase of infection is usually viral which can last up to 10 days and it resolves spontaneously in majority of the cases; however a small number can progress to secondary bacterial infection caused by aerobes. Failure to treat this infection, anaerobes infection will take place over time8.

Diagnosis

History and physical examination:
Two common clinical developments should alert the clinician: (1) Signs and symptoms of a cold that persist beyond 10 days (any nasal discharge, daytime cough worsening at night) and (2) A cold that seems more severe than usual (high fever, copious purulent discharge, peri-orbital oedema and pain)9. Symptoms are often overlapping and vary considerably. Children examination may be challenging. Nevertheless the early diagnosis is key to effective management. Ideally a complete and a thorough general and head and neck exam should be undertaken following a good medical history, which should evaluate for previous history of sinusitis, upper respiratory tract infection (URTI), the potential of nasal foreign bodies, attendance of a day care nurseries, immunization, history of allergy, and exposure to cigarette smoke. Examination should include (orbit, vision and cranial nerve function etc). Anterior rhinoscopy may be performed using an otoscope. In children who are able to tolerate an examination of nasopharynx, it is advisable to complete the examination with fibro-optic-naso-endoscopy (FNE). Nasal swabs for culture are not considered essential unless there is a lack of response to medical therapy within 48-72 hours of treatment, or in immune-compromised patients,
whereby complications may ensue sub-clinically. Where a child may present with severe systemic illness and appear toxic, blood cultures may be useful.10-13

Imaging:
Imaging studies, such as plain radiographs and computed tomography (CT) are not necessary in non-complicated cases, since they are nonspecific and can not differentiate between viral and bacterial sinusitis.14,15

Differential diagnosis:
When a child presents with symptoms of ARS as listed above, the differential diagnosis must include: Intra-nasal foreign body, unilateral choanal stenosis, allergic rhinitis, other causes of facial pain, asthma, dental infection and adenoiditis. ARS is suspected when illness symptoms last more than 10 days. The role of nasal endoscopy is critical at this stage. The differentiation between adenoiditis and ARS in children can, however, be very difficult.

Treatment

Medical:
The goals of medical treatment of ARS are to eradicate infection, reduce the duration of symptoms hence the severity and to prevent any potential complications. Given evidence, albeit inconsistent, that antimicrobial therapy for acute bacterial sinusitis appears to significantly increase the likelihood of resolution of symptoms within 10 days. Authors recommend antibiotic therapy for 10-14 days. Amoxicillin–clavulanate (40 mg/kg/day or 80 mg/kg/day) was the first choice, consistent with Infectious Diseases Society of America (IDSA) and European Position Paper on Sinusitis (EPOS guidelines).1,19 Although there is no consensus regarding optimal duration, a course of 10 to 14 days is considered appropriate.19 Parents should be made aware of common side effects. Clinical improvement in general can be expected within 72 hours.20

If hypersensitivity is suspected, trimethoprim/sulfamethoxasole, azithromycin, or clarithromycin can be prescribed. Those who fail the first-line treatment should be prescribed a second-line treatment after discussion with the specialist microbiologist aiming at an agent with broad-spectrum activity against penicillin-non-susceptible S Pneumonia, ampicillin–resistant H influenzae and other beta lactamase bacteria. Although practically difficult, it advisable to obtain culture from the involved sinuses that failed to improve with empiric treatment.

Adjuvant therapy:
Intranasal steroid spray can offer a modest improvement with minimal adverse effect.21 It can be recommended if there is history of concomitant allergic rhinitis, however its delay onset of action and clinical improvement may take longer than 10-14 days. Nasal douching, antihistamines and decongestants have not been shown to have significant benefit.22,23

Surgical:
There is no role of surgery in uncomplicated cases of ARS/ARS

Complications:
Complications of ARS are rare and uncommon; however, some patients may descend into developing complications as a result of either an extending, untreated, inadequately treated, or partially treated ARS. Our preferred classification of sino-nasal complications would be as local (bony), orbital or intracranial. Orbital complications can often precede intracranial extension.

Orbital complications:
Authors emphasis on orbital complications with its management because of its serious sequelae, especially if the diagnosis is unclear. These cases can present with other serious complications such as meningitis, epidural/subdural abscess and intracranial abscess. In very rare cases there may be visual impairment, blindness and even death. Blindness can result from retinal artery occlusion, direct compression or inflammation of the optic nerve, corneal ulceration or pan-ophthalmitis due to an orbital inflammatory response. Infection most commonly spreads directly from the ethmoids through lamina papyracea, or via the communicating valveless blood vessels. It is unclear how common orbital complications are, as there isn’t a consensus in the literatures; nevertheless there is a large variation in presentation from 0.3 cases per month up to 1.31 in any specialist tertiary centre.25

Managing orbital complications
The key to managing the orbital complications is early diagnosis and treatment with a multi-disciplinary approach from the outset and identifying the differences between peri-orbital and orbital cellulitis (Table 1).

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<tr>
<th>Table 1: Factors differentiating peri-orbital from orbital sinusitis</th>
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<tr>
<td>Obvious external cause</td>
</tr>
<tr>
<td>Fever</td>
</tr>
<tr>
<td>Leukocytosis</td>
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<tr>
<td>Ethmoid sinusitis</td>
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To understand these two completely different conditions, one has to be aware of the orbital septum (Figure 1), which is a connective tissue structure that attaches peripherally at the periosteum of the orbital margin and inserts into the tarsal plate of the upper lid; it centrally fuses with the lid retractor structures near the lid margins, thus acting as a diaphragm and as a barrier to the penetration of infection from front to back. Infection anterior to the orbital septum is defined as pre-septal or peri-orbital cellulitis, whilst disease processes posterior to the orbital septum is described as post-septal or orbital cellulitis. Therefore, the etiology and management of these two conditions differs considerably.26 Patients with orbital cellulitis are systemically unwell, toxic, pyrexial and often irritable upon presentation. They can also present with erythema and induration of one or both lids, often respecting the orbital septum with significant pain on pressure over the lid. The globe may appear injected with significant pain induced upon eye movement. Infection may spread directly from the sinuses into the adjacent orbit but remain superficial to the periosteum as a collection- a subperiosteal orbital abscess (SPOA) (Figure 2). This can cause exotropia, proptosis and restriction of eye movement.

Chandler et al in 197027 proposed a classification of orbital complications, which included the following:

1. Group I – Preseptal cellulitis
2. Group II – Orbital cellulitis
3. Group III – Subperiosteal abscess
4. Group IV – Orbital abscess
5. Group V – Cavernous sinus thrombosis

Jain and Rubin in 2001 simplified this classification28:

1. Pre-septal cellulitis
2. Orbital cellulitis (with or without intracranial complications)
3. Orbital abscess (with or without intracranial complications)
   a. Intraorbital abscess, which may arise from collection of purulent material in an orbital cellulitis
   b. Sub-periosteal abscess, which may lead to true infection of orbital soft tissues

An orbital cellulitis is an emergency that requires an immediate attention of the multi-disciplinary professionals (Paediatrician, Otolaryngologist, Ophthalmologist and Microbiologists) and it requires an urgent referral/admission to the hospital. Given the uncertainty and the difficulty in differentiating between peri-orbital and orbital cellulitis, the majority of these cases may need admission under the paediatric service and the commencement of intravenous antibiotics. Medical management may take effect within 12 hours to 36 hours; therefore, initial observation of a decline in the signs and symptoms may be expected.

When a CT Scan is showing evidence of a collection or deteriorating vision, or non-improvement despite adequate medical treatment, surgical intervention must be considered. Upile et al24 in their study emphasises that Magnetic Resonance Imaging (MRI) may be required as an adjunct to CT if intracranial complications are suspected.

The goals of any surgical intervention are to drain the pus, obtaining a culture and release any pressure on the orbit.
Understandably, Endoscopic Sinus Surgery (ESS) in acutely infected patients is difficult because of the bleeding that may impair the surgical field visibility.

However authors still advocate endonasal approach in the following selected cases:
- If an experienced endoscopic sinus surgeon is available.
- Being able to locate the site of the pus accurately on CT (small-medium subperiosteal medial abscesses).
- Nevertheless, the surgeon should be prepared to opt for external approach if endonasal approach proved to be unfeasible.
- Non-medial subperiosteal or intraorbital abscess are best drained by external approach (Table 2).

**Management of Inpatient Paediatric Peri-Orbital Cellulitis**

This care pathway is a framework of key steps in the management of peri-orbital/orbital cellulitis in children, with the necessary first-line investigations and treatments.

Children may enter this pathway after referral to different teams e.g. A&E, ENT, Ophthalmology, General Paeds or I.D.

This pathway does not replace sound clinical judgement but it will help us to make sure that all relevant teams are involved at an early stage to optimise care for both systemic and operative interventions.

**Fig 3: Management of Inpatient Paediatric Peri-Orbital Cellulitis**
There are some evidences that medical treatment can cure less than 4 mm on CT medially located (SPOA). As mentioned above, loss of visual acuity, non-medial abscess, clinical deterioration and failure to improve within 48 hours of antibiotic treatment can be considered as criteria for surgical treatment. In the absence of these criteria, a trial of antibiotic treatment can be considered with a strict close MDT monitoring of the patient. Oral antibiotics may need to be continued post-operatively for at least 10-14 days to ensure a complete resolution of the sinusitis. Ancillary therapy like topical nasal steroid and nasal decongestant may also be needed. It is important to be aware that almost half of patients with intracranial complications of ABRS may present with a periorbital cellulitis or abscess.

It is apparent from several reviews that the criteria for referral to ophthalmologists or ENT surgeons are unclear. More importantly, there is no clear indication as to why certain patients received a CT scan and what specific settings were requested. In an audit done at an authors’ trust, a group of 25 patients (17 had surgery) were presented with a history of orbital cellulitis between the years 2010-2012.

For audit purposes, we applied the following standards:

1. Paediatric lead
2. Ophthalmology opinion
3. ENT senior opinion
4. Blood test
5. Pre antimicrobial microbiology
6. Ceftriaxone and Metronidazole and decongestant pending microbiology
7. Twice-daily assessments of colour vision, acuity, eye movement, pupil reflexes (hourly if gross proptosis or ophthamoplegia)
8. CT scan indication:
   - Central signs
   - Unable to accurately assess vision
   - Gross proptosis, ophthamoplegia, deteriorating visual acuity or
   - Colour vision, bilateral oedema
   - No improvement or deterioration at 24 h
   - Swinging pyrexia not resolving within 36 h.

Although no harm occurred to any of our patients, neither of them fit all these criteria in combination. Thus we proposed the following algorithm to help junior clinicians to be vigilant when it comes to dealing with ABRS orbital complications (Figure 3). This algorithm should provide a clear pathway to the management of sinonasal/ orbital complications. We are aware that many departments have created their own algorithms to initiate safe and clear guidance of practice with the initiation of a multidisciplinary approach from the outset, and that should be the case even though clinical symptoms sometimes do not correlate well with the severity of the disease.

**Conclusion:**
Viral infection of URT is the most common presentation of ARS and most of the cases resolve spontaneously. Diagnosis is based on history and examination. However, diagnosis can be a challenge due to symptoms and signs. Patients who develop ABRS, an early and appropriate course of antibiotics directed against the most common pathogens is essential, taking into consideration antibiotic resistance and hypersensitivity reaction. Ancillary therapy can also be useful. There is no role for surgery in uncomplicated cases of ABRS. If complications happen then a serious sequelae is likely to result, thus an urgent recognition is required and prompt treatment under a pre-assigned MDT.

**References:**
Iatrogenic facial nerve paralysis in mastoid surgery

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Abstract
Facial nerve damage in mastoid surgery may be the immediate result of trauma in soft tissue dissection, inadvertent burr contact or a delayed phenomenon due to nerve oedema. It is avoided by a thorough knowledge of facial nerve anatomy, recognition of predisposing risk factors in disease and modern tools for imaging and monitoring. Early diagnosis and expert management is essential if disfigurement and handicap is to be minimised.

Key words
Facial nerve paralysis; iatrogenic; mastoidectomy complications.


Introduction
A facial paralysis as a result of mastoid surgery is the complication most dreaded by surgeons operating on the middle ear or parotid area and one which we all hope to be spared. If not corrected in good time, the resulting disfigurement, the obvious loss of facial expression, so fundamental to our personality and communication, is a disaster for the patient. If resulting from excision of a parotid tumour, even a benign adenoma, it somehow seems more acceptable a risk than following surgery for this strange concept of cholesteatoma, so foreign to most lay folk. Curiously it is suggested that the risk is greater in maxillofacial procedures and especially in TMJ replacement, so otologists should not feel unduly persecuted1.

Despite technical advances in imaging, monitoring and repair, the best protection is still familiarity with the anatomy of the facial nerve, appreciating which procedures carry the greatest risk, operating in safe fashion, recognising when things have gone wrong and knowing how to proceed in that event.

High Risk Procedures;
Although a high speed cutting burr is a truly fearsome tool adjacent to the facial nerve, there are probably as many palsies caused by dissection of cholesteatoma or granulations, producing traction on the nerve.

Even a simple post aural incision in the newborn can divide the facial nerve trunk as the mastoid process is underdeveloped and the stylomastoid foramen is located subcutaneously. Posterior tympanotomy, as for cochlear implantation and often in tight acellular mastoids, forces the operator to deliberately drill close to the descending nerve trunk. The chorda tympani suffers trauma in many an otologic procedure, whether drilling or not, but fortunately with less dramatic consequences2. However, it has been hypothesized that facial nerve palsy has occurred due to back bleeding into the nerve trunk after transection of the stapedius and the chorda tympani (MH, Personal communication John Groves)

A loss of surgical anatomy and landmarks is expected when performing surgery in patients with atresia or exostoses and, especially, in revision mastoidectomy. The facial nerve may well run an anomalous course (especially in the congenitally abnormal temporal bone) and just about every pattern of division and relationship to the oval window, lateral canal etc has been described.

The nerve should normally lie safely in its Fallopian canal, but minor degrees of dehiscence are identified almost universally, even in healthy ears. A few millimetres in most cases, these appear especially over the oval window, in the region of the second genu or in the anterior tympanic space adjacent to the processus cochlearformis. A major exposure may be evident on CT scanning, but the image sensitivity and specificity is poor. Cholesteatoma surgery on a patient with a pre op facial palsy should be a very relaxing undertaking, as exposure is to be expected and surely one cannot make things any worse. There is a pitfall here however. Always consider the “fistula/facial” association. The patient with a palsy has a higher risk of a fistula into the lateral semicircular canal. If unrecognised during surgery, the result could be a deafer, dizzy and a permanently palsied patient post op! The same association
warns us that the patient with the nystagmus on raising middle ear pressure, surely also has an exposed facial nerve trunk. Worse still, that guardian landmark of the second genu, the prominence of the lateral canal may now be a concavity. The nerve may well be the more lateral of the two.

**Surgical error;**

It may seem counterintuitive to suggest that length of a surgeon’s experience may be a relatively minor factor. Trainees, short of accreditation must, in these authors’ opinion, be supervised during procedures that risk facial nerve injury, resulting in paralysis. It is often said that it is the qualified surgeon, at the two extremes of a career, that encounters the most surgical complications in any field.

In routine surgery a common error is to immediately tackle the obvious pathologic disease process, failing to first find the facial nerve in a relatively safe area, and then follow its tympanic course. Exploration should therefore start safely in the anterior attic and, by dissecting posteriorly, find the entry point of the nerve above the processus cochleariformis. The digastric ridge is equally valuable in leading to the stylomastoid foramen and the facial nerve’s exit. If the facial nerve has been identified in the region of either of these basic landmarks, it may still be permissible to damage a nerve that is dehiscent or running an anatomically abnormal course.

In the transmastoid approach to the antrum, the finding of a low dura can drive the surgeon progressively more inferiorly. Fear of dural damage and the resulting uncontrolled “irrigation” of the cavity may send the unwitting surgeon into a far more dangerous territory, the second genu and the descending trunk of the facial nerve, the most common site of iatrogenic injury. The combination of a left ear, low dura and a right handed surgeon can require some contortion to stay high when approaching the tegmen.

**Surgical Tips;**

In drilling, use the largest possible burr and avoid pressing on the bone using the tip (which achieves nothing useful) but instead use the side of the burr. Avoid over heating the drilled bone by use of copious irrigation and favour using cutting burrs. However, we must accept that a diamond burr will (possibly anyway) do less damage to the facial nerve trunk, if contact is made. The use of either burr heads has its proponents. The cutter keeps air cells empty and the bone relatively translucent. The bone dust of the diamond fills the cells, renders the bone more opaque, whilst also heating it. Whichever you use in the danger areas, use the drill working from within outwards and parallel to the expected course of the facial nerve trunk.

When removing diseased soft tissue, curiously, sharp dissection with needles is considered safer than the risk of traction associated with blunt elevation and use of a dissector. Again, work parallel to the nerve and remember the fistula/facial association.

**Recognise the nerve;**

Hopefully the reader does not need an anatomical account of the location of the processus cochleariformis, the oval window, the lateral canal, the second genu, the chorda, the pyramidal eminence and the stylomastoid foramen. If he/she knows ear anatomy, the operator should appreciate where the facial nerve is supposed to be. There are some confirmatory features (vessels, air cells etc) to help with identification, but these are best appreciated in the pneumatised, blood free cadaveric temporal bones - unfortunately.

**Nerve Monitoring;**

Swan, Narula, Hawthorne and Flood represent the dinosaurs who still argue that nerve monitoring is not essential in “routine mastoid surgery”. They will probably concede that
for high-risk cases and accept that trainees now feel distinctly uncomfortable without the nerve monitor being used as a routine. The argument that it can do no harm is widely held, but is worth considering further!

Nerve monitoring must be distinguished from the use of a nerve stimulator, of which more anon. EMG electrodes on the orbicularis oculi and oris, with a common ground, will passively sit there awaiting some insult from the unwitting surgeon and will warn one that surgery is being performed in the wrong place or doing the wrong thing. The stimulator requires that the surgeon be alert to this risk and make a conscious decision to check it by picking up this instrument and applying it.

All proponents of monitoring stress that it is no substitute for a sound knowledge of temporal bone anatomy and practice of temporal bone dissection. The sceptics will further point out;

- The signal may come too late or never. One author (MH) notes that, in his medico-legal practice, his last three cases advising on facial nerve paralysis all involved use of monitors. A signal requires a functioning nerve. Traction or early nerve bundle trauma with the drill should produce the characteristic tone burst. A complete transaction is greeted with stony silence. Monitoring is probably of greater value in soft dissection than in bone drilling.

- Complacency. The idea that what I am doing to these granulations must be safe, drilling down this long dark hole must be OK, as I hear nothing........I’ll just carry on.

- “The wretched thing keeps going off and I am sure I am nowhere near the nerve” (almost certainly true). Pearl Harbor 1941 was the classical illustration of the perils of new monitoring technology. A signal that makes no sense, as it is too big, has never been encountered before and it is a Sunday morning, so switch off the radar and go for breakfast.

- Warn the anaesthetist. Neuromuscular blockade at induction of anaesthesia prevents and EMG activity of course. If it has been used, the anaesthetist might be asked to confirm it has worn off by ulnar nerve stimulation.

- Diathermy. Even bipolar diathermy can upset monitors. A wise surgeon leaves the face exposed but covered with a clear adhesive drape to observe facial movements (but the poor scrub nurse has enough to do already).

- Cost. Leads are disposable and costly. Litigation and compensation averages at about £100,000 per incident and leads cost approximately £50, so one would need to palsy roughly 1 in 2000 ears negligently, to if one was to try to make a purely financial case. There are papers that look at this in more detail which include hidden costs of facial palsy and produce an elegant argument that routine facial nerve monitoring is financially sensible. MH feels that probably the greatest argument is to monitor those with the most expensive face however, clearly, there is an ethical argument against this. Although some years ago, it is worth noting that the RCS national audit reported a remarkable 0.8% rate, possibly influenced by a small study population of 55 surgeons and only 611 operations.

- Availability. Our UK nuclear deterrent requires four ICBM submarines to keep just one “boomer” at sea permanently, around the clock. All technology needs service and repair. Neurosurgeons and Otologists will compete for the sets that remain. An ENT colleague recently found the only remaining monitor was unserviceable, fortunately before induction of anaesthesia and felt ethically unable to proceed with the mastoidectomy. Op postponed........

The counter argument is that, when used appropriately, it gives an extra level of security. It is a passive observer that may warn you that you are going wrong! If it is to be used in special cases, then it is best to be totally familiar with the technology, so use it for all. Routine operations have a way of turning “special” with little warning.

The nerve stimulator is curiously overlooked, despite reliability and low cost. It requires surgical suspicion and a decision to apply it, but a response does find the nerve, even if the mastoid segment does require more current than the proximal nerve, in the internal auditory canal IAC. If there is nerve damage, progressive application along the course of the nerve, working distally till a response is obtained, identifies the site of lesion during a three day window of opportunity. Ingenious designers have of course now combined the two, manufacturing surgical tools which provide constant electrical signals for nerve stimulation, while the monitor watches over the whole process.

Now, what if despite all this the worst has happened? Facial nerve damage and/or paralysis may be immediately recognised at surgery, only discovered on recovery from anaesthesia or present as a remarkably late phenomenon (even at 10 days post op).

**Damage immediately recognised:**
Keep calm and that is not easy. At least you did spot the problem, which required a degree of competence. Stop
the operation and irrigate the cavity created. Call for expert help, if immediately locally available; if not, at least ask a colleague to confirm and document your findings. Use any video or photographic assets you have to record your handiwork and misfortune. Whether to complete the operation depends as much on your resilience under terrible pressure as your level of experience. You will not now be at your surgical best. Can your friend take over?

A bruised, oedematous, exposed nerve obviously carries a better prognosis than two stumps. Despite lack of any evidence for systemic steroids, IV dexamethasone can do no harm, in most cases. Use that stimulator proximal to the injury and, if you get facial movement, great the response with prayer to your God. You may still be tempted to incise the sheath, and should certainly do so if there is no response. Partial nerve section of the trunk may be salvaged by approximation of nerve fibres, even in inexperient hands.

The challenge is complete transection. The need for a donor graft requires exceptional surgical expertise, harvesting and sacrifice of other nerves and all without explicit patient consent. The everyday otologist is best advised to wake the patient, explain what has happened, what can be done with informed consent and seek expert help. The subsequent surgery itself is well documented, with freshening of the nerve edges, harvesting of the sural nerve, lateral cutaneous nerve of the thigh or greater auricular nerves and suture anastomosis. The former can produce a longer cable graft and only produces a minor area of anaesthesia on the lateral lower leg. The last is the ideal diameter and near to hand of course. A House Brackmann of Grade III at 12 months is the best that can be expected.

**Recognition immediately post op:**
Facial nerve function must be checked at the earliest opportunity in recovery and documented in the patient’s clinical notes and signed. If the surgeon can honestly say that the face was moving, even temporarily, then subsequent management is based on the conviction that nerve is still in continuity. Beware of delusion and confusing contralateral movement for a flicker of function on the operated side. Remember that a functioning occulomotor nerve can still allow some degree of eye closure, by relaxing the levator palpabrae superioris!

Keep calm and again discover the power of prayer. So often this is just the result of overuse of local anaesthetic infiltration in external soft tissue dissection. In an hour or two all will surely be right....

Traditional advice is also to at least loosen any packing, possibly disturbing all your careful grafting in the process? If there is no recovery then radio opaque packing, such as BIPP, should be removed and the cavity cleared. Seek expert help. A CT scan may help identify the site of lesion. Electroneuronography is of value in estimating the degree of nerve degeneration. If greater than 95% at 6 days, our advice is re-explore. If there is < 95% nerve loss, but then no recovery at 16 weeks, perform an EMG. If this shows no reinnervation potentials, re-explore now.

All too often the expert is called in after that six day threshold. Much then relies on the records and reliability of the operation notes. If of poor quality, consider exploration now. Often the note says that the surgeon was sure the nerve was intact at the end of surgery, so they are sure exploration is not necessary. This overlooks the potential for major thermal or traction damage, which might still be salvaged by early decompression of the sheath. With later expert involvement, if CT suggests the nerve canal is intact, wait until 16 weeks to check the EMG as above. If there are no reinnervation potentials, explore. If a better outcome, repeat at 20 weeks and determine which areas are showing recovery. Innervation of the orbicularis occuli and major muscles of the lips take priority and lack of recovery here again could prompt reoperation.

**Delayed facial palsy:**
A recognised phenomenon in neurosurgery as much as simple otology, this surely represents viral reactivation rather than very late onset nerve oedema. Management is as for Bell’s palsy, but there may yet be a stronger case for antiviral therapy in this situation8.

**Conclusion:**
It is far commoner to find that litigation centres on inappropriate management of the injury rather than the
fact of surgical nerve trauma itself. The consent form should document the risk, however low the rate, as it is of material importance to the patient. The information leaflet (please use and document it; this at least as important as your nerve monitor) should at least touch on what might be done in the event, if only saying “further surgery might be needed to ...”. It would be excessive to suggest that every consent form says "you might awake with scar on your ankle, should we prang the nerve because we need to..."

Above all do not avoid your complications. It is human nature to keep off the ward and dodge the patient whose smile or frown reminds you of the damage done. “Phone a friend” is that game show phrase, seek help, be open and honest and appreciate why you pay those increasing annual defence society premiums.

References:
Intratympanic pharmacology for dizzy patients

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Abstract
In this paper we discuss the current use, delivery methods and success rate of intratympanic pharmacology for the treatment of vertigo. This includes the use of aminoglycosides and steroids for the treatment of Ménière's Disease as well as the novel use of intratympanic aminoglycosides for other conditions.

Key words
Management, Vertigo, Intratympanic, Aminoglycosides, Steroids.


Introduction
Peripheral vestibular pathology can be challenging to treat. Whilst most patients can be managed in a conservative fashion some fail to respond to medical treatment. Patients whose symptoms are not controlled by conservative measures have the options of surgery or intratympanic treatment. Compared to surgery, Intratympanic treatments are less invasive and do not typically require an in-patient stay. Intratympanic treatment also does not preclude later surgery so this option still remains if relapse occurs. As with any intervention designed to influence unilateral vestibular function, before injection the clinician must be certain of the diagnosis and certain which ear is active.

In this paper we will discuss the current indications, techniques and outcomes of intratympanic therapy to treat vertigo.

Intratympanic treatment of Ménière's Disease
Two drugs have been used for the control of vertigo in Ménière's Disease:

- Intratympanic aminoglycosides (gentamicin)
- Intratympanic steroids (dexamethasone)

Both medications have been deemed safe and acceptable methods for treating Ménière's Disease in a recent Cochrane review, although there is a risk of hearing loss using gentamicin and there is only limited evidence for the use of steroids.

<table>
<thead>
<tr>
<th>Uses of intratympanic treatment for vertigo</th>
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<tr>
<td>Unilateral Ménière's</td>
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<td>Bilateral Meniers (active side known)</td>
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<td>&quot;Pre-habilitation&quot; prior to any surgery that will result in a possible vestibular upset</td>
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<tr>
<td>Medically unfit patient with CPA tumours</td>
</tr>
<tr>
<td>Delayed endolymphatic hydrops</td>
</tr>
<tr>
<td>BPPV unresponsive to medical treatment and unfit for surgery</td>
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<tr>
<td>Post stapedectomy vertigo</td>
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<td>Vertigo following idiopathic hearing loss</td>
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Table 1: list of inner ear pathology from common to rare, in which intratympanic therapy can be utilized to alleviate the symptoms of vertigo.

Intratympanic Aminoglycosides
The aim of this therapy is to cause a degree of paralysis of the diseased labyrinth such as to stop the fluctuating malfunction of the labyrinth resulting in the Ménière's vertigo attacks. The treatment also aims to create a lasting situation of stable hypofunction from which the brain can compensate and provide relief from symptoms of persistent imbalance. This chemical ablation of the labyrinth has some advantages over the classic surgical ablation (labyrinthectomy, vestibular or cochleovestibular nerve section): it can be performed in the outpatient clinic under local anaesthesia, so no major surgery is necessary and gentamicin is more vestibulotoxic than cochleotoxic, so preservation of hearing can be achieved.

This vestibulotoxic effect of aminoglycosides was first used by Fowler in 1948 to treat vertigo. Following that, in 1956, Schuknecht became the first person to use intratympanic streptomycin for patients with unilateral Ménière's Disease. His success rate controlling vertigo was 62% but most of the patients had hearing loss.
Once instilled into the middle ear, gentamicin diffuses into the perilymph and endolymph through the round window membrane. Within the vestibule, type I cells are more susceptible than the type II cells. In low doses gentamicin also affects the vestibular dark cells thus reducing the production of endolymph, which is probably responsible for the reduction of vertigo in Ménière’s patients.

The precise action of cellular damage by gentamicin is unknown. Damage may be caused by binding to plasma membrane phospholipids, inactivation of cellular enzymes or binding with iron to form reactive oxygen species and free radicals. All of these processes result in ultimate cell apoptosis and necrosis.5

**Delivery Methods and Dosing Regimes**

Numerous methods have been used to deliver gentamicin including:

- Direct injection using a fine bore needle
- Tympanostomy tube (Injection or drops)
- Surgical catheters
- Silverstein MicroWick

Although in all techniques gentamicin is applied into the middle ear, great differences exist in the number of applications and the amount of gentamicin used. This can be largely categorised into four different groups:

- High dose technique- multiple daily dosing in which three daily doses of gentamicin are given or weekly injections given for four weeks
- Low-dose technique in which one or two injections are given with repeat treatment only for recurrent vertigo
- Continuous microcatheter delivery
- Titration technique in which daily or weekly doses are given until onset of vestibular symptoms, change in vertigo symptoms, or hearing loss occurs.

No consensus exists on the best dosing schedule to minimize hearing damage, but many authors argue that intermittent dosing with long intervals between injections to check whether hearing loss has occurred is a safer approach in preserving hearing.

Our approach to intratympanic gentamicin treatment is based on the desire to control symptoms with the minimum risk to underlying hearing. Only patients with definite Ménière’s are offered this and we adopt a conservative approach in those with possible or probable disease. We do not feel ablation is necessary and treat according to the frequency and severity of vertigo symptoms. Also we do not consider injection of gentamicin for control of fluctuating hearing, tinnitus or aural pressure symptoms. Vestibular function tests including the calorice test are of value in assessing the function of contralateral ear but we have not found this of benefit in determining the need for intervention in the target ear. If a canal paresis is identified in the contralateral ear then the potential risks of persistent imbalance after injection may be higher and the patient should be made aware of this and counselled accordingly.

Currently in our practice a low dose method is favoured in which 1-2mls of gentamicin (40mg/ml) is injected through the tympanic membrane using the operating microscope and a fine bore spinal needle. The tympanic membrane is anaesthetised prior to this using a topical agent such as EMLA or phenol.

The gentamicin can be buffered using 0.5mls of 8.4% sodium bicarbonate and 0.5mls of local anaesthetic in order further reduce middle ear discomfort, however we have not found this necessary and currently inject the solution unaltered.

The patient is then instructed to lie supine with head turned to the contralateral side. The patient maintains this position for half an hour.

It is explained to the patient, that after a delay of 3 or 4 days, symptoms of imbalance are to be expected. These symptoms typically resolve after 6 weeks and our patients are reviewed in clinic two months after injection for a decision with regards to whether or not a second injection is necessary. Further injections are considered in those having persistent attacks of vertigo and vestibular rehabilitation offered to those with symptoms of persistent imbalance. A In our experience this method works in up to 90% of patients with control of vertigo with little evidence of sensorineural hearing loss.

**Outcomes**

The key issues in terms of outcome are the risks of hearing loss and imbalance, and the control of vertigo. The injection does not achieve a “cure” and it would be expected that after a successful injection that the hearing fluctuations continue along with the anticipated natural history. Many patients do in fact bear this out and after injection will describe “attacks” characterised by changes in hearing, tinnitus and aural pressure without vertigo. This is typically indicative of a favourable response to injection and implies good chemical vestibular control. It is thus important that any recorded hearing changes after injection are regarded in the context of a fluctuating condition.
In a meta-analysis by Cohen-Kerem et al, intratympanic gentamicin (irrespective of treatment regime) achieved complete and partial vertigo control in 74.7% and 92.7% of the patients respectively with no adverse effect on hearing level and word recognition6.

In a similar paper by Carey J, titration therapy with intratympanic gentamicin offered control of vertigo in 87% (range, 75%-100%) of patients with unilateral Ménière's disease. The risk of additional hearing loss was about 21% (range, 0-37%). Vertigo recurred, however, in nearly one third of patients over time7.

In a review by Diamond C et al, overall pooled results on vertigo control revealed complete or substantial control in 89% of patients (study range 73-100%). Hearing was worsened in 26% (0-90%). Subjective improvement in tinnitus was seen in 57% of patients (0-82%). Different treatment protocols all resulted in similar rates of vertigo control8.

Chia et al in 2004, concluded that the titration method of gentamicin delivery demonstrated significantly better complete (81.7%, p = 0.001) and effective (96.3%, p < 0.05) vertigo control compared with other methods. The low-dose method of delivery demonstrated significantly worse complete vertigo control (66.7%, p < 0.001) and trends toward worse effective vertigo control (86.8%, p = 0.05) compared with other methods. The weekly method of delivery trends toward less overall hearing loss (13.1%, p = 0.08), and the multiple daily method demonstrated significantly more overall hearing loss (34.7%, p < 0.01) compared with other groups. No significant difference in profound hearing loss was found between groups9.

Using the Round window M-catheter and a low dose continuous effusion Hoffer et al achieved up to 93% control of vertigo with 3.7% risk to hearing10.

Suryanarayan et al using a Silverstein microwick achieved a vertigo control rate of 76.8-80%11,12.

It is possible to treat bilateral Ménière’s Disease with intratympanic gentamycin provided the active ear can be identified. There is a very low risk to hearing provided a low dose regime is used. Patients with a contralateral canal paresis need to be aware of the increased risk of long term imbalance and oscillospia before treatment is commenced13.

Dexamethasone

There is limited evidence in the long term effectiveness of intratympanic dexamethasone. In a recent Cochrane review, one trial with low risk of bias demonstrated a significant improvement in vertigo (82%) over a 24 month period using intratympanic dexamethasone (4mg/ml once daily for five days)1.

Since then Lambert et al, in a double-blinded, randomised study, demonstrated a 73% reduction in vertigo in patients with unilateral Ménière’s Disease using slow release intratympanic dexamethasone (OTO-104). The study was only over a three month period14.

However when Casani AP et al, compared a low dose of intratympanic gentamicin to dexamethasone in a randomised controlled study they found that after 2 years although there was a 12.5% reduction in hearing, gentamycin had a better vertigo control than dexamethasone (81% versus 43%)15.

Other use of intratympanic treatments for vertigo

An alternative use of intratympanic gentamicin is to ablate remaining vestibular function in those patients who are awaiting surgery to remove cerebellopontine angle lesions.

In a small study by Magnusson et al,12 patients with near normal vestibular function were treated with intratympanic gentamicin (1.2 mls of 30mg/ml buffered gentamicin 4 doses over 2 days) in a combination with vestibular 'prehab' to achieve preoperative vestibular ablation and compensation. All subjects were compensated before surgery and no patient complained of dizziness or vertigo after surgery16.

A similar study by Tjernström et al, concluded that the subjects pre-treated with gentamicin had significantly less postural sway at the follow-up, both compared with the preoperative recordings and compared with the other groups17.

Bauer et al, treated two patients suffering from delayed endolymphatic hydrops including one post stapedectomy case successfully with intratympanic gentamycin18.

Brantberg et al, used intratympanic gentamicin to successfully treat vertigo other than Ménière’s in 2 cases of vertigo attacks caused by vestibular dysfunction in deaf ears in 1 of brief sensations of linear acceleration in a patient who had suffered idiopathic sudden hearing loss a few years earlier, in one of disabling benign paroxysmal positioning vertigo and 1 case of severe and frequent attacks of vertigo in an elderly patient with a medium-sized acoustic neuroma who did not want surgical extirpation of the tumour19.

Similarly in a recent paper by Giannuzzi et al, intratympanic gentamicin was used with good effect to control symptoms of disabling vertigo in 4 elderly patients with small
(< 1cm) Vestibular schwannoma) with good effect. This treatment represents an additional option in patients with small not-growing tumour affected by vestibular symptoms to be combined with a wait-and-scan policy.

**Conclusion**

When medical treatment of vertigo fails, it is worth considering intratympanic treatment in carefully selected patients. Patients have to be aware that there is a risk to remaining hearing, that they will experience symptoms of imbalance that may require vestibular rehabilitation and it may be necessary to repeat intratympanic treatment if they relapse.

**References**

Stenosing chronic otitis externa

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Abstract
Chronic stenosing otitis externa is a rare pathological entity that is preceded by chronic otitis externa. It is a chronic inflammatory condition of the external ear canal that results in irreversible sub-epithelial fibrosis and narrowing of the canal lumen, leading to an acquired atresia of the external auditory canal. Patients either present at the active immature phase complaining of chronic discharge with episodic inflammation or at the later mature stage of the disease with a conductive hearing loss. Once the condition has developed and becomes quiescent the patient can be managed with hearing aids if the conductive hearing loss is significant enough to warrant their use or undergo a canalplasty that aims to widen or restore patency to the ear canal.

Key words
Otitis externa, fibrosis, ear canal, stenosis, chronic infection


Introduction
Stenosing chronic otitis externa (SCOE) is a chronic inflammatory condition of the external ear canal that results in irreversible sub-epithelial fibrosis and narrowing of the canal lumen, leading to an acquired atresia of the external auditory canal. The condition develops when acute otitis externa (AOE) persists and recurs repeatedly. It is a rare condition with an estimated incidence of 0.6 per 100 0001. It is a condition that has been described by a number of different names including: post-inflammatory medial canal fibrosis, obliterative otitis externa2, recurrent acquired atresia, post-inflammatory acquired atresia3 and idiopathic inflammatory medial meatal fibrozing otitis4. Acquired atresia of the external auditory canal without an inflammatory insult also exists and its aetiology includes traumatic, post-operative and neoplastic causes5. The focus of this review is stenosis secondary to chronic otitis externa (SCOE).

The condition may be bilateral, with a frequency varying between 12.5% and 67%1,3-8. It seems to be more prevalent in females than males. Keohane et al postulating that the more common usage of hair sprays and other cosmetic preparations by women might be a contributing factor7, however he provided no evidence to support this hypothesis. The mean age at presentation seems to be consistently in the fifth decade2, 3,6, although there have been reports in children3, 4, 7.

No unifying features have been identified that explain why some patients with chronic otitis externa (COE) develop stenosis and others do not. Some patients have a history of chronic dermatitis such as eczema, lichen sclerosis or psoriasis, with others having an allergic component to their condition. The predominant allergens are therapeutic agents such as neomycin and topical corticosteroids9 which produce a type IV hypersensitivity skin reaction. Immunosuppression has also been postulated as a contributing factor3, although this is not demonstrated in all studies7. Microbiological cultures of the discharge commonly identifies Pseudomonas aeruginosa, Proteus mirabilis and Staphylococcus aureus all of which are non-specific, as they are frequently seen in AOE and chronic otitis media2,10. Underlying chronic supplicative otitis media, use of hearing aids, surgical trauma and high humidity are also thought to predispose to disease progression6,10. Alkaline ear canal skin is also a risk factor for the progression of AOE to COE11. Patients who develop COE in response to Pseudomonas infection have also proven resistant to treatments as the bacterium organizes itself in a ‘biofilm’ where it can be protected from both antibiotics and immune cells12.
SCOE as demonstrated is a specific entity, with particular symptoms, this condition should be confirmed histopathologically by performing a biopsy, to differentiate it from the many other pathological diagnoses that can affect the external auditory canal. These include: Histiocytosis X, tuberculosis, fibrous dysplasia, sarcoidosis, tertiary syphilis, lupus erythematosus and primary carcinoma of the skin of the ear canal.

The specific pathophysiology of CSOE remains uncertain, and this is compounded by the lack of an experimental animal model. It appears that patients pass through a number of different stages prior to canal stenosis.

1. An insult to the external auditory canal and/or the tympanic membrane epithelium initiates the process.

2. This initial insult produces extensive granulation tissue on the tympanic membrane and external auditory canal wall epithelium. The loss of squamous epithelium on the lateral surface of the tympanic membrane results in exposure of its fibrous layer.

3. The continuous superinfection and iatrogenic treatment of the condition causes progression to maturation of the granulation tissue on the fibrous layer of the tympanic membrane into a thick fibrous plug. This is especially evident in the narrow anterior tympanomeatal angle where granulations on the two adjacent surfaces may come into contact and with subsequent epithelialisation blunting can occur.

4. The stenotic process does not seem to extend laterally past the bony/cartilaginous junction and this may be a factor in the condition’s aetiology. There is the possibility that features of the interaction of bone and chronic infection lead to the development of CSOE, and this is an area that needs further research. Otitis externa can be largely confined to the outer canal but CSOE never is.

Patients either present at the active immature phase complaining of chronic discharge with episodic inflammation where the granulations flare up or at the later stage of the disease with a conductive hearing loss. Examination during this later dry stage identifies a shortened external auditory canal with the appearance of a lateralisied tympanic membrane and no evidence of ongoing inflammation (Figure 1.). Palpation is painless and demonstrates a soft tissue plug. Audiometry identifies a 10-40 dB conductive hearing loss with a flat tympanogram.

Eliciting an appropriate history and examination, with audiometry enables the diagnosis to be confirmed. Computed Tomography (CT) scanning is essential to ensure that there is no erosive bony process that may indicate a more sinister pathology. It is also important to exclude middle ear disease because the surgical repair will be less successful if the tympanic membrane has been perforated, that may result in the fibrous layer may be deficient. This makes stripping the fibrous plug off virtually impossible during surgical correction of CSOE. CT scanning characteristically reveal a core of fibrous tissue abutting the tympanic membrane, extending laterally into the external auditory canal, with the middle ear and mastoid antrum appearing normal.

**Management of the pre-stenosis stage**

AOE and COE are common dermatological conditions that affect all aspects of patients’ lives, including employment. Ali et al demonstrated that the quality of life (QOL) in those with COE was moderately affected and in AOE patient’s QOL scores were significantly affected. Chronic stenosing otitis externa is preceded by COE, a disease entity that is defined as inflammation of the ear canal lasting > 3 months. As mentioned previously, no unifying features have yet been identified that predict why canal stenosis should develop in some cases of otitis externa and not others. However, halting the disease progression is paramount and should be actively pursued.

Two novel therapies have been used in the treatment of COE, tacrolimus with its immunosuppressive effect acting on the non-steroidal pathway and chemical ear peels.
which comprise ciprofloxacin and cortisone drops with acetic acid. Whilst both studies show efficacy the treatment groups were small and the use of these treatment regimens is not widespread.

Referral to an ENT specialist should be considered when:

1. Otitis externa does not respond to appropriate treatment in primary care.
2. Contact sensitivity is suspected and patch testing would be useful to guide further management.
3. The ear canal is occluded or becoming occluded.
4. Necrotising otitis externa is suspected.

Occasionally, the symptoms and signs of chronic otitis externa persist in spite of proper and intensive medical treatment with topical application and regular suction toilet. At this late stage, when the fibrous plug has developed, patients generally cease to have any further problems with infection. Patients may opt to do nothing after appropriate investigations and manage their deafness conservatively, especially if it is not severe. A study from the House Ear Institute identified that once fibrosis had developed patients who did not undergo (or plan) surgery were a) patients whose hearing loss was not great enough to warrant surgery or b) they refused surgery.

Hearing aids, as well as being implicated in the development of the condition, can be difficult to fit and are prone to feedback due to the foreshortened canal and whilst some patients will have no further problems others re-develop otorrhoea with their use. A solution to this is the use of a bone anchored hearing aid (BAHA). BAHA implantation has been demonstrated to significantly improve the quality of life as measured by the Glasgow benefit inventory when implanted into patients with chronic otitis media a condition with similar symptomatology. There will also be a place for the new implantable transcutaneous bone conductor hearing implants that minimize adverse events and implant loss.

If on careful counseling the patient wishes to follow a surgical path they need to be aware that the condition can be difficult to treat and success is not guaranteed. Patients must take into consideration that they are committing themselves to intensive and prolonged follow-up to ensure re-epithelialisation. In the series published by the senior
There was a patient average of 15 visits to the aural care service prior to discharge.

The main aim of surgery is to restore and maintain patency of the canal for normal sound conduction and to be self-cleaning. The procedure can also allow the surgeon to identify and treat canal wall cholesteatoma. Paparella and Kurkjian first demonstrated the technique in 1966 and whilst subsequent surgeons have modified parts of the procedure the basic steps remain the same:

1. Excision of all fibrous tissue
2. Preservation of the fibrous layer of the tympanic membrane
3. Widening of the bony canal
4. Grafting or skin flaps to cover bare bone and drum
5. Packing to maintain patency

The most popular material used to cover the raw areas of the denuded bony canal wall is a split-thickness skin graft overlaying a layer of temporalis fascia to aid graft placement. The skin graft is usually harvested from either the upper arm or postauricular region, and the way in which it is applied differs between authors however all recommend that the graft overlaps from the wall of the canal onto the tympanic membrane. The skin of the graft is however non-migratory and some patients may need regular aural care to remove keratin accumulation even though they become symptom free.

In the reporting of case series, a number of factors have been specifically highlighted as being crucial to the success of the procedure, and include the features below that need consideration to prevent re-stenosis:

1. Adequate exposure is necessary, and this can be achieved by an endaural incision, postauricular incision or a combination of the two.
2. The complete removal of all fibrous tissue from the tympanic membrane by the identification of a plane of dissection superficial to the fibrous layer of the tympanic membrane.
3. Widening of the bony canal is recommended, and this consists of drilling down the spine of Henle, the tympanomastoid suture and widening the lateral bony canal until mastoid air cells are encountered. Care must be taken so that the capsule of the tempromandibular joint is not breached which in extreme cases can cause prolapse of the head of the mandible into the canal and mastoid air cells should not be encountered for fear of the development of a canal wall cholesteatoma.

The creation of a meatoplasty at the lateral opening of the external auditory meatus preserves normal lateral migration of cerumen and desquamated keratin, allowing it to extrude easily and enabling good ventilation to the canal.

4. Initially authors used stents or plugs to keep the newly created canal open, although this has proved unnecessary. The emphasis has now been placed on the importance of early cauterization of granulations in the healing phase to prevent further stenosis.

5. Elocon ointment (0.1% mometasone furoate - Merck, Sharp and Dohme Ltd) in the postoperative period should also be used in combination with aural care to prevent re-stenosis.
The major risk of this procedure is re-stenosis and this varies according to the technique and length of follow up recorded. The re-stenosis rates vary from 9-27% \(^1,3\), however further surgical correction can be performed. Another outcome is a continually moist ear that does not re-epithelialise and these patients may have an improvement in their hearing but are dependant on 3-6 monthly aural care appointments.

**In Summary:**

CSOE is a rare condition, and long-term success rates are not frequently reported as studies are small, however the aim of surgery is to prevent recurrence of the problem, and improve the conductive hearing loss patients’ experience. The senior author’s own series has a mean follow-up duration of 2 years and 11 months. At 3 months post-operatively, the four-tone average threshold had improved by a mean of 13.9dB in the operated ear and the mean Glasgow benefit inventory score of 20 was indicative of an overall improvement in quality of life following the procedure. Careful consideration of post operative management must be taken into account although in over 80% of cases a successful outcome can be anticipated.

**References:**

Current opinion on Vestibular Migraine

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Introduction

Definitions

Migraine - This is a chronic neurological disorder characterised commonly by recurrent moderate to severe headaches in association with other symptoms. These are often symptoms of autonomic origin, such as nausea, vomiting, sweating, diarrhoea and increased sensitivity to light (photophobia) and noise (phonophobia). Symptoms of dizziness often accompany the headache. Other forms of migraine exist that are not associated with headache.

Vertigo – This is defined in the Oxford English Dictionary as a hallucination of movement, such as spinning or swaying1. This may be described subjectively, as the outside world moving, i.e. the room spinning, or an internal feeling of movement. It is the cardinal symptom of vestibular dysfunction.

Vestibular Migraine – This is now the accepted term for migraine presenting with primary vestibular symptoms following classification by the International Classification Committee for Vestibular Disorders of the Barany Society and the International Headache Society2. Older terms such as; Migraine-associated Vertigo, Migrainous Vertigo and Migraine-related vestibulopathy are now obsolete. Vestibular Migraine is a separate disease entity from Basilar-type migraine and the terms are not synonymous. However, different dizzy and migrainous diagnoses may co-exist in the same individual.

Key words
Migraine, Vertigo, Vestibular.

Epidemiology

Migraine – This common condition affects 23-29% of females and 15-20% of males3. In the adult population, 16% will suffer from migraine at some point in their lives4. Migraine is a headache disorder as described by the International Classification of Headache Disorders (ICHD-II).

Vertigo - A presentation with dizziness as the primary symptom is a very frequent occurrence in the outpatient department as well as in primary care. In fact, it is a symptom experienced by 20% of the working population5. It is also one of the most common presenting complaints in elderly patients. Dizziness, however, may describe a myriad of non-specific symptoms and does not have a precise medical definition. Additional information is typically required to further define the patient's problem. Distinctions must be made between vertigo, near-syncope (a feeling of impending faint), disequilibrium (loss of balance), and ill-defined light-headedness (an inability to concentrate or focus the mind)6. Vertigo is the prime symptom in vestibular pathology, whether peripheral or central, whereas other forms of dizziness may indicate non-vestibular system disorders7. Vertigo is a multisensory syndrome induced either by stimulation of the intact sensorimotor system by motion (eg, physiological vertigo as in motion sickness), or by pathologic dysfunction of any of the stabilizing sensory systems (eg, peripheral vestibular as in vestibular neuritis, or central vestibular as in vertebro-basilar ischemia)8.

Vestibular migraine – This entity has gradually been recognised as a major cause of vertiginous symptoms over the past twenty years and it is now understood to have an annual prevalence of around 1%9. It represents the diagnosis in 11% of patients in specialist dizzy clinics and it is described by some authors as the third most common diagnosis after Benign Positional Paroxysmal Vertigo and panic disorder10. The close relationship between migraine and vertigo has been well established. It has been shown that when compared to controls, the presence of migraine is 1.6 times higher in dizzy patients, (38% of 200 dizzy clinic patients vs. 24% of 200 matched controls. p<0.01)10. Also vertigo is reported as presenting in a greater proportion of migraine sufferers when compared to other headache entities, (27% of 200 migraine patients vs. 8% of 116 tension headache patients. p=0.01)10.
Neuropathophysiology
There are many well established theories on the pathophysiology of migraine.

Neurovascular
The original vascular theory proposed changes in the cerebrovascular system with vasoconstriction leading to aura effects followed by a rebound dilatation causing the classic migraine headache. This was based on observations that vasoconstrictive medications such as Ergot, resolved the attacks and vasodilators provoked attacks. However, imaging modalities and further work has shown an inconsistency in the blood flow which disputes this theory. This led to the Neurovascular theory which holds that a complex series of neurovascular events initiates migraine with only secondary changes in cerebral perfusion. The theory suggests that there is a state of neuronal hyperexcitability in the cerebral, and specifically the occipital cortex, at rest in a migraine patient. This increases the susceptibility to an attack when exposed to a trigger.

Cortical Spreading Depression
First suggested by Leao in 1944, this forms the basis of the presumed cause of migrainous aura. It suggests that a wave of neuronal excitation spreads from a site in the occipital region across the cortex. The release of potassium and glutamate from neural tissue depolarizes adjacent cells, which, in turn, release neurotransmitters, propagating the spreading depression across the cortex. This wave of depolarization causes the phenomenon of aura and releases parasympathetic neurotransmitters causing the classic parasympathetic symptoms. The depolarization also activates trigeminal neurons and stimulates nociceptive fibres on dural blood vessels. These release calcitonin gene-related peptide, substance P, vasoactive intestinal peptide, and neuropeptides such as Serotonin, Noradrenaline and Dopamine, which are known to regulate vestibular neurones and may have a role in the associated vertigo. These excite the sensory epithelium of the inner ear and brainstem vestibular centres. Peripheral sensitization may lead to vertigo on movement whereas central stimulation may lead to a general dysequilibrium.

Aetiology
There is some postulation of a familial cause for migraine. Indeed, approximately 70% of migraine patients have a first-degree relative with a history of migraine. The risk of migraine is increased 4-fold in relatives of people who have migraine with aura.

Genetics
A rare form of migraine with aura, Familial hemiplegic migraine, is associated with mutations in a gene located on chromosome arm 19p. This gene codes for a neuronal calcium channel, and defects involving this gene are also implicated in Episodic Ataxia type 2 (also known as periodic vestibulocerebellar ataxia). This presents with migraine and vertigo. Interestingly, in a single family with multiple sufferers, a gene locus was identified for Migraine associated vertigo mapped to 5q35.

Triggers
As described above, the spreading depression theory with associated release of vasoactive neurotransmitters requires a stimulus. These stimuli are known as trigger factors and are widely accepted, however, there is little solid evidence to prove their effect. Triggers may be internal, such as lack of or excessive sleep, stress, fasting or missing meals and hormonal changes such as menstruation, menarche and menopause. They may also be external such as, ambient lighting and ventilation, smoking, strong odours, weather changes and of course, dietary triggers. Classic dietary triggers include caffeine, monosodium glutamate, artificial sweeteners, citrus foods, cheese and alcohol. However, some authors have disputed chocolate and tyramine as trigger factors for migraine. Table 1 shows trigger factors in order of their reported effects following a study in 2010. This study also identified that 62% of actively cycling women noted menstrual periods were a trigger and 67% of patients with menstrual migraine observed that their migraine attacks were more severe, refractory or longer than their non-menstrual attacks. Others studies have also shown that these are the most commonly reported triggers.

Table 1

<table>
<thead>
<tr>
<th>Trigger</th>
<th>Percentage reporting effect*</th>
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<tbody>
<tr>
<td>Stress</td>
<td>59%</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>53.5%</td>
</tr>
<tr>
<td>Odours</td>
<td>46.5%</td>
</tr>
<tr>
<td>Missed meals</td>
<td>39%</td>
</tr>
</tbody>
</table>

* Of 200 patients 91% reported at least one and 82.5% multiple triggers.
Diagnosis

Diagnosis of Vestibular Migraine is based almost entirely on a careful detailed history and examination, with only occasional need for further investigations to rule out other differential diagnoses. As has been mentioned, there is a strong link between migraine and vertigo. However, the two can co-exist, and the vertigo may be caused by other vestibular conditions such as Meniere’s disease, benign paroxysmal positional vertigo, vestibular neuronitis and episodic ataxia type 2. A careful history will usually eliminate these other conditions, but they must be borne in mind, as multiple balance disorders may occur simultaneously. A history of headaches either concurrently or separately to the vertigo is key. The principle differential diagnosis is Meniere’s Disease, and the two conditions co-exist in a large number of patients. Table 2 provides a useful comparison.

The differences in Table 2 can help distinguish Vestibular migraine from Meniere’s disease, but occasionally, electronystagmography (ENG), Vestibular evoked myogenic potentials (VEMPs), Electrocochleography (ECochG) and imaging in the form of a Magnetic Resonance scan (MRI), may be required. Other factors in the history may be more specific for Vestibular migraine than other differentials. Aura with the migraine or vertigo is diagnostic, with patients often reporting visual aura such as flashing lights or zigzag lines when prompted. Patients may report concurrent headaches or other migraine symptoms such as photophobia or phonophobia in 25-50% of cases, suggesting vestibular migraine. Light sensitivity is a very strong predictor of Vestibular migraine, with odds for disease 41.1 times higher in patients reporting the symptom (95% CI = 15.8—108.2). Another helpful predictor is a positive personal or family history of migraine.

In June 2012 a consensus document was jointly formulated by the Committee for Classification of Vestibular Disorders of the Barany Society and the Migraine Classification Subcommittee of the International Headache Society (IHS). The classification includes vestibular migraine and probable vestibular migraine. Vestibular migraine will appear in an appendix of the third edition of the International Classification of Headache Disorders (ICHD) as a first step for new entities, in accordance with the usual IHS procedures in 2014. This therefore, now makes a diagnosis of Vestibular migraine much more straightforward and simplified.

Table 2. Vestibular Migraine: Diagnostic Criteria

<table>
<thead>
<tr>
<th>Course</th>
<th>Vestibular Migraine</th>
<th>Meniere’s Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vertigo</td>
<td>Associated with headaches in 2/3 of patients. May be positional</td>
<td>Not usually associated with headache. Not usually positional</td>
</tr>
<tr>
<td>Duration</td>
<td>Seconds to days</td>
<td>Minutes to hours</td>
</tr>
<tr>
<td>Hearing Loss</td>
<td>May be &gt;24hrs</td>
<td>Up to 24hrs</td>
</tr>
<tr>
<td>Tinnitus</td>
<td>Tends to be bilateral Non-obtrusive</td>
<td>Must be present diagnostically – unilateral in the affected ear Can be obtrusive during attacks</td>
</tr>
<tr>
<td>Photophobia</td>
<td>Often present</td>
<td>Never present (Unless concurrent migraine)</td>
</tr>
<tr>
<td>Personal or family history of migraine</td>
<td>Yes</td>
<td>No (Unless concurrent migraine)</td>
</tr>
</tbody>
</table>
Behavioural modifications may be required to achieve a reduction in trigger exposure, but psychologists advocate learning to cope with triggers rather than total avoidance. As can be seen from Table 1, good stress management, sleep hygiene and regular meals and nutrition should be highlighted. Counselling for those with significant stress or sleep disturbance can be life changing. Alternative therapies including massage and relaxation techniques can be very effective. Root extract of the Butterbur plant is the only alternative medication with evidence of efficacy. Dietary triggers can be identified from a well kept symptom diary. These can then be controlled to reduce the burden of symptoms related to them. Dietary changes alone may achieve significant resolution of symptoms in as many as 72%. Abortive Medications

These medications aim to stop or significantly shorten the duration of attacks. Simple analgesics and Non-steroidal anti-inflammatory drugs are frequently used for headaches in migraine, but have also been shown to help with vertigo of vestibular migraine. Serotonin or 5HT1 agonists known as Triptans have been shown to be efficacious in vestibular migraine. A randomised double blinded placebo controlled trial showed response rates of 38% versus 22% for placebo. However, it has been suggested that Triptans could worsen or induce headache in vestibular migraine, but with amelioration of the vertigo. Intravenous steroid has been used successfully in prolonged vestibular migraine. Ergot alkaloids are not recommended in migraine with aura, and basilar migraine and are therefore not recommended in vestibular migraine.

Prophylactic Medications

When abortive treatments are insufficient or where the symptoms are prolonged or especially severe and impairing daily activities, prophylactic treatment may be required. There are various classes of medication and it is usually suggested to try one class at a time for a period of around 3 months. If proven helpful, the treatment should be continued for a year after which there can be a trial off treatment. Should the symptoms recur, the patient is likely to require long term therapy. Tricyclic antidepressants are often used as first line treatments, especially in those with significant pain profiles. Amitriptyline is usually used starting at a low dose of 20mg, but this can be substituted with Nortriptyline if the side effect profile proves problematic. Topiramate is a commonly used migraine treatment that has been shown to be effective in vestibular migraine at a dose of 50mg/day. Sodium Valproate at a
low dose has also been shown to useful\textsuperscript{43}. Low dose propranolol at 20mg is a good choice for patients with associated anxiety issues. Lamotrigine and Acetozolamide have also been shown to be effective in small studies\textsuperscript{44-45}.

**New Treatments**

Neurostimulation and nerve decompression have been used for common migraine headaches\textsuperscript{46-47}. As yet, however, they have now been used specifically for vestibular migraine. Botulinum toxin has also been used for headache migraine and has been used by the author very effectively for vestibular migraine\textsuperscript{48}. Calcitonin gene related peptides (CGRPs) are known to play a role in the pathogenesis of the pain associated with migraine and is possibly involved in vertigo. CGRP receptor antagonists, such as Olcegepant and Telcagepant have been investigated both in vitro and in clinical studies for the treatment of migraine\textsuperscript{49}. Transcranial magnetic stimulation also shows promise in migraine headache and may be effective in vertigo\textsuperscript{50}.

**Summary**

Vestibular Migraine is now the accepted term for vertigo associated with migraine. It is the third most common diagnosis made in dizzy clinics and has an annual prevalence of 1%. The theory of cortical spreading depression associated with neurovascular hyperexcitability in the brain is thought to be the cause and neurotransmitter release is implicated in the aetiology of the vertiginous symptoms. Ischaemia of the labyrinth from vasoconstriction may also be involved.

There is a strong familial association with some evidence of causative gene mutations, however, many trigger factors exist which can precipitate attacks. The diagnosis is made almost entirely with a careful detailed history and examination. There are now clearly established diagnostic criteria.

Once diagnosed, treatment may involve dietary modification, abortive treatments and prophylactic medications, but there is no substitute for adequate patient education, advice and understanding.

**References:**

Pathology and management of transitional cell papilloma of the sinonasal cleft

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Abstract
Transitional cell papilloma of the sinonasal cleft are benign epithelial nasal tumours that originate from the Schneiderian membrane of the nose and paranasal sinuses. Inverted papilloma, the most common subtype, usually originates from the lateral wall and histologically shows inversion into the underlying stroma rather than proliferation outwards. These tumours have a high tendency to recur and therefore optimal management is complete resection of the lesion, its underlying attachments and surrounding normal mucosa. In this article we aim to describe the common presentations of such tumour, methods of investigations and the complexities surrounding surgical management and minimizing recurrence of these lesions.

Key words
Inverted papilloma, Sinonasal papilloma, Schneiderian papilloma, Human Papillomavirus (HPV).


Introduction
Transitional cell papillomas of the sinonasal cleft also known as Sinonasal papilloma or schneiderian papilloma, were first described by Ward in 18541 and are benign tumors of the sinonasal tract. There are three histological subtypes: Inverted papilloma is the most common (47- 78%) followed by the cylindrical (2-26%) and lastly the fungiform (6-50%) subtypes. They are a rare and distinct histological entity with a tendency to recur hence management is focused on complete removal of the lesion and surrounding normal tissues.

Pathogenesis:
Inverted papilloma (IP) is a benign, epithelial neoplasm originating from the Schneiderian membrane of the nose and paranasal sinuses. They comprise 0.5-4% of all primary nasal tumours with an incidence of between 0.5- 1.6 cases per 100,000 people per year2 Usually seen in males in the fifth and sixth decades of life, this tumour generally originates from the lateral nasal wall around the middle meatus extending into the ethmoid and maxillary sinuses. However as the disease advances extension into all paranasal sinuses can occur. Origins from the paranasal sinuses occur in order of frequency from ethmoids, maxillary regions, sphenoid and frontal sinus (48%, 28%, 7.5% and 2.5%). Sinonasal papillomas arising from the nasal septum are exceedingly rare and are most likely to represent the fungiform subtype.

Histologically, as first noted by Ringertz in 19383, inverted papilloma is a tumour in which there is inversion of the neoplastic epithelium into the underlying stroma rather than proliferation outwards, with a clear basement membrane between the epithelial and stromal component. It is thought that this inversion may be the cause of the high rates of recurrence often observed with such tumours. The pathogenesis of IP is unclear but human papilloma virus (HPV) have been implicated. HPV DNA types 6,11,16 and 18 have been identified in transitional cell papilloma and its neighbouring normal mucosa, with a preponderance to the fungiform or exophytic type, hence the importance of complete removal of the lesion, the mucoperichondrium and adjacent normal looking mucosa during treatment4-6.

Figure 1: low power view (H&E, x40) showing an endophytic growth pattern of surface squamous/transitional epithelium in keeping with inverted papilloma.
The cylindrical subtype behaves similarly to the inverted type and microscopically its epithelium consists of layers of eosinophilic ciliated columnar cells. The fungiform subtype however is more distinct clinically and microscopically as an exophytic lesion with preponderance to the nasal septum (Figures 1 and 2).

**Clinical Aspects:**

IP most commonly presents as unilateral nasal obstruction combined with rhinorrhoea and epistaxis. A combination of computerised tomography (CT) and magnetic resonance imaging (MRI) is most useful (Figures 3 and 4). CT will identify the disease and any underlying bony erosion, hyperostosis and calcium deposits, which may suggest a malignant component. An MRI will further define the IP and whether opacification of the sinuses is due to disease or mucous from obstructed paranasal sinuses. Characteristic streaking or stranding on MRI may also imply malignancy. Pre-operative imaging is essential when planning surgery particularly in sites such as the frontal sinus, which are often difficult to access and may involve a complex combination of open and endoscopic procedures.

A number of staging systems for IP exist, which are based on the origin of the tumour rather than its volume, however to date no single system has been universally accepted (Table 1).

**Malignant Transformation:**

The incidence of associated squamous cell carcinoma varies widely in the literature but it is reported that malignancy tends to affect the inverted and cylindrical subtypes. Carcinoma may be synchronous when there is no history of surgery or metachronous when it occurs at a site of previously excised IP. Mirza et al reviewed 63 case series comprising 3058 patients and reported the incidence of associated malignancy. Atypia was noted in 1.1%, dysplasia in 1.9% and synchronous lesions in 7.1%. The transformation rate for metachronous lesions was 3.6% and the mean time interval to developing such lesion was 52 months (6-180mths). It has been reported that HPV infection is likely to increase the malignant transformation rate with HPV DNA being more likely to be identified in malignant lesions than simple IP.

**Management:**

IP has been associated with a very high rate of recurrence.
Recurrence often is the representation of residual disease and so the main problem facing the clinician is adequate initial treatment. This involves resection of the disease, its attachment to and including the underlying mucoperiosteum and adjacent normal mucosa. In cases of HPV infection recurrence may be due to changes within the mucosal field but complete initial resection is still the mainstay of treatment. Removal has been described by a number of approaches from intranasal endoscopic procedures to a lateral rhinotomy, mid-facial degloving and sub-cranial approach. The method of resection should be based primarily on achieving complete removal and secondarily on minimizing surgical morbidity.

Endoscopic versus open approach:
The treatment of inverted papilloma has evolved over the years with an initial preponderance to open, aggressive procedures prior to the widespread availability and use of endoscopes. Lateral rhinotomy and en block excision of the lateral nasal wall with removal of all the mucosa of the ipsilateral paranasal sinuses was deemed appropriate with groups in the 1980s advocating midfacial degloving, medial maxillectomy, Caldwell-Luc and other various approaches to the frontal sinuses. Follow up by such groups were deemed to show recurrence rates of between 20-30% thus supporting aggressive surgical excision. Vrabec reported recurrence rates of 2% using a lateral rhinotomy and Dolgin et al suggested the choice between lateral rhinotomy and midfacial degloving is based on the exact location and extension of the lesion. Such findings were supported by multiple groups in the 1990s. With the widespread introduction and availability of endoscopes and advances in modern CT and MRI imaging, more precise tumour localization has lead to an increase in endoscopic management of inverted papilloma with more than comparable recurrence rates. An early study by Kamel noted total intranasal endoscopic removal of localized unilateral lesions with limited extension into the sinonasal region in three cases with no reported recurrence at an average of 23mths follow up. However one of the largest early studies by Waitz and Wigand demonstrated no difference in recurrence rates of intranasal endoscopic treatment versus extranasal management even in the treatment of large lesions involving the posterior ethmoids, sphenoid sinus and nasofrontal duct. The recurrence rate following endoscopic resection was 17% as compared with 19% after the extranasal approach. Homer et al reviewed their 12 year experience of nasal neoplasia noting 61 cases of inverted papilloma. 7 underwent endoscopic treatment, 6 of which using the technique described by Waltz and Wigand and 5 of these remained symptom free at 22 months. The patient with recurrent disease had extensive paranasal and intraorbital tumour and the endoscopic approach was used to control the disease which would otherwise have been unresectable or would have required extensive surgery resulting in major comorbidity.

The case for endoscopic excision of IP over more open aggressive approaches continued to be made by a number of groups. Lawson et al reviewed 160 cases of IP and reported recurrence of 18% amongst 112 patients who had undergone lateral rhinotomy and 12% with those who had...
undergone conservative approaches. Lund’s review of 1287 cases reported recurrence of 58% after conservative intranasal removal, 14% after radical removal and 18% after endoscopic removal. Finally Busquets et al reported a recurrence rate of 12% versus 20% for endoscopic and non-endoscopic resection although it should be noted that the mean follow-up time for the endoscopic groups are often shorter than the open groups. In addition to the lower reported recurrence rate advantages of the endoscopic approach include a preservation of the external bony structure of the nose, improved cosmesis, the absence of an external incision, limited mucosal clearance hence minimal disruption of the normal mucociliary clearance and function of the nose and paranasal sinuses as well as reduced post-operative pain and a shorter in patient stay.

The success of an endoscopic procedure is inevitably related to preoperative localization and accurate and complete visualization using a variety of optical angulated endoscopes. Underlying bone may require further treatment using a drill with a diamond burr. It would therefore seem obvious that groups have opposed the intranasal endoscopic approach in cases where the lesions are in the anterior of floor of the maxillary sinus, there is extension into the extranasal tissues such as skull base, intraorbital and intradural extension, a high tumour stage or suggestion of malignant transformation.

Use of the KTP-532 laser has been described in the resection of IP. Kaluskar et al describe their experience of 9 patients with unilateral IP without intracranial or intraorbital extension. The KTP-532 laser was used to resect the tumour by incising the mucosa 5mm anteriorly to the tumour which was then elevated using a Freer elevator. The underlying attachment was dissected using the laser again. Involvement of the ethmoid or sphenoid sinus was followed by complete endoscopic sphenoorhmoidectomy and follow up at a mean of 4.9 years showed only one incidence of asymptomatic recurrence in a patient at 12months.

The follow up of patients with inverted papilloma seems to be highly variable amongst surgeons. The only consistency noted is that those patients undergoing endoscopic procedures tend to average shorter follow-up periods. As the time in which recurrences manifest is unclear it is difficult to suggest how long a patient should be followed up for but it would seem sensible to base this decision on the type of transitional cell tumour identified, its site, extent and complexity of management.

**Sphenoid sinus Inverted Papilloma:**
Isolated lesions of the paranasal sinuses are rare and particularly those reported in the sphenoid sinus are few. Inevitably sphenoid sinus disease detection has increased with advancing endoscopic visualization and imaging techniques and the close anatomical relations of the sphenoid sinus makes disease detection increasingly important. The most common presenting symptoms in these patients are headache followed by visual disturbance, hearing loss, nasal obstruction and epistaxis. Guillemaud & Witterick describe a series of 8 cases of sphenoid sinus IP that were managed endoscopically with a recurrence rate of 12.5%. A literature review by the group noted a much higher recurrence rate worldwide (20.5%). As described by Hyung-Ju et al, who also noted an extremely high rate of recurrence after endoscopic removal of sphenoid sinus IP, this is likely to be related to difficulty in accessing the most lateral portion of the sphenoid sinus where relations to other vital structures makes treatment challenging.

**Frontal sinus Inverted Papilloma:**
Sinosal papilloma is thought to arise in the frontal sinus in between 1-16% of cases. Management of such tumours is more complex due to the surgical challenge of access to the frontal sinus via the frontal recess, the degree of pneumatisation and pathway of sinus drainage and proximity of critical structures such as the orbit and anterior skull base. Approaches to the sinus have included a number of endoscopic procedures, the traditional osteoplastic flap, endoscopic frontal trephination and a combination of the endoscopic and open approaches. The use of angled endoscopes and median drainage procedures have made endoscopic access to the frontal sinus easier. Frontal sinus IP has also been noted to more likely be bilateral in nature possibly due to the intersinus septum being a poor barrier to tumour spread. Such complexities have made consensus on the approach to manage frontal sinus IP difficult and a recent systematic review by Walgama et al has attempted to untangle this. They included a total of 49 patients across 11 studies with 47 cases of benign IP and 2 with squamous cell carcinoma. 49% of cases were primary lesions and 51% secondary. Surgical approach to the tumour was endoscopic frontal sinusotomy (EFS) in 21 cases, endoscopic modified Lothrop (EML) in 10, osteoplastic flap (OPF) in 12 and endoscopic frontal trephination (EFT) combined with another endoscopic approach in 5. Recurrence was 22.4% at a mean follow up of 27mths however no single factor such as approach, site of attachment of tumour, unilateral versus bilateral disease or other patient variables was shown to be statistically significant of recurrence. It would seem sensible that the approach to frontal sinus is based on detailed review of the site of origin and attachment with each technique offering advantages in different cases. OPF allows wide surgical exposure especially in malignant cases, bilateral or multifocal disease. EML may be useful.
for attachments to the medial wall, posterior wall or intersinus septum with less morbidity than the OPF and can be combined with EFT.

EFS alone may be utilized best in limited unilateral frontal disease in cases where tumour can be adequately visualized and accessed. The frontal drainage pathway consists of the frontal infundibulum and the frontal recess. Superior attachments may require a more extended approach whilst those originating from the frontal recess may be suitable for a total endoscopic procedure\textsuperscript{34,35,26}. In Zhang's series of 9 patients those that have tumour located on the lateral wall of the frontal recess underwent a Draf IIA procedure. Those that had tumour originating on the posterior wall as well as the medial or lateral wall or intersinus septum underwent a Draf IIB procedure and finally two patients with bilateral sinus disease underwent a Draf III (EML). At 15 mths follow up all patients remained disease free\textsuperscript{36}.

**Conclusion:**

Transitional cell or Inverted papilloma of the sino-nasal region is a benign disease that provides interesting management challenges for ENT surgeons. Its inverting nature, which is thought to be the major causative factor in the observed high rates of recurrence, suggests that thorough initial excision of the tumour, its underlying mucoperichondrium and the adjacent normal mucosa is vital. With advances in imaging techniques and the widespread availability of optical endoscopes, disease is often managed intranasally and endoscopically with results comparable to the open, aggressive procedures historically employed. However the surgical strategy should always be dictated by a combination of histology, adequate imaging and preoperative localisation, accurate and complete visualisation of the tumour at operation and surgical skill.

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**References:**

Balloon sinuplasty

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Abstract
Balloon sinuplasty has been licensed for the treatment of chronic rhinosinusitis since 2006. Balloon dilation enlarges the sinus ostium by creating micro fractures of the surrounding bone and compressing soft tissue such that no mucosa is removed. The device is designed to dilate maxillary, frontal and sphenoid sinuses, and has been widely used in the management of patients with recurrent acute and chronic rhinosinusitis. Indications for use and limitations of the technique are discussed. With the evolution of the technology Balloon sinuplasty can be performed under local anaesthesia in an out patient setting, potentially leading to accelerated care and cost savings.

Key words
Para nasal sinuses, balloon catheter, dilation, chronic sinusitis, acute sinusitis.


Introduction
Chronic rhinosinusitis (CRS) remains one of the most common chronic illnesses in Europe and the United States, affecting 10% of the UK population1. Symptoms include nasal obstruction, rhinorrhea, anosmia, facial pain and sleep disturbance. CRS has been recognised to have a significant negative impact on the quality of life, worse in some respects than heart disease, chronic obstructive pulmonary disease and back pain2. For all these reasons effective treatment is sought focusing on eradicating, reducing or simply controlling symptoms. The introduction of endoscopic sinus surgery (ESS) over three decades ago aimed to treat patients who fail maximum medical therapy for CRS. A key principle of ESS is that of mucosal preservation; to facilitate mucosal preservation the available instrumentation has matured, with smaller forceps, through-cutting instruments and powered instrumentation for a more precise approach to the surgical treatment of chronic rhinosinusitis. The development of balloon technology complements the philosophy of ESS, managing chronic rhinosinusitis using less invasive techniques and with mucosal preservation. The nature of the balloon catheter instrumentation provides the sinus surgeon the opportunity to dilate selected sinus ostia with minimal manipulation of the surrounding tissue and preservation of sinus anatomy.

How does it work?
Balloon sinuplasty employs a Seldinger technique (adapted from cardiac angiography) in order to achieve minimally invasive dilation of the sinus ostia with maximum anatomy preservation. A catheter tailored to each peripheral sinus (maxillary, frontal and sphenoid) is delivered into the nose endoscopically and the natural ostium is cannulated with a transilluminated thin guidewire passed through the catheter. The guidewire is very flexible, and ‘seeks’ the natural ostium. Correct placement is confirmed by transillumination of the forehead (in frontal sinuses dilation) or cheek (in maxillary sinus dilation). A balloon is advanced and inflated to high pressures in order to dilate the ostium and outflow tract and affect sinus drainage. Rather than removing inflamed and diseased tissue, mucosa is compressed and tiny fractures in the underlying bone are made by the action of the balloon. The balloon, guidewire and catheter are removed (Figure 1). Dilatation may be undertaken in the frontal, maxillary and sphenoid sinuses.

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Figure 1: Introduction of guidewire, balloon inflation, catheter retraction and resulting sinus ostia dilation
a. Guide wire is introduced; b. Balloon is inflated; c. Catheter retracted and sinus ostia dilated.
Trans-sinus illumination is a recent modification to the original balloon sinuplasty system. Previously the position of the balloon was confirmed fluoroscopically, using radio-opaque iodine to fill the balloon. This resulted in concerns being expressed regarding the potential dosage of ionizing radiation used, particularly regarding exposure to the lens of the eye, although studies found exposure to be well within safe limits. Transillumination eliminates the risk of radiation exposure to the patient and surgeon, and reduces time (and costs) by eliminating the need for a radiographer. Furthermore, it can be more demanding to determine the position of the balloon fluoroscopically, whereas transillumination, provided it is interpreted correctly and in conjunction with anatomical knowledge from CT scans, reduces the risk of placement errors (Figure 2).

Cadaveric and simulator training is currently available from manufacturers of the balloon technology. It has been our experience that the technique is easily mastered, even in the frontal sinus where complex anatomy can make conventional techniques challenging. Dependent upon ability of the operating surgeon, it may reduce operative time and intraoperative bleeding.

**Indications:**
Balloon sinuplasty is simply another instrument on the tray available to sinus surgeons. It is crucial to state that the choice of surgical instrumentation does not change the indications for sinus surgery. Rather, patients should be considered for surgical intervention based on persistent symptoms, endoscopic evidence of disease and radiological findings of CRS on CT scan, despite maximum medical therapy, as recommended by the European Position Paper on Rhinosinusitis (EPOS) 2012 guidelines on the management of CRS.

Thus any patient who fails to respond to maximum medical therapy for 12 weeks may benefit from surgical intervention; the choice of balloon technology or conventional instrumentation is then based on discussion between patient and surgeon.

Overall, patients with more limited anterior mucosal disease involving the maxillary, frontal and anterior ethmoids in isolation or combination would be ideal candidates for balloon sinuplasty alone. Patients with extensive ethmoidal disease with or without nasal polyposis may still benefit from a balloon sinuplasty as part of “Hybrid” procedure in which the ethmoidal disease is formally addressed by conventional endoscopic sinus surgery and the nasal polyps are removed in a traditional way. The decision to use sinuplasty technology may in part depend on the surgeon’s confidence and ability to adequately address the frontal sinus in particular with conventional instrumentation. However, as there is a small failure rate in cannulation, the surgeon must have the ability to convert to conventional techniques when required.

The importance of surgically addressing ethmoid disease is controversial; some investigators have anecdotally noted ethmoid disease resolution in some patients when peripheral sinuses were dilated without ethmoidectomy. There is limited support for this concept in the literature. Chan et al studied 5 patients with chronic frontal sinusitis who had failed medical management and also presented with ipsilateral anterior ethmoid sinusitis. After balloon dilation of the frontal stenosed ostia without ethmoidectomy, all patients showed complete radiographic clearing of both the dilated frontal sinus and the anterior ethmoid. Stankiewicz et al demonstrated that patients with both maxillary and anterior ethmoid disease had statistically and clinically significant improvement in QOL with just maxillary dilation. Karanfilov reviewed 203 patients who underwent balloon sinuplasty, 102 of which had ethmoidal disease and reported complete radiographic resolution by dilating peripheral sinuses without ethmoidectomy. It is the current practice of the authors to perform a conventional ethmoidectomy when there is evidence of ethmoidal disease on CT, regardless of what instrumentation is being used for the frontal or maxillary sinuses.

Surgical management of recurrent acute rhinosinusitis (RARS), defined by at least four acute episodes per year separated by symptom free intervals, remains contentious. Smith et al demonstrated that ESS for RARS significantly reduces utilisation of antibiotics and health care expenditure, as well as reducing risk of both antibiotic related morbidity and development of bacterial resistance. In this setting in particular, obstruction of sinus ostia in an acute setting plays a significant role, and dilatation
without tissue removal would seem to be an ideal adjunct to treatment. Another setting where balloon sinuplasty is ideal is for recurrent sinus barotrauma.

**Safety of sinuplasty:**

In 2008, Levine et al published a multicenter registry of 3276 sinuses dilated with balloon sinuplasty, in which 2 cases of CSF leak attributed to conventional FESS instruments in patients undergoing hybrid procedures were reported. There were no major adverse events in this study attributed to the balloon per se. Only one case of CSF-leak after frontal balloon sinuplasty was reported in the Manufacturer and User Facility Device Experience Database (MAUDE) adverse event report database by the Food and Drugs Administration (USA) in 2006, again caused by a traditional instrument in a hybrid procedure. Bolger et al published a multicenter study in 2007 The Clinical Evaluation to Confirm Safety and Efficacy of Sinuplasty in the Paranasal Sinuses (CLEAR study) including 115 patients with 358 sinuses operated. Of these, 124 frontal recesses had been balloon-dilated. There was no evidence of CSF leak at 24 week follow up and no other adverse events were reported at 2 years follow up reported by Weiss et al.

In contrast, Tomazic et al reported a case of CSF leak in a 36 year old patient who underwent “only balloon sinuplasty” of her frontal sinus. The thin lateral lamella of the cribriform plate was penetrated with the tip of the sinus catheter whilst attempting to dilate the frontal recess. Post operative examination confirmed a circumscribed dural herniation indicative of trauma. Conventional ESS is associated with a 1 in 1500 risk of CSF fistula, thus it would seem that balloon technology is at least as safe as conventional instrumentation.

As with ESS, it is mandatory to review CT scans preoperatively in order to evaluate the anatomy in great details. Anatomic variations such as middle turbinate concha-bullosa or a deviated nasal septum are not contraindications to balloon catheterisation but may make sinus access more difficult. A low lying cribriform plate (Keros type 3) or a dehiscent skull base should be identified preoperatively, and the surgeon needs to be aware of the risks of such variations regardless the instrument used in sinus surgery. It is essential to obtain full informed consent in the same manner as that obtained for conventional endoscopic sinus surgery, particularly as some times it may become necessary to change to conventional instrumentation during a procedure.

**What is the evidence?**

The largest prospective study to date is the CLEAR study with follow-up intervals of 24 weeks, one year and two years respectively. After two years, 195 dilated sinuses in 65 patients (initially 115 patients) showed significantly improved SNOT-20 scores and Lund-Mackay scores. Initially 347 of 358 (96.9%) sinuses were successfully dilated. 50% of the patients involved in this study underwent a hybrid procedure.

Batra notes in his review that the “Hybrid” group in the CLEAR study showed better SNOT-20 outcomes after two years compared with the “Balloon-Only” group (0.64 vs 1.09) and they had started with a higher preoperative SNOT-20 (2.42 vs. 2.14) showing that patients additionally benefitted from the surgical part in “Hybrid” procedures. Another multicenter study (BREATHE) was performed to assess the safety and outcomes of balloon dilation of the maxillary and ethmoidal sinuses. The mean overall SNOT 20 scores at 1-week, 3-month, and 6-month follow-up were 0.8 ± 0.8, 0.7 ± 0.8, and 0.8 ± 0.9 respectively (Fig 3). It also reported a 95% sinus patency confirmed by CT scan imaging at 3 months.

Koskinen et al performed a retrospective controlled study looking at 208 patients with CRS without Nasal polyps comparing symptom outcomes after maxillary sinus surgery with either the ESS or the balloon sinuplasty technique. He reported a slightly better outcomes for ESS in acute exacerbations and in patients with occupational or CRS-Related risk factors.

In comparison, Hopkins et al reported a significant improvement of the mean SNOT-22 scores following conventional ESS, with improvement largely maintained over the 5 year follow-up period. The results reported in

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**Figure 3: Comparison of the baseline and post operative SNOT-20 scores from the CLEAR (Hybrid), CLEAR (Balloon Only), and BREATHE 1 study groups**
the BSP studies reported above certainly appear comparable with those shown in Figure 4.

Plaza et al\textsuperscript{18} performed a randomised control study of 34 patients, comparing balloon dilation of the frontal sinus plus conventional ethmoidectomy with conventional ESS of the frontal sinuses and ethmoids. Outcomes measured were improvements of CT images and permeability of the frontal recess on endoscopic examination. At 12 months follow up they reported 63\% improvement of both CT resolution and permeability in the ESS alone group compared to 73\% in the frontal BSP + ESS group. Unfortunately no symptomatic outcomes were recorded.

**Limitations:**
Stammberger et al has emphasized the need for continued training in a wide range of sinunasal techniques and procedures to overcome any unexpected intra-operative findings that would place a balloon only trained surgeon in a very difficult position. The Graz experience looking at the feasibility of Balloon sinuplasty was abandoned following an unexpected high failure rates. The study initially intended to cover 200 patients with CRSsNP who had a refractory medical therapy and were referred to the Graz to consider surgical intervention. 45 consecutive patients were included in whom 112 sinuses were approached by BSP. Of the 112 sinuses, 68 (60\%) were planned as a “Balloon-Only” procedure and 44 (40\%) were planned as a “Hybrid” procedure. Of the 68 sinuses in the “Balloon-Only” group, in 44 sinuses BSP failed, equating to a failure rate of 65\%. Forty-four sinuses were planned for “Hybrid” procedures. In 29 of these sinuses BSP failed, giving a failure rate of 66\%. Based on these initial results the study was abandoned\textsuperscript{19}.

Difficulty to cannulate the frontal sinus, failure to inflate the balloon and creation of accessory ostium when dilating the maxillary sinus were amongst the reasons for failure, although also included were a number of cases where sinuplasty was not even attempted. In contrast, failure rates have not been a problem in our own experience. Hopkins et al\textsuperscript{20} reported successful dilation in 98\% of 67 sinuses in our first 27 patients, while still on a learning curve, and successful cannulation rates have been maintained at this level. We do not usually use the balloon in cases of CRS with nasal polyps, and rarely in revision cases, which may account for some of the differences with the Graz experience.

Since introduction to the market, sinuplasty has generated significant controversy, on contrast to the quiet acceptance of other advances in instrumentation such as powered microdebriders. Perhaps, in different market environments such as the U.S., where direct marketing to patients is permitted, and financial reimbursements are higher, there has been a corruption in the indications for surgical intervention in some cases. It is essential to consider this new technology as an adjunct to the current ESS and not a replacement; the development of new technology should not change the indication for surgery per se.

Under current austerity measures and demands for efficiency savings, several NHS Trusts have concerns with regards to the additional disposable costs of sinuplasty when compared with ESS. The same balloon may be used for each sinus to be dilated, but the disposable cost per patient is currently in the region of £900, despite a number of different manufacturers now competing for market share. However, use of balloon technology may reduce operative time for some surgeons, and the potential to move treatment out of the operating theatre has further potential for cost-saving; a recent US study reported reduced operative costs for balloon sinuplasty when performed in office compared to standard operative room cost\textsuperscript{21}.

Finally, use of the balloon is no substitute for careful analysis of the scans and expert knowledge of sinus anatomy. Thoughtful interpretation of the site of transillumination is essential to ensure correct placement, as cannulation of large Kuhn cells or supraorbital cells may still allow transillumination, and may lead to inadvertent inflation of these cells, further obstructing the frontal sinus outflow. The examples in Figure 5 were referred to us having undergone sinuplasty elsewhere, and we believe incorrect placement occurred in both cases for the reasons above. This may have been avoided with careful interpretation of the scans. As with any technique, adequate training is essential, and the instrument is only as good as the surgeon applying it.

**Future developments:**
The USA has seen an explosion of balloon sinuplasty being performed in an outpatient setting under local

**Figure 4:** Comparison of the pre and post operative SNOT-22 scores in the national audit of surgery for rhinosinusitis and nasal polyposis
anaesthesia. Further studies are needed to assess whether the clinical outcomes and patient satisfaction are comparable to doing it in theatre, but early results are very encouraging. It has been suggested that doing balloon sinuplasty under local anaesthesia as an outpatient leads to quicker recovery times, patients reporting back to work quicker, and a decreased use of man power, leading to overall procedural cost savings.

Conclusions:
Balloon sinuplasty is an adjunct to and not a replacement to functional endoscopic sinus surgery. It should be performed according to international guidelines already existing for the management of chronic rhinosinusitis and following careful evaluation of a pre-operative CT scan. The technology appears to be safe and effective, and there and there are promising results in the literature on BSP being widely used as an office-based procedure for selective cases in the US.

References:

Figure 5: CT scans of 2 patients referred for ‘failure of sinuplasty’ due to incorrect placement of guidewire.
Nasal septal perforation: causes and management options

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Abstract
This article reviews the aetiology and assessment of patients presenting with perforation of the nasal septum. The need for investigation and place of septal biopsy is still controversial and is discussed.

Conservative means of controlling symptoms are described and the use of septal obturation is discussed. The surgical management includes the use of a partial septectomy to enlarge the perforation. The indications and techniques for surgical repair and reconstruction of the perforation are then discussed.

Key words
Septal perforation, nasal septum, septal reconstruction.


Introduction
Perforations of the nasal septum are often seen in ENT clinics but the exact prevalence is unknown. They can incidental and asymptomatic but some are very challenging to manage. This article will deal with the various practical issues that we face as ENT surgeons in assessing and managing septal perforations.

Aetiology of septal perforations
Texts on septal perforation often provide a daunting long list of potential causes of septal perforation but in clinical practice, most are either idiopathic or traumatic following direct nasal trauma or septal surgery (Table1). However, uncommon causes secondary to tumours, chronic inflammatory disease and infections must also be considered and excluded.

The bony septum consists of the perpendicular plate of the ethmoid bone superiorly and the vomer inferiorly. The mucoperichondrium and mucoperiosteum are held firmly against the septum at the fibrous junction between the two. The posterior edge of the bony septum forms an arch in the anterior section of the nasopharynx, and extends superiorly to form the thick bony rostrum superiorly as it abuts up to the sphenoid sinus.

An understanding of the blood supply of the septum is essential knowledge prior to contemplating surgical repair of a septal perforation. The posterior section of the septum is supplied by branches of the sphenopalatine artery that run in a horizontal plane. The mid and anterior septum is supplied by a rich anastomosis of vessels from the following feeding vessels: the sphenopalatine artery; the anterior ethmoidal arterial branches from the anterior cranial fossa; the labial branches from the facial artery; a palatine branch from the greater palatine vessels that run on the inferior surface of the hard palate.

Aetiology of septal perforations
Texts on septal perforation often provide a daunting long list of potential causes of septal perforation but in clinical practice, most are either idiopathic or traumatic following direct nasal trauma or septal surgery (Table1). However, uncommon causes secondary to tumours, chronic inflammatory disease and infections must also be considered and excluded.

Trauma includes direct trauma to the external nose or nasal septum, or surgical trauma from septal surgery, cautery and nasal packs. Submucosal resection of the septum is reported to have a much higher incidence of septal perforation than septoplasty, and estimates quote 17 – 25% and 1.4 – 5% respectively1,2. A perforation is much more likely to arise if the mucosa has been torn or removed in adjacent parts of the mucosa.
Digital trauma from recurrent picking with a finger nail is associated with a pick ulcer. The patient is often said to have caused the perforation from persistent picking but in reality they are probably only trying to keep the nose clear of crusts that block the nose and embarrasses the patient.

Mucosal trauma from irritants and particularly substance abuse may progress to perforation. Cocaine causes intense vasoconstriction of the mucosa and may induce massive defects in the nasal septum as well as external nasal collapse and saddle deformity. Irritants at work from chronic or sulphuric acid fumes are reported to cause septal perforation.

Steroid nasal sprays are also reported to cause anterior septal perforation, probably from the trauma from the jet of the actuated spray, but the incidence is likely to be extremely low.

A number of chronic inflammatory and granulomatous diseases, including sarcoidosis, relapsing polychondritis, systemic lupus erythematosus, Crohn’s disease and dermatomyositis are associated with septal perforation. However, the most likely and most important diagnostically is Wegener’s Granulomatosis, now known as granulomatosis with angiitis. The latter is potentially lethal due to the risk of renal failure and can also destroy most of the nasal septum resulting in very large perforations (Figure 1) and external saddle deformity. Cocaine abuse can be associated with a Wegener’s type reaction and cause massive septal perforation and perforation of the hard palate.

**Specific infections such as tuberculosis and syphilis are now rare causes of septal perforation.**

Malignant tumours by nature are destructive and may cause septal perforation. Tumours such as squamous cell carcinomas, mucosal melanoma and adenocarcinoma should always be considered and excluded.

**Prevention of septal perforation**

Having acknowledged that symptomatic septal perforations are difficult to manage, all efforts should be made to prevent iatrogenic perforation. Cautery should be applied with caution: this applies specifically to monopolar diathermy applied to the nasal septum in patients with

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**Figure 1:** Massive perforation extending to posterior section of nasal cavities following cocaine abuse. Both middle turbinates are visible. Inferiorly, mucosa overlies the maxillary crest. The posterior edge of the perforation is thick and covered by moist crusts.
difficult epistaxis. Nasal packs should be inserted with care and attention to avoid mucosal trauma and excessive prolonged pressure. The septum is particularly at risk in patients with hereditary haemorrhagic telangiectasia who undergo multiple episodes of cautery or septodermoplasty, sometimes combined with septoplasty.

Simple cautery with silver nitrate is very unlikely to lead to a perforation but it is good practice to avoid applying this to both sides of the nasal septum simultaneously, as may arise in children with bilateral nose bleeds. Furthermore, it is not necessary to apply silver nitrate on the nasal mucosa for more than 5 seconds. There is good level evidence that 75% concentration silver nitrate is preferable to 95% as it is more effective in the short term and causes less pain.

Whilst performing septal surgery, care and attention should be given to preserving the mucosa and avoiding tears if at all possible. Sometimes, mucosa over a septal spur is so thin and atrophic that a tear in inevitable, but care should be taken to avoid a tear on the mucosa directly opposite, especially if the cartilage and bone between the two has been removed. If this has been the case, the defect should be repaired and the cartilage replaced.

**Patient assessment and Clinical features**

Patients with perforations of the nasal septum are typically referred with a combination of rhinological symptoms but most are initially unaware of the presence of the perforation. Symptom complaints include whistling, nasal airway obstruction, bleeding, crusting, and mucus clearance problems. Whistling is a particular feature of a small anteriorly placed septal perforation. The persistence of a dry nasal crust, coupled with repetitive manipulation and attempts at clearance can lead to progressive enlargement of the defect. Documenting these symptoms by linear analogue scales and/or the Sinonasal Outcome Test – 22 is helpful in monitoring the effect of any intervention.

A full rhinological assessment is necessary to exclude other sinonasal pathology or chronic inflammatory disorders.

After a complete medical history, attention should be turned to the external nose and oral cavity before assessing the intranasal septum and nasal cavities endoscopically. Most patients will have a normal external nose. However, external nasal trauma may result in deviation or deformity of the nasal dorsum. Large perforations may cause a saddle deformity, tip ptosis and columella retraction.

Mucosal vasoconstriction with phenylephrine or xylometazoline spray will facilitate a clear accurate view of the nasal septum and any potential deviation. The nasal cavities should then be examined with an endoscope, looking specifically at the perforation, residual nasal septum and ethmoid regions. Perforation of the anterior cartilaginous septum is the commonest most easily seen defect (Figure 2) but perforations of the mid and posterior septum may only be noted on endoscopy.

It is important to assess the proportion of septum around the perforation as the proportion that remains determines the likely success of surgical reconstruction. The dimensions of the perforation should be measured with a small ruler. The margins should be inspected for drying, crust formation and evidence of bleeding. Thickening and inflammation of the marginal mucosa should be noted. The cartilaginous defect may be much greater than the mucosal defect and this can be assessed by palpation with a blunt probe.

**Investigations**

Controversy exists as to whether or not to investigate all patients with a septal perforation routinely, and if so, and which investigations should be done. The objective of investigation is to determine a specific condition that is responsible for the perforation and to exclude a tumour.

If there is a clear history of nasal trauma or surgery in a patient who is otherwise fit and well and the perforation margins do not look thickened, inflamed or suspicious, then there is probably no reason to perform detailed investigations. If the perforation is crusted, a culture from site of the anterior nasal cavity to look for staphylococcus colonization and guide medical treatment may be helpful.
However, should investigation be the preferred option, then systematic consideration should be given to blood tests, imaging and nasal biopsy (Table 2). Firstly, a vasculitic screen that includes the following tests should be arranged: erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), centrally accentuated ant neutrophil cytoplasmic autoantibody (c-ANCA), perinuclear antineutrophil cytoplasmic autoantibody (p-ANCA) and angiotensin-converting enzyme (ACE), autoantibodies, calcium levels, urea and electrolytes. A urine sample for urinalysis should be obtained and a chest radiograph arranged. A CT scan of the sinuses should also be considered.

The question of biopsy is perhaps the most controversial topic. A biopsy is not without risk and may induce crusting and bleeding in a stable perforation. Biopsy can also enlarge a perforation, and if taken from the dorsal edge, may induce saddle deformity. However, should a chronic granulomatous condition be likely, the biopsy should be taken from an area of abnormal mucosa prior to starting the patient on medical treatment. Nasal biopsies in patients with Wegener’s granulomatosis are however, often non-diagnostic and show only chronic inflammation. Malignant tumours are unusual but their appearance is generally suggestive of a destructive or invasive process and biopsy will be essential and diagnostic. Tuberculosis and syphilis are extremely rare in the UK but should there be any suspicion then targeted investigation is required. This will include septal biopsy as well as a Heaf/Mantoux test for tuberculosis and serology for syphilis.

**Table 2. Investigation of septal perforation**

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>Initial investigation</th>
<th>Subsequent investigation</th>
<th>Diagnostic Imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior perforation / healthy edges / no crusting / history of trauma or surgery</td>
<td>No identifiable cause</td>
<td>If markers are positive, then perform targeted biopsy</td>
<td>Consider CT sinus scan / chest radiograph then chest CT</td>
</tr>
<tr>
<td>Anterior perforation / crusting / inflamed thickened edge</td>
<td>Vasculitic screen / urinalysis / culture swab</td>
<td>Wegener’s granulomatosis / Sarcoïdosis</td>
<td></td>
</tr>
<tr>
<td>Perforation of anterior and posterior septum with granulations / crusts</td>
<td>Include syphilis serology / Mantoux or Heaf test</td>
<td></td>
<td>CT sinus / MRI head / CT neck and chest according to histology</td>
</tr>
<tr>
<td>Suspected tumour</td>
<td>Urgent targeted biopsy</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Observation and conservative therapy

Small asymptomatic septal perforations need no active intervention other than assessment of size and review. Such perforations are more likely to reside in the mid-section of the nose.

Perforations near the anterior part of the nose are much more likely to be symptomatic and will need interventional management. The objective of treatment is to keep the perforation clean and encourage the margins to develop healthy mucosa. A prolonged course of topical antibiotic / antiseptic nasal cream ((chlorhexidine dihydrochloride 0.1%, neomycin sulphate 0.5%; Naseptin) or mupirocin (Bactroban) ointment for 4-6 weeks is often effective. Long-term application of petroleum jelly is also frequently advised. Saline sprays and rinses should be helpful in removing and controlling crust formation.

**Septal obturators**

Occluding the perforation with a silicone polymer (Silastic®) septal obturator is a popular method of treating a symptomatic septal perforation. Perforations of about 1 – 2cm are usually suitable for this device, although experience using two splints to obturate larger perforations have also been described in the literature. The obturator is fitted in the operating theatre and it is important to cut the flanges to an optimum size to avoid subsequent irritation (Figure 3). However, the success in alleviating symptoms is variable, and not all patients benefit from this device. Long-term follow-up studies have shown that many patients do not tolerate the device well and eventually seek removal of the septal button. Nasal hygiene to prevent or remove crusts is important once an obturator has been fitted.

Custom-made obturators are reported to have a more effective outcome but the patient will need high resolution...
CT scanning of the septum to enable such a device to be made\textsuperscript{9}.

Even though an obturator has limited success, a decision to try such a device may be taken prior to proceeding to operative repair, given that surgery has variable success in closing septal perforations.

\textbf{Surgery for septal perforations}

Surgical procedures are designed either to close the septal perforation or paradoxically enlarge the perforation in a posterior direction.

\textbf{Septal perforation enlargement surgery}

This procedure is ideal for perforations that are deemed to be too large to repair but are subject to crusting and bleeding. By moving the posterior margin back to the posterior part of the nose and ensuring that the margin is covered by healthy mucosa, the crusting is normally controlled\textsuperscript{10}.

The technique includes raising and preserving a mucosal flap that is long enough to wrap around the posterior margin of the extended perforation, once the edge has been resected and moved to the back of the nose.

Perforations of 2cm diameter or larger are suitable for this procedure, but once done, there is no possibility of returning to repair the perforation.

\textbf{Repair of septal perforations}

Septal perforations of the anterior cartilaginous septum are most likely to be symptomatic compared to perforation in the posterior part of the nose. However, attempts to repair perforations of the cartilaginous septum are invariably challenging and difficult, with variable success\textsuperscript{11}. Some patients may wish to take this chance to avoid long-term medication and the variable effects of an obturator.

Several techniques have been described but the principles are common to all. Firstly, the edges of the perforation should be as healthy as possible, having controlled crusting and infection with the conservative therapy described above. The dimensions of the perforation should be recorded; there should be an adequate area of intact septum superior to the perforation between the perforation and the nasal dorsum; the mucosa surrounding the perforation should be healthy and robust. The site relative to the nasal valve should also be noted and it is important to avoid inducing a narrowing the nasal valve. Access to the surgical site should be optimized and mucosa should be widely elevated to permit closure that is not under tension. An interpositional middle layer should ideally be inserted to replace the cartilaginous defect and serve as a scaffold. Several graft materials are described and include septal, conchal or rib cartilage, temporalis fascia, peristeum, acellular dermal allografts and bioglass. Mucosal incisions should be horizontal to avoid transecting branches of the sphenopalatine artery. Absorbable polyglactin (Vicryl\textsuperscript{TM}, Ethicon inc) sutures on round body needle are recommended and prevent unnecessary tearing of the mucosa at suture points. Post-operatively, it is important to prevent infection and keep the nose clean. Oral antibiotics, saline sprays and topical antibiotic/antiseptic cream are all important adjuncts.

Generally, perforations up to 2cm diameter are suitable for repair. Small anterior perforations of less than 5mm diameter can be approached via the anterior nares, carefully elevating mucoperichondrium through a hemitransfixion incision. Larger perforations up to 2cm diameter will need much more surgical access and an open rhinoplasty approach is recommended. Bilateral alar incisions have also been described. A midface degloving technique has also been utilized but access is not that much greater than the open rhinoplasty approach, but complications are more likely. Large perforations require much wider elevation of posteriorly based mucosal flaps that may include the floor of the nose up to the origin of the inferior turbinates.

Alternative means of transposing tissue to close the perforation include the use of mobilized inferior turbinate based on a posterior pedicle, or elevation of oral mucosa that is passed through a channel under the upper lip to reach the nose. Inferior turbinate flaps may cause significant nasal obstruction and a second stage procedure to release the posterior attachment will be necessary. Oral mucosal flaps may necrose or leave a residual oronasal fistula.

\textbf{Figure 3: A silicone polymer septal button with flanges in situ.}
A vascularized flap may be required to repair large perforations in patients with poor nasal tissues as may arise after radiotherapy. Examples include a free flap based on the facial vessels and a musculomucosal flap based on the facial artery.

**Conclusion**

The surgical repair of septal perforations is an uncommon procedure that is often difficult, fraught with limited success and easy to missjudge. Many techniques have been described and include pedicle flaps, rotation and advancement flaps with free grafts to create a middle layer.

Although the success following repair and reconstructive surgery is quoted at 80-90%, authors publishing such data generally have a specialist interest in this particular type of surgery. Given that it is very easy to under-estimate the difficulty of septal perforation repair, it is probably wiser to refer on to a colleague with experience in these techniques in order to achieve the greatest chance of a good surgical outcome for the patient.

**References:**

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Adults: Two sprays per nostril once daily (total daily dose, 110 micrograms). Once symptoms controlled, use maintenance dose of one spray per nostril once daily (total daily dose, 55 micrograms). Reduce to lowest dose at which effective control of symptoms is maintained. Children aged 6 to 11 years: One spray per nostril once daily (total daily dose, 55 micrograms). If patient is not adequately responding, increase daily dose to 110 micrograms (two sprays per nostril, once daily) and reduce back down to 55 micrograms daily dose once control is achieved.

Contraindication: Hypersensitivity to active substance or excipients.

Side Effects: Systemic effects of nasal corticosteroids may occur, particularly when prescribed at high doses for prolonged periods. These effects are much less likely to occur than with oral corticosteroids and may vary in individual patients and between different corticosteroid preparations. Potential systemic effects may include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, cataract, glaucoma and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children). Very common: epistaxis. Epistaxis was generally mild to moderate, with incidences in adults and adolescents higher in longer-term use (more than 6 weeks). Common: headache, nasal ulceration. Uncommon: rhinorrhoea, nasal discomfort (including nasal burning, nasal irritation, and nasal soreness), nasal dryness. Rare: hypersensitivity reactions including anaphylaxis, angioedema, rash, and urticaria. Not known: transient ocular changes, growth retardation.

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The pathology and management of antrochoanal polyps

Natasha Choudhury FRCS, Hesham A. Saleh FRCS.

Abstract
Antrochoanal polyps (ACP) are benign lesions that originate from the mucosa of the maxillary sinus, and extend into the nasal cavity, choana and nasopharynx. They are almost always solitary, unilateral lesions, and rarely arise from other sinus groups. The treatment of ACPs is surgical, with a number of different surgical techniques having been described. The pathology, presentation and management of ACP are described.

Key words
Antrochoanal, Polyp, Sinus, Antrum.

Introduction
Antrochoanal polyps (ACP) are benign lesions that originate from the mucosa of the maxillary sinus, and extend into the nasal cavity to reach the choana and nasopharynx. The first reported case was in 1753 by Palfyn1 although it was Killian who later described the lesion in detail in 1906. ACPs are relatively uncommon and account for just 4-6% of all nasal polyps, although they are much more frequently encountered in children, with an increased incidence of up to 35% in the paediatric population. Even among adults, they usually present at a younger age, as compared with nasal polyps; Larsen and Tos conducted a comparative study between patients with nasal polyposis and antrochoanal polyps and found that the mean age at diagnosis was 50 years and 27 years respectively. They are also reported to occur twice as commonly in males, although there are some conflicting reports claiming no noticeable difference in incidence between males and females in children.

Antrochoanal polyps are almost always solitary, unilateral lesions, with only a few reported cases of bilateral ACPS having been reported in the literature to date, mainly in children, although more recently there has also been similar cases reported in adults. It has been suggested that most ACPs originate from the posterior antral wall of the maxillary sinus. In one published series of 37 cases, 38% were reported to originate from the posteromedial wall and 19% from the posterior wall. In a minority of cases, other sites of origin were described including 8% from the anterior wall, 8% from the anteromedial wall, 8% from the floor, 5% from the lateral wall, 5% from the roof, 3% from the anterolateral wall, 3% from the posterosuperior wall, and 3% from the inferolateral wall. In our own series of 29 adult patients with antrochoanal polyps, we similarly identified the posterior wall to be the most frequent site of origin, in 55% of our patient cohort (unpublished data).

Although antrochoanal polyps typically originate from the maxillary sinus, there are some rare reports of them arising from other sinus groups including the sphenoid and ethmoid sinuses, from which they can also extend into the nasal cavity and choana. Clinically, they usually present with unilateral nasal obstruction, but a variety of other sinonasal symptoms have also been reported such as epistaxis, rhinorrhea and postnasal drip, as well as other rarer aerodigestive symptoms including snoring, obstructive sleep apnoea, dysphonia, and dysphagia.

Clinical examination:
Using a nasal endoscopy will typically reveal a smooth polypoidal swelling originating from the middle meatus and extending posteriorly into the choana. Stammberger and Hawke found that 70% of ACPs emerge through an accessory ostium. Aydin et al studied 37 patients with ACPs and found that 51% originated from an accessory ostium, 43% from the natural ostium and 6% from both.

Very large ACPs can be seen to be filling the nasopharynx or even extending down to the oropharynx.

Radiological imaging:
Radiological imaging should be performed before considering treatment, in view of the unilateral nature of the disease. CT scanning typically shows a soft tissue mass filling the maxillary sinus with opacification of the middle meatus and extension into the choana (Figure 1).
Histological findings:

Although such radiological features are typically suggestive of an underlying antrochoanal polyp, there are a number of other diverse disease processes that should be considered as part of the differential diagnosis, in patients with such unilateral nasal pathology or choanal lesions. A study by Lopatin et al evaluated 20 cases of choanal polyps and from these, they identified two cases of inverted papilloma among them, highlighting this as an important differential, which also typically presents as a unilateral choanal lesion \(^\text{16}\). We have similarly reviewed all patients with a presumed antrochoanal polyp who have been managed at our institution, and in our own experience we have identified 18% of these patients to have discrepant histology with a different underlying histological diagnosis made following surgical biopsy (unpublished data). These have included a diverse range of both benign and malignant pathologies, of which the most frequent pathology was also inverted papilloma.

Therefore, in any patient with clinical features suggestive of an antrochoanal polyp, radiological imaging with a CT scan of the paranasal sinuses should always form part of the diagnostic work up, but even in cases with features consistent with an antrochoanal polyp, other differential diagnoses need to be borne in mind. From our experience we have found important radiological features of bony sclerosis, erosion and destruction to be non specific for the underlying histological diagnosis, in such cases. Histopathological analysis should therefore always be performed following biopsy of any unilateral nasal pathology, including suspected antrochoanal polyps.

**Pathology of Antrochoanal Polyps:**

Macroscopically, antrochoanal polyps consist of two parts, namely a cystic component which fills the maxillary sinus and solid part within the nasal cavity, which together form a typical dumb-bell shaped polyp (Figure 2). Microscopically, the ACP shows a number of typical histological features (Figure 3). The polyp surface is lined with respiratory epithelium and includes a central cystic cavity surrounded by a homogenous, oedematous stroma, with few cells. In contrast to inflammatory nasal polyps, ACPs have less inflammatory infiltrate with significantly lower eosinophils \(^\text{17}\). An ACP also exhibits significantly higher fibrous inflammatory changes with proliferation of fibroblasts and collagen, and a lymphocyte inflammatory infiltrate. It has been postulated that the latter is related to

![Fig. 1: Computed Tomography images of paranasal sinuses, showing features consistent with an antrochoanal polyp. (A): Axial view showing soft tissue opacification within the right maxillary sinus with extension via the posterior fontanelle, into the nasal cavity and choana. (B): Sagittal view showing extension of soft tissue lesion from the nasal cavity into the choana.](image1)

![Fig. 2: Macroscopic appearance of an antrochoanal polyp, demonstrating a typical 'dumbell' appearance.](image2)
the long evolution of an ACP that leads to a scarring stage. The surface epithelium of an ACP is mostly intact in contrast to some disruption that is seen in inflammatory nasal polyps.

**Pathogenesis:**
The underlying aetiology of antrochoanal polyps is still not fully understood. Chronic rhinosinusitis and allergy have both been implicated, but there are conflicting reports regarding their association. Lee and Huang determined that 65% of their paediatric patients with ACPs had co-existing chronic sinusitis. Similarly, some authors have also identified an association of ACPs with allergic disease. Most notably, Cook et al identified 67% of their patient cohort, which included a total of 33 patients as being diagnosed with concomitant allergic rhinitis, and this association was found to be statistically significant. However, many other studies have found no positive association between allergy and ACPs, and therefore the true significance of these co-existing pathologies remains unknown.

Our understanding of the cellular aetiology of antrochoanal polyps is also still evolving. The molecular biology of ACPs has been studied by some authors. Urokinase type plasminogen activator (u-PA), which is related to proliferative changes of the mucous membrane in inflammatory tissue, has been identified in ACP tissue extracts. Other reports have shown that the expression of basic fibroblast growth factor (bFGF) and transforming growth factor (TGF) β was significantly higher in ACPs than in chronic rhinosinusitis and healthy mucosa. Some also showed increased expression of matrix metalloproteinase-9 (MMP-9), which is involved in mucous membrane inflammation in ACPs.

**Management of Antrochoanal Polyps:**
The treatment for antrochoanal polyps is surgical removal. A variety of different surgical approaches have evolved with time and been used with varying success. Simple avulsion is the simplest form of surgery for antrochoanal polyps. However, it is associated with high rates of recurrence because the maxillary portion is not removed, and therefore this surgical technique should be avoided in current day practice. To reduce the risk of recurrence, other surgical approaches have been described including the Caldwell Luc approach. This offers good exposure to facilitate complete, simultaneous removal of the mucosa of the maxillary sinus and the ACP under direct vision. However, there is a recognised morbidity from risks of infraorbital paraesthesia and also to developing dentition in children with this approach, but it is still reserved as a considered approach, particularly in revision cases where there has been recurrence of the antrochoanal polyps following previous surgery. The most widely established and accepted surgical approach now is endoscopic sinus surgery due to the significantly less associated morbidity. However, with this more conservative surgical approach, there is the potential for residual disease, and subsequent recurrence. Some authors therefore advocate a combined approach using a Caldwell-Luc approach together with an endoscopic procedure in select cases. Alternatively, El-Guindy and Mansour have described another combined approach using both endoscopic middle meatal surgery together with transcanine sinoscopy to resect the antral part in recurrent cases. This has been further modified by Hong et al, with powered instrumentation with a microdebrider through the canine fossa for broad based resection of the antral component at its attachment.

In our own practice, we use an endoscopic approach for all cases of antrochoanal polyps. We have used this approach in a total of 29 adult patients to date, with no recurrences over a mean follow up period of 14.7 months (unpublished data). This series included 4 patients who were referred to us with a history of previous antrochoanal polyps surgically managed elsewhere. Some of these individual patients had undergone numerous previous operations for their antrochoanal polyps (up to 7 previous surgeries) but we
have successfully managed all of them using the same endoscopic approach. This select group of patients have had a more protracted follow up period of up to 2 years, also with no recurrences.

The principles of an endoscopic approach for surgical resection of an antrochoanal polyp should include creating a large middle meatal antrostomy in order to access the maxillary portion. Where the antrochoanal polyp has already created an auto-antrostomy, this should be enlarged further. This will facilitate removal of the nasal component and cystic antral part en bloc, where possible. A nasal snare can be tightened around the nasal portion close to the antrostomy and gradual “to and fro” movements can lead to the complete removal of the whole ACP (Figure 2). The next, and most important step of the surgery is close, direct inspection of the maxillary sinus cavity, using angled endoscopes (30°, 45° and 70°), in order to inspect the site of origin of the antrochoanal polyp. This is crucial to assess for any residual mucosal remnant, which must be removed to reduce the risk of recurrence. For this, either angled curetting instruments or a curved microdebrider (60°, 90° and 120°) can be used (Fig. 4), set at 1500rpm, to debride the underlying mucosa at the site of origin.

Summary:
Antrochoanal polyps are a benign sinonasal condition that can present with a number of symptoms, the most frequent being persistent unilateral nasal obstruction. The diagnosis is usually obvious from the clinical examination with nasal endoscopy, but it should be investigated with cross sectional imaging with a CT scan of the paranasal sinuses. Radiological features of soft tissue opacification filling a single maxillary antrum, with extension into the nasal cavity and choana will typically confirm the diagnosis. However, histological confirmation is required to exclude any other underlying pathology.

The definitive treatment for antrochoanal polyps is surgery, with an evolution in surgical techniques from previously described open approach surgery to more recent endoscopic techniques. All surgeries aim for complete removal of the ACPs and to avoid future recurrences. Of the different approaches, the endoscopic technique is now most commonly favoured, with the advantages of reduced operating time and hospital stay, and reduced morbidity. The key steps of the endoscopic approach include creating a large antrostomy to allow careful inspection of the antrum, following removal of the polyp. This will allow subsequent removal of the underlying mucosa at the site of origin of the ACP, in order to reduce the risk of future recurrence.

References:
The principles of upper eyelid blepharoplasty

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Abstract
Blepharoplasty of the upper eyelids when undertaken appropriately can completely rejuvenate the individual. In this paper, we describe our approach to the patient with upper third aging. The approach should be tailored to the individual's needs trying to achieve a natural result that will not in any way affect the function of the eye.

The anatomy, preoperative assessment, decision-making, surgical planning, eyelid marking, and various techniques associated with current concepts in aesthetic upper blepharoplasty are described.

Key words
Blepharoplasty, Blepharoptosis, Eyelids.

Introduction
Upper eyelid blepharoplasty is one of the most effective procedures in aesthetic plastic surgery. Upper third aging can falsely project an appearance of tiredness, sadness, anger, or lack of interest. Upper eyelid blepharoplasty must be customized to the individual's requirement and desire. Upper lid blepharoplasty includes the restoration of a natural sharp and crisp pre-tarsal fold and a pre-tarsal show¹. Evaluation of the upper eyelid must include an evaluation of the eyebrow². Brow ptosis should be corrected, residual brow ptosis compounds upper lid hooping and if ignored blepharoplasty result will be sub standard³. Aging causes the eyebrow fat and thick skin to descend over the upper lid, giving it a full appearance. Tailored blepharoplasty, resecting the appropriate tissue planes will deliver a rejuvenated look. Lack of a clear plan and a one-size fits all approach may result in sub par result in a significant number of cases. This results in a more aged appearance. It is important to assess the patient on an individualized basis and ensure the correct approach is applied to the correct patient.

Some important Anatomical Concepts of the Eyelids:
The pre-tarsal eyelid show is often less than 4 mm in the aesthetically attractive eye.

The upper eyelid is considered as tarsal and orbital portions at the level of the supra-tarsal fold. The skin crease in Caucasians, is located approximately 8 to 10 mm from the palpebral margin and results from a fusion of the levator aponeurosis, orbital septum, and fascia of the orbicularis oculi into the dermis. In males it is usually lower. This area degenerates with age, which may lead to a high fold (Figure 1a), with or without upper lid ptosis, and/or skin laxity of the lid (Figure 1b). Qualitative and quantitative changes may result in the loss of crease attachments and cause the skin drop beyond the upper eyelid/lash margin, with a tendency to interfere with upper outer visual fields³.

Clinical Evaluation:
The surgical approach must take into consideration the repositioning of underlying soft tissue and the re-draping of skin. Evaluation of the upper eyelid must include an evaluation of the eyebrow. Brow ptosis should be corrected to achieve repositioning of heavy eyebrow skin, which may be compensated by frontalis contraction to keep the eyebrows above the orbital rim. Aging causes the eyebrow...
fat to descend over the upper lid, giving it a full appearance (Figure 1b). Once the visual obstruction has been removed by eyelid skin resection, the brows may look even heavier since elevation is no longer needed for the visual field. This results in a more aged appearance. Any underlying true lid ptosis should also be corrected. The skin mobility of the upper eyelid is essential to avoid lagophthalmos, so resection must be conservative, especially in the nasal half.

Pre-operative Markings:
Preoperative markings are critical in assessment of the patient and are made with the patient sitting upright and in neutral gaze. The brow needs to be elevated to the proper position before any marks are made. The supra-tarsal fold is located at approximately 8 to 10 mm above the ciliary margin in women and at 7 to 8mm in men. A mark should be made on this fold (Figure 2). The upper marking must be at least 10 mm from the lower edge of the brow and not include any thick brow skin. The use of a pinch test with a non-toothed forceps for re-draping the skin is helpful (Figure 3). The index of safety is much higher laterally (one can remove more skin) and becomes more critical as the incision proceeds medially. The incision may need to be extended laterally with a larger excision, but extension lateral to the orbital rim should be avoided if possible to prevent a prominent scar. Similarly, the medial markings should not be extended medial to the medial canthus for larger resections because extensions onto the nasal sidewall result in webbing. If excessive skin is present medially, a more vertical resection may be considered. It is important to ensure that the preoperative markings, especially medially, disappear when the eye is open in the primary position. This ensures that any unsightly scars will be avoided. The amount of fat to be resected should be determined preoperatively, with the patient in up-gaze, down-gaze, and medial and lateral ranges of motion, with photographic documentation. We often use cross-hatching to indicate the amount of fat to be removed as this can become difficult to assess after local infiltration however in the majority of cases no fat is removed as most blepharoplasties will not require fat resection.

The Standard Upper Eyelid Blepharoplasty Surgical Technique in the Older Patient:
Subcutaneous injection with 2-3 cc of a pre-made mixture of 4cc of lignospan (2% lignoaine with 1:80,000 adrenaline), 4 cc of bupivacaine and 2cc of dexamethasone (8mg) is injected subcutaneously using a 27G- gauge needle by firstly pinching the skin and then rolling the orbicularis off the skin to ensure that the injection is just subcutaneous. The speed of injection is crucial in avoiding patient discomfort. This improves patient satisfaction rates. A rubber corneal shield is used in all eyelid procedures to avoid inadvertent damage to the cornea. Incisions are made using a monopolar microdissection needle. The skin, without muscle, is dissected off the underlying tissue maintaining rigorous haemostasis (Figure 4 a, b, c). Once the skin has been removed a strip of orbicularis is then removed. The upper 1/3 of muscle is removed (Figure 5). If lateral brow elevation is required more orbicularis muscle is removed at the lateral corner. If pre-septal muscle is left under the skin excision, there will be muscle over muscle when the final closure is performed. This redundancy can cause a heavier, fuller lid postoperatively and
interfere with the creation of a clean, distinct supra-tarsal fold. If fat removal has been deemed necessary a small incision is made into the medial compartment of the eyelid. The fat is teased out and resected using a clamp, cautery and curved scissors. It is rarely necessary, in our experience, to remove fat from the central and lateral fat pads though lacrimal gland repositioning is often required (Figure 5).

In cases where reformation of skin crease is necessary the sutures should include the subcutaneous aponeurotic/septal tissue. Figure 6 shows pre and postoperative appearances of a blepharoplasty in an older patient.

Upper Lid Blepharoplasty in the Young Patient:
The surgical approach is exactly as described above however we do not remove the orbicularis muscle in these patients.

Post-operative Care:
Preservative free ocular lubricants are prescribed four times per day for two weeks. Chloramphenicol ointment is used topically on the eyelid incision and in the eye for 2 weeks at night. The sutures are removed at ten days, when the monopolar needle is used as it takes longer to heal.

Contraindications to surgery include patients with psychological issues, dry eyes, uncontrolled inflammatory skin conditions such as eczema and psoriasis, multiple redo surgeries and in situations where removing skin would lead to lagophthalmos.

Conclusion:
Blepharoplasty is a highly successful aesthetic surgical procedure that requires careful preoperative planning and examination of the patient’s concerns and desires. Standard resections of fat and muscle have been replaced with conservative and careful resections of only redundant soft tissue. Ptotic soft tissues are relocated rather than resected. The eyelid must always be considered in conjunction with the eyebrow, and correction of periorbital aging may require brow repositioning as well. Careful perioperative technique, meticulous haemostasis, and attentive postoperative management of blood pressure will prevent most complications.

The ten most important principles in Upper eyelid blepharoplasty are as follows
1. Know which patient should NOT have blepharoplasty
2. Always obtain a detailed and informed written consent before the procedure
3. Be cautious if patient is taking anticoagulants. If fat resection anticipated then anticoagulants should be stopped.
4. Mark the skin prior to surgery with the patient in an upright position ensuring that good eyelid closure is possible when performing the ‘pinch test’.
5. Ensure that a minimum of 20 mm of skin is retained between the upper lash line and the brow at the mid pupil position, in the absence of significant brow ptosis
6. Meticulous haemostasis should be ensured during surgery.
7. The upper 1/3 of orbicularis can be removed to achieve good skin - septum-skin crease forming closure.

Figure 4a, b, c: Figures show steps in skin only excision with Colorado monopolar diathermy needle.

Figure 5: Upper 1/3 orbicularis muscle is removed showing lacrimal gland prolapse (arrow).

Figure 6a, b: pre and post operative blepharoplasty.
8. It is rarely necessary to remove fat except in the medial fat pad and in patients with thyroid eye disease
9. Correct underlying ptosis and lacrimal gland prolapse
10. Lubricants, topical artificial tears and antibiotics ointment should be given to ensure patient comfort post operatively.

References:
Squamous cell carcinoma of the temporal bone

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Abstract
Squamous cell carcinoma of the temporal bone, usually of cutaneous origin, is a rare entity, and it accounts for most of the malignancies arising from this region. The complexity of the neighboring anatomical structures and the lack of a standardized management approach make treating this tumor difficult. This text will review the clinical presentation, staging systems, treatment options and results from recent studies.

Key words
Squamous cell carcinoma, temporal bone, ear canal, lateral temporal bone resection, chemotherapy, radiation therapy.

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Introduction
Malignant tumors of the temporal bone are rare with a reported incidence of 1-5 cases per 1 million population annually1. Squamous cell carcinoma (SCC) is the most common type of cancer occurring in the temporal bone1- 4. Tumors involving the temporal bone may either originate primarily from the external auditory canal, middle ear or mastoid or they may extend to the temporal bone from adjacent sites such as the parotid gland, the pinna or the periauricular skin. This review will focus on SCC arising primarily from the temporal bone.

The surgical treatment of SCC of the temporal bone has evolved over the last century, but the literature has been limited by the rarity of this tumor. En bloc resections were initially performed in the 1950’s5. Total en bloc temporal bone resection was then described in the 1980’s6. The current trend has been to favor lateral temporal bone resection for disease limited to the ear canal and to reserve subtotal or total resections only for the more advanced cases7. Recent improvements in microsurgical techniques and skull base surgery have greatly improved the safety and effectiveness of these procedures.

Clinical presentation
The mean age at presentation of patients with a primary SCC of the temporal bone is between 50 and 60 years7,9. This malignancy mimics common benign pathologies such as otitis externa and chronic otitis media. Indeed, the 3 most common presenting symptoms are otorrhea (51-62%), otalgia (26-52%) and hearing loss (18-43%). The clinician treating presumptive otitis externa must therefore include malignant pathologies in his differential diagnosis when symptoms do not respond to standard therapy such as ear cleaning and topical antibiotics. In these cases, a biopsy is warranted. Facial nerve dysfunction occurs in 11-15% and is a sign that the tumor has extended beyond the ear canal, more medially into the mastoid or anteriorly-inferiorly into the parotid gland. Other less common symptoms include bleeding from the ear, trismus, an ear canal mass or ulcer, itching, tinnitus, vertigo, dysphagia, hoarseness, and tongue dysfunction7,10. Of these symptoms, facial nerve dysfunction is associated with a poorer prognosis10,11. Regional metastasis to neck lymph nodes is variable (1.4-23%)7, 10, 12, 13. The presence of positive local or cervical lymph nodes is considered a sign of aggressiveness.

Clinical Evaluation
Otomicroscopic examination is essential to determine if the tumor extends beyond the membranous cartilaginous canal. This assessment is critical because the subcutaneous tissue is much thicker lateral to the bony-cartilaginous junction, allowing deep margins to be taken during surgery. On the other hand, the skin over the bony canal is very thin and does not lend itself to deep surface margins.

Assessment of cranial nerve function is important in these patients. Facial nerve function has important implications in the treatment and staging of disease. Lower cranial nerve deficits (IX-XII) are a sign of far-advanced disease that might be beyond surgical resection.

Accuracy evaluation of disease extension is often difficult on physical examination alone. Preoperative assessment of patients with SCC of the temporal bone should include multiplanar imaging with high-resolution computed tomography (HRCT) and magnetic resonance imaging.
Close attention is paid to invasion of the dura, brain, facial nerve, jugular foramen, carotid artery, temporomandibular joint and parotid gland. Modern imaging also allows better assessment of regional lymph nodes metastasis. An example of erosion of the anterior wall of the external auditory canal as seen on HRCT is showed in figure 1. Such erosion is not detectable on physical examination alone.

Preoperative audiometry should also be obtained. Sensorineural hearing loss on the side of the lesion can suggest cochlear or labyrinthine invasion. It also allows better counselling of patients presenting with a SCC that involves an only-hearing ear.

**Staging**

Having an appropriate staging system is essential for adequate treatment planning. Many staging systems have been proposed, however, since 1990, the Pittsburgh staging system has become the most commonly used. The more recent literature reports results using the latest revision as described by Moody et al. (Table 1) Staging for tumors arising from the periauricular skin is based on the American Joint Committee on Cancer (AJCC) system. Whereas the previous edition utilized only measurements in centimeters to categorize lesions, the newest revision now considers high-risk features and involvement of specific bony structures to better account for the aggressiveness these lesions. (Table 2 and 3)

**Management**

The study of SCC of the temporal bone has been limited by the rarity of this disease. The literature lacks prospective multi-institutional, randomized studies comparing treatment strategies. Presently, there is no consensus for the optimal management algorithm for cutaneous malignancies of the temporal bone. Limitations of previous studies include small number of patients, retrospective design, and heterogeneity in patients’ population and management strategies. We present below a standardized approach for tumor resection and reconstruction that was adopted by our multidisciplinary team at the UT MD Anderson Cancer Center.

**Early stage disease**

For early stage disease (Stage I or II), a lateral temporal bone resection (LTBR) with superficial parotidectomy is performed. A limited selective neck dissection (level IIA, IIB, and III) is also included, not only for known cervical disease but also for appropriate staging and selection for adjuvant radiotherapy. The LTBR includes a mastoidectomy with the en bloc removal of the bony external auditory canal, the tympanic membrane, the malleus and the incus. The facial nerve, stapes, inner ear and uninvolved portion of the auricle are all preserved. The defect can be closed with a temporalis muscle flap and a split thickness skin graft. For limited T1 lesions that only involve the membranous, cartilaginous ear canal, a wide local excision can be considered. An example of a lesion amenable to wide local excision is showed in figures 2 and 3.

Evaluation of margins by frozen section is essential, and positive margins have to be addressed at time of surgery. If the tumor is found to involve the ear canal medial to the bony-cartilaginous junction, then the procedure must be converted to a LTBR.

Generally, surgery alone is curative for T1 lesions. Postoperative radiotherapy is given to patients with T2 disease especially when there is bone invasion or erosion.
positive or close margins, perineural or vascular invasion, or cervical nodal metastasis.

**Intermediate stage disease**

For select patients with intermediate-stage disease (stage III [T3N0] or stage IV [T1-3N1-3]) that does not involve the middle ear, treatment includes lateral temporal bone resection, parotidectomy, neck dissection and postoperative adjuvant radiotherapy. Frozen section is important to guide the extent of the dissection. Often a large soft tissue defect is created requiring microvascular free flap reconstruction. An example of a lesion eroding the anterior canal wall into the temporomandibular joint as seen on HRCT is showed in Figure 4. The resection included a LTBR and removal of the condyle (Figure 5), and the defect was reconstructed with a free flap (Figure 6).

If the tumor involves the middle ear space, a LTBR is not sufficient by itself. LTBR may be the initial first step since removal of the external auditory canal allows better visualization and access to the more medial structures. Several structures can be explored including the infralabyrinthine and supralabyrinthine air cells, eustachian tube, jugular bulb, carotid canal and temporomandibular joint. The tumor is followed and removed in a piecemeal fashion. If the tumor extends into the cochlea and labyrinth, these structures must be resected leading to a subtotal temporal bone dissection (STBR). For these more medially based tumors, reconstruction can be performed with temporalis muscle flap and fat obliteration or microvascular free flap.

**Advanced stage disease**

Patients with advanced disease (T4) present a significant challenge. Surgery alone often fails to eradicate the disease and achieve negative margins. The addition of postoperative radiotherapy is essential but not sufficient in achieving durable long term survival. Consideration can be given to induction chemotherapy. A subtotal or total temporal bone resection (TTBR) is reserved for those with stable or responding disease. TTBR goes beyond STBR by removal of the petrous apex and internal auditory canal and is performed for those tumors involving these structures. The en bloc total resection of the temporal bone is no longer advocated as it is associated with significant morbidity with no added benefits. Carotid encasement, brain invasion, lower cranial nerve deficits and distant metastases are signs of advanced tumor that are not surgically resectable. Microvascular free flaps are used to reconstruct these defects, especially when dural resection has been performed.

Other authors have described a somewhat similar approach with some notable differences. In a recent retrospective study evaluating patients with SCC originating from the temporal bone and periauricular skin, Lassig et al reported a similar management paradigm for early-stage disease. However, they treated advanced disease with combined chemotherapy and radiation or radiation alone.
They did not perform subtotal or total temporal bone resections as they considered these procedures to have significant morbidity and mortality with unclear benefits to survival and quality of life.

Shiga et al.\(^\text{25}\) have recently suggested the use of concomitant chemoradiotherapy as a standard primary treatment for SCC of the temporal bone in a pilot study that included 14 patients. Patients with stage I tumor received either radiation alone or oral 5-fluorouracil (5-FU). One patient with stage II disease was treated with radiation therapy and weekly treatment of low-dose docetaxel. Patients with stage IV cancer received concomitant chemoradiation therapy, a regimen that included 5-FU, docetaxel and cisplatin (TPF). The study reported a 5-year disease-specific survival rate of 78% overall and 67% for patients with T4 tumors. Despite these promising results, the sample size of this study was small and more studies are required to compare concomitant chemoradiotherapy to surgical protocols.

**Facial nerve**

Every attempt should be made to preserve the facial nerve when it has normal function. However, patients who present with facial weakness or paralysis will often require facial nerve sacrifice. In these patients, facial nerve decompression is performed lateral to the geniculate ganglion. The facial nerve is divided in its mastoid portion, and the proximal margin is sent for frozen section. More proximal segments of the nerve can be sampled to reach a negative margin, but our group does not perform labyrinthectomy for the sole reason of trying to achieve a negative margin in the facial nerve. In this circumstance, any remaining microscopic disease in the nerve would be controlled with radiotherapy.

Facial nerve reconstruction is considered in every patient who undergoes facial nerve sacrifice. Nerve grafting has a reasonable chance of success even in the setting of postoperative radiotherapy\(^\text{26}\) or a positive nerve margin\(^\text{27}\). When the facial nerve is resected and repaired by cable grafting, some return of function can be expected in the majority of patients, with some authors reporting at least some improvement in up to 97% of their patients\(^\text{28}\). Hanasono et al. found a recovery of function to a House-Brackmann score of 3 or better in 42.9% of their patients with a mean time of 7.9 months before reinnervation. They also determined that the return of function was not influenced by the degree of preoperative weakness, postoperative radiation or age\(^\text{26}\).

Adjuvant surgical treatments for facial nerve rehabilitation include upper eyelid gold weight placement, direct brow lift, lateral canthoplasty, lateral tarsorrhaphy and static reanimation with fascial slings. The goals of these procedures are to prevent ocular complications such as exposure keratitis, to assist with oral closure and to improve facial symmetry\(^\text{26}\).

**Prognosis**

Survival rates from recent studies of patients with SSC of the temporal bone are presented in table 4. Several studies have showed a significant difference in the survival of patients with T1 and T2 tumors compared to those with T3 or T4 lesions, with most authors reporting a 5-year survival between 48 and 100% for early stage tumors\(^\text{7, 10, 24, 29, 30}\). LTBR has been shown to have superior results compared to local canal resection alone. In a study examining patients with T1 or T2 disease, Zhang et al. demonstrated a lower recurrence rate in patients receiving LTBR (recurrence rate 0%) versus patients treated with local canal sleeve resection (recurrence rate 46%)\(^\text{31}\).

The importance of achieving negative margins must be emphasized. Gillespie et al.\(^\text{4}\) reported a survival rate of...
78% for patients who had negative margins while none of those with a positive margin survived. Furthermore, patients with recurrent disease do worse compared to those who were previously untreated, highlighting the need for complete resection and aggressive management of more advanced disease. According to some authors, the presence of regional nodal disease is associated with a poorer prognosis and a higher rate of recurrence. In addition to margin status and regional nodes involvement, Morris et al. determined that extratemporal spread of disease to the parotid gland and mandible was another independent factor predicting survival.

**Conclusion**

SSC of the temporal bone remains a rare disease whose optimal management approach is yet to be defined. A multidisciplinary team effort is essential in the treatment of these often complex tumors. Multi-institutional studies are required for a better understanding of the roles of radiotherapy and chemotherapy in the management of these lesions.

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**References:**

Minor salivary gland neoplasms

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Abstract
Minor salivary gland neoplasms [MSGN] are uncommon neoplasms of the head and neck region with an unpredictable clinical history. They are heterogeneous neoplasms with a widespread anatomic location in the upper aero-digestive tract. The anatomical location of the primary will dictate when in the tumor growth will symptoms manifest. Punch or incisional biopsy will clinch the diagnosis of salivary origin and histopathology. Radiological investigations will delineate the tumor extent and resectability. Statistically the probability of malignancy is higher than a benign one in minor salivary gland tumours. Staging and complete excision with clear margins is the gold standard. Post-operative radiation therapy is indicated for close or positive margins and in high grade or advanced stage of the malignancy. Radical resection for oncological clearance may be challenging due to proximity to vascular and neural elements and may have a poor functional outcome. Treatment of neck is indicated if there evidence of disease and in high grade malignancy in selected subsites. Management of MSGN is still evolving and requires a multi-modality targeted approach for optimal outcome.

Key words
minor salivary gland tumors, heterogeneous, prognosis, stage, treatment.

Introduction
World literature reports salivary neoplasms account for 3 - 6% of head & neck tumors. Minor salivary gland neoplasm [MSGN] accounts for 9 - 23% of all salivary neoplasms. They manifest with considerable pathological diversity and this makes it one of the most heterogeneous neoplasms of the head and neck region. The relative scarcity, widespread anatomical location and heterogeneity of these tumors contribute to its complexity and limited understanding. Various methodologies have been employed to report MSGN with regard to histology classifications and anatomical versus pathological grouping [oral cavity cancers as opposed to classifying them as minor salivary gland tumors] and hence the true incidence of minor salivary gland still remains unclear.

Bradley and McGurk studied the prevalence of salivary gland neoplasms in the UK by analyzing the pathology records from two university hospitals across two, ten-year periods. They concluded that from a total of 861 salivary neoplasms, 81% occurred in the parotid, 9% in the submandibular region and 9% in the minor salivary glands which conforms to the rule of 10:1:1 distribution pattern.

Ratio of benign to malignant is universally believed to be 20% benign and 80% malignant in MSGNs. However, some authors believe the higher malignancy ratio may possibly be attributed to the “harvesting effect” due to the higher referrals for malignant conditions to tertiary centers.

Anatomy
There are about 600 - 1000 estimated minor salivary glands located in the upper aero-digestive tract. The highest density of minor salivary glands are found in the oral cavity & oropharynx, but are conspicuous by being absent on the gingiva, midline & anterior part of the hard palate. Other locations where they are located are in the nose and paranasal sinuses, middle ear, pharynx and larynx. The basic unit of the minor salivary gland comprises of acinar-ductal unit surrounded by myo-epithelial cells on the outer aspect embedded in the sub mucosal connective tissue. These cell types form the basis of neoplastic process. Functionally they can be classified according to the type of secretion and consist of groups of mucous acinar, serous or mucouserous demilune cells and typically lack true capsule and in comparison to major gland have an abbreviated duct system.

Diagnosis
Minor salivary gland tumours predominantly presents in the fifth or sixth decade of life. Though infrequent, studies where age is reported claims 5% or less of MSGNs afflict the paediatric population, with malignant tumors almost representing 46-55%.

(Table 1)
Tumours of salivary gland origin should be a part of differential diagnosis in every painless, non-ulcerative submucosal swelling in the upper aero-digestive tract. However, due to their widespread anatomical location, the site and size of the tumor will also dictate the other co-existent symptoms and signs specific to the region during presentation. The site of primary and histologic grade, will dictate when in the tumour growth will symptoms arise, and this will impact the stage of presentation.

The most common sites of MSGN are the oral cavity & oropharynx, and the most frequent sub-site is the hard palate due to the increased population of the number of glands, especially at the junction of hard and soft palate\textsuperscript{15}. Site distribution pattern revealed that the palate, buccal mucosa, and upper lip were the most common locations of intra-oral MSGN\textsuperscript{16,17}. Minor salivary gland tumors were mostly benign on the upper lip but malignant on the lower lip\textsuperscript{15,16}.

Nerve involvement is an ominous sign and may present as either pain or numbness. Adherence to and ulceration of the overlying mucous membrane may also signify an underlying malignant potential.

<table>
<thead>
<tr>
<th>Table1: Salient differences between minor and major salivary glands.</th>
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<tbody>
<tr>
<td>Minor</td>
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<tr>
<td>Estimated 600 – 1000 minor salivary glands</td>
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<tr>
<td>Widespread anatomical location in the upper aerodigestive tract</td>
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<tr>
<td>Unencapsulated with an abbreviated ductal system</td>
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<tr>
<td>Low volume of saliva is produced continuously day and night and via parasympathetic stimulation</td>
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<tr>
<td>Ratio of malignant to benign is higher.</td>
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<tr>
<td>Grading minor tumors is fraught with high inter-observer variability, and lack of consistency between tumor grade and biological behavior.</td>
</tr>
<tr>
<td>Considering it has a widespread anatomic location, there are various surgeries involving the various organ systems in the upper aerodigestive tract. No standard surgical procedures.</td>
</tr>
<tr>
<td>First echelon lymph node involvement depends on the site of primary, this will dictate lymph node groups to be dissected. Elective neck dissection not recommended and considered unnecessary.</td>
</tr>
<tr>
<td>Rare to have metastatic cancer involving minor salivary glands.</td>
</tr>
</tbody>
</table>

Investigations

While dealing with MSGN, the probability of malignancy is high and this dictates the choice of investigations in clinching the diagnosis. Despite that literature quotes a high accuracy rate of FNAC, the primary drawback is the lack of tissue architecture, and inability to accurately grade these tumors. Hence there is diversity of opinion on the role of FNAC in the evaluation of salivary tumours. However, FNA in conjunction with radiological and clinical evaluation may provide a safe guard against false-positive and false negative results\textsuperscript{18}.

Another option is punch biopsy, which may add more clarity to diagnosis and is likely to be more representative of the tumor\textsuperscript{10}. Bradley cautions avoidance of excisional biopsy in the case of MSGN\textsuperscript{10,19}, since positive margins and confusion with orientation of the tumor may confound treatment planning. Though incisional biopsy is avoided in major salivary glands, it adds more valuable information in the management of MSGN.

To the surgeon pre-operative imaging plays a key role in disease staging, surgical planning, and patient counseling. Radiologically one cannot reliably define and differentiate malignant versus benign, but there are strong indicators of...
malignancy. Well-established features are irregular margins or extension of tumor along nerves. Smooth sharp margins favor a benign disease but it can be deceptive since this feature can also be seen in malignant lesions, particularly in low-grade histology\(^\text{20}\) [Figure1].

Imaging can be in the form of CT or MRI. MRI is particularly recommended in demonstrating the interface of tumor and surrounding soft tissues for determining surgical resection margin. Cortical bone erosion of the mandible, maxilla or skull base is best visualized on CT, although infiltration of the marrow is better demonstrated on MR. However, in neck evaluation both studies can assess for nodal metastatic disease with an accuracy of 80\%\(^\text{21}\). PET scan can increase accuracy to more than 90\%\(^\text{21}\). Body imaging may be indicated in high-grade or locally advanced disease to stage and screen for distant metastasis.

Pleomorphic adenoma requires special mention since it is the most common benign tumor. It displays gradual enhancement on CT contrast, if one images early after injecting the contrast it may be almost invisible. Delayed enhancement is commonly seen in this tumor and can be a useful diagnostic feature\(^\text{22,23}\). Tumor of malignant interest with specific appearance is adenoid cystic carcinoma [AdCC], on account of peri-neural invasion. When it occurs in proximity to the posterior hard palate palatine nerves can carry the tumor to the pterygopalatine fossa and further all the way via foramen rotundum with extension right up to Meckel’s cave [Figure 2].

Enlargement of the canals carrying the nerve, enhancement of the nerve and compression of the fat pad in the fossa are typical signs of perineural spread\(^\text{20}\). Thus it is evident that pre-op evaluation aids in therapeutic planning and is crucial in the management of MSGN.

**Histological Classification and Grading in MSGN**

World Health Organization has classified salivary gland tumors, based on the type of cellular, architectural and organizational pattern, into well-defined entities and they comprise of 13 benign and 24 malignant tumors\(^\text{24}\). Almost all of the described malignant tumours have been reported to occur in the minor salivary gland sites. Malignancies originating from ducts are purely epithelial and highly malignant, whereas those originating from terminal ducts which are composed of epithelial and myo-epithelial cells behave less aggressively.

Histopathology classification of salivary gland tumors has a high inter observer variability and is fraught with complex morphology and overlapping histologic patterns. Hence distinction between benign and malignant entities can be challenging.

Grading the tumor is an additional guideline to predict the biological behavior of a tumor within the same histo-type. However in contrast to major salivary gland tumors, its prognostic value is controversial in MSGN\(^\text{25,3}\). This has been evidenced by clinical experience that there is no consistent correlation of certain carcinomas to their histopathology classification since they have variable outcomes.

The commonest benign neoplasm is undoubtedly pleomorphic adenoma and infrequently other benign tumors that occur are cylindrical adenoma, monomorphic adenoma, basal cell adenoma and myoepithelioma\(^\text{26,27,28,29}\). Amongst the malignant neoplasms the two most common are adenoid cystic carcinoma [AdCC] 30\% - 45\% and mucoepidermoid [MEC] 30\% - 50\%, and the others

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**Figure 1:** Teenager with a mass in the nasopharynx. Sagittal post contrast T1W sequence demonstrating an enhancing mass in the nasopharynx (broad arrow) – low-grade mucoepidermoid carcinoma.

**Figure 2:** Axial Post contrast T1W demonstrating peri-neural spread to the left Meckel’s cave (broad arrow) and along the left trigeminal nerve (slim arrow). Primary from adenoid cystic carcinoma of the hard palate.
polymorphous low-grade adenocarcinoma [PLGA] & acinic cell carcinoma [AcCC] 4% - 9% occurs less frequently\textsuperscript{30,16,31}.

Commonest benign salivary tumor in children is pleomorphic adenoma and malignant is mucoepidermoid carcinoma\textsuperscript{11} and the majority tend not to be high grade most are amenable to complete resection with clear margins\textsuperscript{32}.

**Adenoid Cystic Carcinoma [AdCC]**

Adenoid cystic carcinoma though a rare head and neck cancer, is considered the most common malignant tumor of the minor salivary glands with an incidence as high as 70\% in certain studies\textsuperscript{33,34}. It is often diagnosed in an advanced stage due its propensity for indolent yet progressive local growth and unique neuro-trophic property. It is histologically classified into 3 patterns, cribriform, tubular and solid. Poor prognosis is associated with higher extent of solid component. Treatment involves complete radical resection to achieve clear margins; this can be challenging due its proximity to vital vascular and neural structures and skull base. Adjuvant post-operative radiation therapy to the tumor bed is often given to achieve good local control.

The many paradoxical features of AdCC make it an interesting tumor model to study. The natural course of this disease is punctuated with multiple recurrences. It is puzzling that metastases to the lungs and bone may be frequent although nodal metastasis is uncommon. Classically characterized by the possibility of late recurrence even more than 10 and 20 years after initial “curative” therapy due to distant metastasis\textsuperscript{4,35}. Another intriguing feature is patients may survive for many years with local recurrence and distant metastasis without treatment\textsuperscript{36}.

Other poor prognosticators are positive margins, perineural invasion, proximity to skull-base [nasopharynx & maxilla] and advanced stage at initial presentation. Despite the vast amount of research on AdCC, the consistent feature that remains unchanged based is that it continuous to follow an unpredictable course with an uncertain prognosis after surgical resection.

**Mucoepidermoid Carcinoma [MEC]**

MEC account for almost 40 - 50\% of MSGNs\textsuperscript{37}. The clinico-pathologic behavior of MEC is highly variable, ranging from slow-growing indolent tumors to locally aggressive and highly metastatic carcinomas. It can be composed of different histologic cell types of varying portions, mucous, undifferentiated small [intermediate], and epidermoid [squamoid], columnar and clear cells, often demonstrating prominent cystic growth\textsuperscript{38}. MEC’s are graded on a three-tiered system low, intermediate and high grade based on pattern of invasion, coagulative necrosis, atypia, and cystic component <20\%. Histologic grading of MEC and its clinical biologic behavior correlate more predictably and can be a more reliable indicator of recurrence and survival and hence this can guide treatment paradigms. However, consistency associated with grading systems can be problematic\textsuperscript{38}. MEC is also specifically linked to a specific translocation t (11; 19)(q12; p130) resulting in fusion between MECT1 and MAML2 gene\textsuperscript{39}. A study from MD Anderson contend that fusion positive tumors regardless of grade, exhibit a more stable genome and better clinical behavior, while fusion negative MEC characterize relatively aggressive tumors.

**Polymorphous Low Grade Adenocarcinoma [PLGA]**

Considered the second or third most common minor salivary gland tumor, with a female preponderance and commonly located in the palate, buccal mucosa and upper lip\textsuperscript{40}. The natural history of PLGA is that it is slow growing but locally invasive with a low potential for aggressive behavior. The diagnostic dilemma is to distinguish it from pleomorphic adenoma and adenoid cystic carcinoma. Histologically it is characterized by “beads on a string” or as an “Indian file appearance” comprising of a single row of epithelial cells between layers of collagen at the periphery of the tumor\textsuperscript{41,42}. Confused with pleomorphic adenoma due to its myxomatous, mucoid hyalinated stroma and the cribriform areas can be misleading to a diagnosis of AdCC. This is critical as treatment and prognosis vary. Though the initial surgical treatment of primarily wide-resection is the same for all, but adjuvant RT is debatable. There have been reports that RT may transform PLGA to a high grade variant . Metastases are rare and recurrences tend to be local and can occur well after 7 - 10 years of treatment. Thus, reiterating it’s malignant potential and the need for long-term follow-up\textsuperscript{43}.

**Staging and TNM Classifications**

There is no TNM staging for minor salivary glands per se, but if the tumor diagnosed as a salivary malignancy then they conform to the same staging as squamous cell carcinoma of that particular anatomic site\textsuperscript{3}.

**Treatment**

The single most vital factor in the treatment protocol for MSGN is complete resection with clear margins. Operability with clear margins is dependent on histological grade, anatomical extent and most importantly stage of the disease\textsuperscript{38}.
Oropharyngeal MSGNs have a propensity for sub-mucosal spread and can be challenging to operate. Resections are not uncommonly associated with positive margins and require post-op radiotherapy as a routine. Conventionally these tumors were resected through trans-mandibular and trans-cervical approach, which may carry significant surgical morbidity. Tongue base is the most frequently involved sub-site and is amenable to minimal access surgery in the form of transoral robotic surgery [TORS]. This obviates the need for open approach in low-volume tumors and leads to improved functional outcome. Laryngeal MSGNs also exhibit extensive sub-mucosal spread and hence present in an advanced stage with metastasis to the lungs [Figure 3].

Total laryngectomy with post-operative radiotherapy is considered necessary in advanced disease. MSGT located to the paranasal sinus or nasopharynx, their prognosis is dismal. This is due to early involvement of cranial nerves and intracranial structures and radical management may not impact the outcome. Unresectable disease may require primary radiotherapy. Tumors of this site also have a propensity for higher degree of nodal involvement.

Postoperative radiation therapy is commonly used as an adjuvant therapy and is usually effective in preventing or reducing local recurrence. Well-established indications for postoperative radiotherapy are advanced stage [II - IV], invasion of local structures, incomplete resection or positive margins, peri-neural invasion, lympho-vascular invasion, high-grade histology, and primary site with rich lymphatics [oropharynx, nasopharynx, hypopharynx and supraglottic larynx]. For most patients the recommended postoperative dose is 60 Gy to the operative bed for microscopic disease; 66 Gy for gross disease and 46 Gy for elective neck radiation. If there is named nerve invasion, the path of the nerve is treated electively to its ganglion. If local failure occurs, it tends to be a late event.

A study from Yale University concluded on multivariate analysis that there were four statistically significant factors that were identified for nodal metastasis. They were: male gender, T3-T4 disease, pharyngeal site of primary malignancy and high-grade adenocarcinoma or high-grade mucoepidermoid carcinomas as the indices for predicting lymph node involvement.

Currently neck dissection is indicated only if there is clinical or radiological evidence of tumor involvement and elective neck dissection is not routinely done for minor salivary gland malignancies. However in the N0 neck in the presence of high-grade cancer, elective neck dissection may be justified due to the high risk of regional recurrence.

Primary RT is recommended if the patient refuses surgery or suffers from an unresectable or inoperable tumor. While treating inoperable or unresectable tumors neutron, heavy ions or proton beam therapy is recommended.

An equally important factor is the functional outcome and quality of life after radical resection, given the high likelihood of developing distant metastases. A retrospective study from Stanford Cancer Center reviewed 90 patients who received radiotherapy for MSGN and were followed up for a minimum period of 5 years. Of the 24 patients who developed distant failure, 19 of these failures were in patients who had locally controlled disease. Patients with advanced stage III - IV [31%] had a higher failure rate as compared to early stage I - II [11%].

Chemotherapy is not routinely used in the management of MSGN and is reserved primarily for palliation. It may be indicated for metastatic disease, unresectable recurrent tumor and in patients not amenable to radiotherapy.

Future trials investigating concurrent chemotherapy and radiation, as well as the use of targeted agents based on evolving molecular discoveries, will lead to optimal personalized approaches for MSGM disease.

**Outcome and Prognosis**

Advanced stage and high grade portends the worst prognosis. Sub-sites that tend to present at advanced stage with early involvement of cranial nerves and intracranial extension are skull-base and paranasal sinus minor salivary gland cancers. Other independent prognosticators are positive surgical margins, extra-capsular extension, bone invasion, perineural invasion, nodal involvement and distant metastasis. Retrospective data have shown that...
postoperative RT in locally advanced salivary gland cancer improves locoregional control. A raised value of Ki-67, an anti-apoptotic nuclear antigen, is associated with treatment failure in large tumors.

Conclusion
Surgery remains the mainstay of treatment for most minor salivary gland tumors. Adjuvant radiotherapy is given based on the histologic diagnosis and staging. Nevertheless, widespread anatomical location, diverse histological diagnosis, under-powered analyses due to reduced sample size, prolonged study period and lack of randomized multi-center trials all contribute to the complexity in the management of MSGNs. Despite several developments, management of minor salivary gland carcinomas can be challenging. However, emergence of studies on biomarkers, concurrent chemo-radiotherapy and targeted molecular therapy holds hope to improved outcomes in the future.

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Paralytic dysphonia – modern management strategies

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Abstract
Unilateral vocal fold paralysis (UVFP) may be due to one of a number of different pathologies. In this article, the aetiology workup of such patients will be explained. The management of UVFP depends on factors relating to the patient’s comorbidities, life expectancy and voice requirements. A description of the technique of transcutaneous medialisation is presented.

Key words
vocal fold paralysis, dysphonia, management


Introduction
Paresis or paralysis of one or more of the muscles of the larynx can be the consequence of any one of a large number of processes. The clinical picture varies widely according to which muscles, and to what extent, they are affected.

A previous article in this journal1 presented a discussion of the surgical management of unilateral vocal fold paralysis (UVFP). This current paper outlines various aspects of the causes, investigation and management of patients with unilateral vocal fold paresis or paralysis.

Causes and prevention of unilateral vocal fold paralysis
Immobility of the vocal fold may be thought of as either mechanical (direct infiltration of the muscle of the vocal fold or the crico-arytenoid joint) or neurological. Of the latter group, there are four broad categories: trauma (iatrogenic or accidental); neoplastic; systemic disease; or idiopathic.

Systemic causes of vocal fold paralysis are rare, but need to be considered when a patient presents with a seemingly idiopathic case. Systemic causes include stroke, amyotrophic lateral sclerosis, myaesthenia gravis, Arnold-Chiari malformation, tuberculosis and Wegener’s.

Tumours of any part of the recurrent laryngeal nerve can cause vocal fold paralysis: thus, skull base tumours, parapharyngeal space masses, thyroid tumours, oesophageal or lung malignancy can either directly infiltrate or compress the nerve supply to the larynx.

Equally, surgical procedures to any one of these anatomical structures can cause vocal fold paralysis; in addition, surgery of the cervical spine or on the heart or aorta place the recurrent laryngeal nerve at risk.

If a thorough investigation reveals no obvious cause, the paralysis is deemed to be idiopathic.

Assessment
Clinical assessment of the patient will start with a detailed history: most patients with UVFP will complain of a weak and breathy voice. On further questioning, many will comment that they aspirate on swallowing, particularly with liquids. Patients will complain of the effort of phonation and of a subjective feeling of shortness of breath: this is a consequence of the increased airflow required as a result of the glottic insufficiency. Certain situations are particularly problematic: speaking against background noise, for example, and having to sustain the voice for long periods of time, can be difficult. For this reason, some patients become socially withdrawn or are unable to work. Glottic insufficiency leads to a weak and ineffective cough. When combined with a tendency to aspirate liquids, this can lead to aspiration pneumonia.

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Perceptual evaluation of the voice is required to monitor treatment response: the GRBAS scale2, 3 is widely used and is easy to undertake. Diplophonia is common – this occurs as a result of the differing tensions of the two vocal folds, causing each fold to vibrate at a different frequency. Examination of the neck and cranial nerves follows. Flexible or rigid laryngoscopy will confirm the diagnosis. In cases of subtle paresis of the vocal fold, the asymmetry of movement may not initially be apparent: it is therefore important to assess repeated movements of the vocal folds:


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asking the patient to alternate “ee – sniff – ee – sniff – ee – sniff…” will highlight fatigability of a paretic vocal fold.

Patients should self-rate their voices: the most widely used measure is the Voice Handicap Index (VHI). This is a 30-item questionnaire that has been reduced to a VHI-10 for ease of use.

In cases that are not obviously iatrogenic, the workup for patients with UVFP is aimed at evaluating the entire course of the recurrent laryngeal nerve. Cross-sectional imaging of the neck is mandatory: on the right side, where the recurrent laryngeal nerve does not enter the chest, imaging of the neck alone suffices. On the left, the scan should include the upper mediastinum as well as the neck. The choice of CT versus MRI is at the discretion of the clinician.

**Prevention of recurrent laryngeal nerve trauma**
Avoidance of trauma to the recurrent laryngeal nerve is one of the principle concerns during thyroidectomy. There are occasions when sacrifice of the nerve is unavoidable, but for benign thyroid disease, when the nerve is functioning normally prior to the operation, it should be the aim of surgery to leave it working at the end of the surgery.

The recurrent laryngeal nerve should be routinely identified and preserved in the course of thyroidectomy. Nerve monitors now exist to assist the surgeon in confirming the anatomical location and the functional state of the nerve in the course of surgery. However, controversy exists as to the usefulness of these monitors; with some surgeons concerned that over-reliance on technology is diminishing surgical skills and discouraging accurate dissection.

**Superior laryngeal nerve palsy**
The superior laryngeal nerve (SLN) provides two functions: its internal branch provides sensory supply to the glottis and supraglottis; the external branch supplies motor function to the cricothyroid muscle, which is responsible for stretching the vocal folds when raising the pitch of the voice. Many cases of SLN palsy are idiopathic, but some are secondary to thyroid surgery: the SLN is at risk when the superior pole vessels are being ligated. Whilst the recurrent laryngeal nerve is relatively rarely injured in thyroid surgery (with thyroid surgeons acutely aware of the devastating consequences), the superior laryngeal nerve is often overlooked in thyroid operations. Symptoms of SLN palsy include diminished sensation, and hence aspiration and throat clearing. The impact on the quality of voice for a non-performer may be limited; however, professional voice users may complain of a lack of power, along with an inability to reach notes at the top of their registers. Investigation centres on electromyography (EMG) to confirm or refute the diagnosis. Unfortunately, there is little that can be achieved either medically or surgically to help in this situation: the patient is reliant on speech and language therapy to try to regain the flexibility of their vocal range.

**Nonsurgical management of UFVP**
Several factors govern the management of patients with UVFP. Symptom severity, aspiration of liquids and patient requirements are the key factors. For example, a patient with severe aspiration (and possibly being kept nil-by-mouth for that reason) would require early intervention. Equally, a young professional who is reliant on his/her voice for work will wish to have a rapid intervention.

In all cases, the involvement of a speech and language therapist is invaluable: techniques to improve vocal power, to limit compensatory tension and to avoid aspiration of liquids are all required alongside any surgical or injection interventions. This therapy is particularly useful when delivered early.

The choice of intervention is very much a matter of personal experience and preference on the part of the surgeon. In recent years, advances in imaging equipment have led to the development of very high resolution flexible endoscopes: the use of these chip-tip scopes this means that laryngeal interventions can now be carried out under local anaesthetic with endoscopic guidance.

**Local anaesthetic medialisation injection**
Medialisation injection under local anaesthetic has now become (in many centres) the first-line treatment for patients with UVFP. The choice of injection material depends on the clinical situation, but a new-onset idiopathic paralysis would usually lead to the injection of a temporary filler such as hyaluronic acid. On the other hand, a longer-standing permanent palsy would require a long-lasting injectable such as calcium hydroxylapatite (Radiesse Voice).

Various techniques for local anaesthetic medialisation injection have been described: below are the most widely-used methods.

All techniques start with the administration of topical anaesthesia – this must be performed very thoroughly to permit manipulation of the airway. Typically, the patient will receive a nebulised solution of 4% lidocaine via a mouthpiece for approximately 10-15 minutes. The nose should be anaesthetised with a combination of lidocaine and a nasal decongestant such as phenylephrine.
Following this, the skin is anaesthetised with 1% or 2% lidocaine. Having infiltrated the skin, the needle is advanced into the airway and more lidocaine is administered directly to the larynx. This will cause the patient to cough – this action is helpful as it further aerosolises the anaesthetic and provides more comprehensive anaesthesia.

In the transcutaneous technique, three approaches may be used:

Trans-cricothyroid approach
The injection needle is advanced into the airway through the skin, just off the midline, approaching from the opposite side to the paralysis. The vocal fold is entered from inferiorly, aiming directly deep into the muscle of the vocal fold. The aim is to very slightly over-inject, so that the vocal fold takes on a slightly convex appearance. (Figures 1, 2, 3 and 4). Following this, the patient should be asked to cough to spread the material evenly throughout the vocal fold.

Trans-thyrohyoid approach
With the patient’s neck extended, the needle is advanced through the thyrohyoid membrane. The needle is advanced almost vertically inferiorly towards the vocal fold. The needle will be seen to enter the airway just below the petiole of the epiglottis. The needle tip is advanced into the muscle of the vocal fold, and the injection proceeds as for the trans-cricothyroid technique, aiming to slightly over-inject the vocal cord and achieve a convex shape (Figures 5, and 6).

Trans-thyroid cartilage approach
In certain cases, particularly when the patient is unable to
extend his/her neck, the injection can be placed directly into the vocal fold through the cartilage of the larynx. This assumes that the cartilage is easy to penetrate with the needle – this can be difficult to achieve in the calcified cartilage of an older patient (Figure 7).

**Per-oral approach**

Using a long injection needle, the vocal fold can be injected per-orally. This requires a very cooperative patient and a well-anaesthetised upper airway (Figure 8).

Transcutaneous injection techniques are relatively quick and easy to perform and give rapid results. They do, however, require high-quality instrumentation and an experienced endoscopist and injector. Injections under local anaesthetic are particularly useful for patients who require a rapid improvement in their voice, or for those whose intercurrent illness precludes them from having a surgical procedure under general anaesthetic or sedation. For example, patients with bronchogenic carcinoma, who are frequently very unwell and have a limited life expectancy, can achieve a good result which allows them to communicate adequately during their palliative illness\(^{10-12}\).

**Conclusion**

Unilateral vocal fold paralysis has a variety of effects, not only on the voice but on swallowing and the ability to cough. In cases that are not due to surgical injury, a thorough workup is required to exclude malignancy compressing or infiltrating the recurrent laryngeal nerve.

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**Figure 5:** Diagram demonstrating technique of trans-thyrohyoid injection.

**Figure 6:** Aiming the needle inferiorly, the point enters the airway just below the petiole of the epiglottis and is directed into the upper surface of the vocal fold.

**Figure 7:** Diagram demonstrating technique of trans-thyroid cartilage injection.

**Figure 8:** Diagram demonstrating technique of per-oral injection.
The management of such cases depends on a number of factors including comorbidities, life expectancy, and vocal demands. Increasingly, injection medialisation is an excellent option for patients with terminal disease or in those requiring a rapid return to work.

Acknowledgements:
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Nerve monitoring in thyroid and salivary gland surgery

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Abstract
Iatrogenic damage to either the facial or recurrent laryngeal nerve (RLN) has a significant impact on patient quality of life as well as being a relatively common source of litigation for otolaryngologists. Preservation of the nerves by meticulous surgical dissection and good anatomical knowledge may be aided by the use of intraoperative nerve monitoring. The evidence in the English Language literature for the use of nerve monitoring in salivary or thyroid surgery is limited. This article reviews the current literature regarding the application of nerve monitoring and its role in both salivary and thyroid surgery for reducing nerve injury.

Key words
Parotid, salivary, thyroid, nerve, monitor, facial, laryngeal.

Introduction
Nerve injury following either parotid or thyroid surgery is a significant complication. For patients the resulting morbidity can have a significant effect on their quality of life. Facial nerve injury as a result of parotid surgery can result in significant psychological and physical morbidity at any age. In thyroid surgery RLN palsy is most often unilateral resulting in hoarseness. Bilateral RLN is thankfully uncommon but if it does occur then this may result in tracheostomy being required which is a serious adverse outcome.

In 1907 Carwardine first described the need for preservation of the facial nerve in parotid gland dissection. Despite meticulous dissection techniques, temporary facial nerve palsy is reported in up to 65% of cases. In one prospective series by a single surgeon the permanent paralysis rate was reported as 5.6% of cases but has been reported as high as 17%. The marginal mandibular nerve is the most commonly affected branch. Riddell in the 1950s realised the importance not only of preserving the recurrent laryngeal nerve (RLN) in thyroid surgery, but also the need to confidently identify it to ensure its safety during dissection. Temporary RLN palsy rates, like facial nerve injury, vary widely in the literature with rates of up to 13% reported. Permanent palsy is seen in 1-3% of cases post-operatively, increasing to 14% in high-risk cases such as revision surgery. These rates may vary in part due to the fact that many studies include results without having visualised vocal cord movement following surgery and simply assessing voice quality, which may lead to a relative under recording of palsy rates.

Techniques available to potentially reduce nerve injury have been investigated over recent decades. Its use in both thyroid and parotid surgery has remained controversial. In this article we present the evidence and discuss issues around the use of intra-operative nerve monitoring in thyroid and parotid surgery.

What monitoring techniques are available?
Initial monitoring devices used stimulation techniques only, however, continuous monitors are now available allowing real-time feedback regarding the integrity of nerves. There are several devices available on the market currently. The most commonly used monitoring system used in a poll of American thyroid surgeons was the Medtronic Nerve Integrity Monitor (NIM) system (see Figure 1). This machine is multifunctional and can be used for middle ear, as well as thyroid and parotid surgery. This system allows both real-time nerve monitoring as well as intermittent stimulation of the nerve in question. Other systems are also available from Inomed (Figure 2).

Facial nerve monitoring during parotid surgery requires electrodes to be placed in the distribution of the muscles of facial expression and can be combined with a monopolar nerve stimulator for direct stimulation of the nerve.

In thyroid surgery the most common technique is to use an endotracheal tube with an electrode on it, which
senses movement of the vocalis muscle. Other techniques include inserting electrodes directly into the vocalis muscles or alternatively by placing an electrode onto the vagus nerve itself, which requires further dissection. How does it decrease injury?

There are several ways in which a nerve can be injured during surgery: division, laceration, traction, pressure, crush, electrical, ligature entrapment, ischaemia and by suction. All of these injuries are still possible with a nerve monitor in place.

Stimulation alone is helpful to some surgeons. In some cases of parotid surgery there can be confusion between whether structures are fine nerve fibres or fibrous strands and some surgeons (often trainees) may find the monitor / stimulator useful in this scenario.

Continuous nerve monitoring gives real-time feedback regarding the nerve. It may help to alert the surgeon to become aware of inadvertent handling of the nerve and dissection in close proximity to the nerve. Some surgeons using nerve monitoring find it ‘very helpful’ regardless of its effect on nerve injury rates. With regard to trainees, surgical technique was thought to be ‘more gentle’ when continuous monitoring was used. Monitoring in parotid surgery may reduce the need for visualisation of gross facial movement if there is no surgical assistant, although if an assistant is present then this should still take place, as it is important to use all available techniques to minimise the risk of facial nerve damage.

In thyroid surgery use of monitoring is advocated to facilitate identification of the RLN, reduce operative time and reduce nerve palsy rates. Dralle et al found that when signal was lost due to presumed nerve injury in total thyroidectomy during dissection of the initial side, 90% of surgeons would not progress to perform surgery on the
second side, preferring to perform two stage surgery and allow any temporary palsy time to recover\(^3\). A similar approach was adopted by Perie et al\(^18\). The underlying pathology would have to be considered when adopting this technique and it should be noted that all RLN injuries were temporary in Perie’s series.

**How much do they cost?**

Due to the application of nerve monitoring in middle ear surgery and increasing use in parotid and to a lesser extent thyroid surgery, many departments now possess a monitor. Currently the initial capital cost is £13206 (price quoted by Medtronic Ltd, U.K., July 2013). For each procedure there is a further cost for stimulators and electrodes. Parotid surgery supplements are £109 for the disposable stimulator and facial electrodes. The cost for thyroid surgery is higher at £159 due to the increased cost of the endotracheal tube with electrode\(^24\).

Whether or not nerve monitoring is cost effective remains unclear. Grosheva et al found that there was a statistically significant reduction in operative time for superficial parotidectomy, (26 minute reduction) and parotid surgery overall, (reduction of 24 minutes), if intraoperative nerve monitoring was used\(^25\). This could have a significant cost implication. Germillion et al found that the use of RLN monitoring in thyroid surgery did not alter the rate of either permanent or temporary nerve palsy. Further more it did not reduce the operative time for either heni or total thyroidectomy\(^24\). An Italian study by Dionigi et al found that nerve monitoring was an additional cost for a procedure where the tariff was already mismatched with the significantly higher hospital costs\(^26\). In the UK the current NHS tariff for parotid surgery is approximately £2500 and £2400 for thyroid surgery. The costs of nerve monitoring could be considered reasonable if there was a significant reduction in nerve injury with a reduction in on-going additional medical care to manage the palsy as well as a reduction in litigation costs.

**When to use monitoring**

A survey of surgeons in the USA found only 29% were using nerve monitoring for thyroid surgery, compared to 80% for parotid surgery\(^17,27\). Similar results were seen in a similar study from the UK with 24% using monitoring in initial thyroid surgery, increasing to 35% in revision cases, compared with 80% in parotid surgery\(^28\). Of those using monitoring for parotid surgery there was wide variation as to whether stimulation alone was used or stimulation in combination with continuous monitoring. Most who did not use RLN monitoring sited lack of good clinical trial evidence of its effectiveness at reducing nerve injury\(^17\).

There is a relatively higher use of monitoring in revision surgery as this is considered to be more difficult surgery and locating the nerve is often more challenging. Brennan et al advocate the use of monitoring in more difficult cases such as Hashimoto’s thyroiditis, malignancy, the previously irradiated neck and revision cases\(^20\). It is not always possible however to identify which cases will be difficult. Some would argue that if nerve monitoring is to be used, it should be used for all cases, particularly given the practicalities of use in thyroid surgery where the endotracheal tube needs careful placement by an experienced anaesthetist. It is important that theatre staff, anaesthetists and surgeons remain familiar with the use of whichever nerve monitor system is used. Some surgeons (including the senior author) suggest that this is best achieved by using it regularly in all cases and not just occasionally in difficult cases.

**Does it work?**

The evidence for the use of nerve monitoring in the literature is limited. The quality of studies is poor with most being retrospective case series reviews many of which include mixed case complexity e.g. deep lobe and superficial lobe parotid tumours. Those that are prospective are often not compared with a control group\(^20\). Terrell et al found in a series of 56 patients undergoing parotidectomy there was a lower rate of 44% compared to 62% of temporary facial weakness in patients undergoing surgery with monitoring of the facial nerve\(^29\). Lopez et al found similar results\(^30\). These were small studies however. Larger studies do not show any statistical difference between the rates of both temporary and permanent palsy in cases where monitoring has been used\(^20,25\). It is also worth noting work by Meier et al, which shows that abnormalities seen on the monitor do not predict facial nerve outcome in parotid surgery\(^31\).

Similarly in thyroid surgery there is inadequate good quality evidence to suggest that use of a nerve monitor has an impact on nerve injury (either temporary or permanent)\(^22,32,33\). Dralle et al has one of the largest published series of 30000 at risk nerves\(^34\). Patients were divided into those where the RLN was not identified, those where identification alone was used, and a final group where identification was combined with continuous nerve monitoring. There was no statistically significant difference between the latter two groups, although non-identification of the nerve was associated with higher nerve injury rates. This is in keeping with a further large study by Hermann et al of 16443 patients undergoing thyroid surgery who found that exposure of the nerve along the whole thyroid bed was associated with lower risk of nerve injury\(^35\). This was the basis of the guidelines produced by The German Association of Endocrine
Surgeons. Despite the lack of evidence that using a nerve monitor reduced nerve injury rates, its use is now a standard of care in Germany due to its use in large centres and the fact that surgeons find it a useful adjunct to surgery. A 2013 clinical practice guideline from the American academy of otolaryngology head and neck surgery found no evidence to advocate the use of nerve monitoring in thyroid surgery in order to improve voice outcomes postoperatively. The guideline comments that while the use of monitoring adds information regarding the neurophysiologic status of the nerve and potentially aids identification; the cost, extra training requirements and potential for misinterpretation of results make its risk/benefit equivalent.

Despite the fact that there is little evidence to say that nerve injury is reduced by the use of nerve monitoring intra-operatively, many authors still advocate its use. Several authors have commented that while it does not make an unsafe surgeon safe, it is ‘very helpful’. Several authors also advocate its use in more ‘high risk’ cases such as reoperative surgery, massive or retrosternal goitres, Graves disease or advanced cancer. In their recent review of the literature, Sanabria et al considered that use of nerve monitoring in thyroid surgery should not necessarily be considered the standard of care due to a lack of sufficient evidence and considerable variation in its use by thyroid surgeons.

**Medico legal issues**

The most important aspect of preventing damage to the facial or RLN nerve is an excellent knowledge of the relevant anatomy, meticulous dissection and appropriate experience of the operating surgeon. The surgeon should be familiar with all relevant techniques required to identify the nerves e.g. retrograde techniques for finding peripheral branches of the facial nerve.

**Parotid Surgery**

Parotid surgeons who use intraoperative nerve monitoring are less likely to have a lawsuit brought against them. It is important during the consent process to clarify the use of nerve monitoring if it is to be used, as the patient should understand that it is not a proven method of decreasing palsy rate and that it is not always reliable. However if the surgeon informs the patient that a monitor is used it may reassure the patient that all available techniques and equipment to minimise the risk of damage to the nerve is being used. If a nerve monitor is available then the surgeon should consider carefully why he or she is not using it. If it is deemed that a nerve monitor would be useful but is not available then the patient should be referred to a centre with nerve monitoring facilities. Cost or lack of equipment should not be a reason not to use a monitor if it is deemed to be useful in that procedure.

**Thyroid Surgery**

Recurrent laryngeal nerve injury is the most common cause of litigation in endocrine surgery. In a search of a legal database half of those cases involving thyroid surgery were due to injury to the recurrent laryngeal nerve (1989-2009). RLN monitoring was not performed in any of these cases. American insurance companies still consider nerve monitoring in thyroid surgery to be “experimental and investigational because its clinical benefit has not been established.”

With growing internet access patients are becoming increasingly aware of devices such as nerve monitors and may see lack of its utilisation as negligent on the part of the surgeon regardless of the medical literature, especially when in the case of parotid surgery so many surgeons are using monitoring. In time this may become the case for thyroid surgery also as the use of monitoring increases.

From a medicolegal aspect the most robust defence in litigation is a well-kept personal audit of the nerve palsy rates of the individual surgeon. Publication of personal case series with acceptable palsy rates has been shown to provide satisfactory evidence of acceptable clinical practice (personal correspondence, Professor PJ Bradley, Nottingham).

**Training issues**

Brennan et al state that trainees’ dissection was gentler in response to audio feedback from the nerve monitor. Surgeons who were trained using the monitor routinely were three times more likely to use it in thyroid surgery as a consultant. Trainees are encouraged not to become reliant on the monitor in parotid surgery, particularly given the possibility of false positive/negative responses and faulty equipment. It is certainly no replacement for meticulous dissection and good anatomical knowledge, something that the literature reiterates.

**Conclusion**

The use of intraoperative nerve monitoring in both parotid surgery and thyroid surgery remains controversial and currently should not be considered the standard of care, although this may change in the future. The literature for both is limited, made up of small retrospective case series reviews without a control group. Where larger studies exist there is no evidence to suggest that nerve injury resulting in either temporary or permanent weakness is reduced by using nerve monitoring. In the case of parotid surgery a reduction in operative time has been documented which may offset the cost of equipment. Despite this, up to 80% of surgeons are using facial nerve continuous monitoring in
parotid surgery and up to 30% of surgeons for thyroid surgery. This is bound to impact on trainees, who are likely to be trained entirely using monitoring, but should be taught not to rely on it. Therefore the training and experience of surgeons will also be a determining factor in the use of nerve monitoring. With an increasing number of surgeons using monitoring in parotid surgery, patients may begin to expect this as a standard of care for the use of nerve monitoring. With an increasing experience of surgeons will also be a determining factor in the use of nerve monitoring. This is bound to impact on trainees, who are

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Incidence, evaluation and management of synchronous primary malignant tumours of the head and neck

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Abstract
The aim of this review is to look at the incidence of synchronous primary tumours in the head and neck and how they are evaluated and managed. As the presence of a second primary significantly affects prognosis; methods that allow early detection have been assessed, treatment options discussed and recommendations for management made.

Key words
Synchronous tumour, head and neck cancer, second primary tumour, multiple primary malignancies.

Introduction
It is well recognised that patients with head and neck squamous cell carcinoma (HNSCC) are at an increased risk of developing second primary malignant tumours1, 2. The incidence of second primary malignant tumours in patients with (HNSCC) ranges from 5 to 16% 1-3. The high incidence of second primary tumours is thought to be due to ‘field cancerisation’ as all mucosal surfaces of the upper aerodigestive tract are exposed to the same carcinogens, alcohol and tobacco, and therefore there is a risk of multiple primary cancers4. The wide range of incidence quoted most likely represents variation in the timeframe post diagnosis of index tumour that incidence of second primary is measured. A more useful measure is the incidence rate i.e. the diagnosis of new second primary tumours per year which is approximately 2-4%1. The wide range in incidence rates may also be due to the variation in methods used to screen for second primaries among different departments.

The risk of developing a second primary tumour appears to be steady throughout the follow up period1. Due to a cumulative effect the overall incidence of second primary tumours steadily increases in the years following diagnosis of the index tumour2. After 4 years post treatment for a primary head and neck malignancy the chance of mortality from a second primary is greater than from the initial tumour2. Therefore as survival from head and neck cancer improves the incidence of second primary tumours will most likely continue to increase. Indeed, after 4 years follow up it could be argued that the focus of surveillance should change from the identification of local recurrence to the early detection of a second primary malignant tumour.

Warren and Gates set out criteria for diagnosis of second primary malignant tumours: in that both tumours must be a histopathological proven malignancy, with at least 2 cm of normal tissue between the tumours, unless of the same site but greater than 5 years apart and one tumour must not be the metastasis of the other 2, 5.

Depending on which definitions are being used a synchronous malignant tumour is generally accepted as one that arises within 0 and 6 months of diagnosis of the index tumour. This can be divided further into a sub-group of simultaneous primary malignant tumours, which occur within 1 month of the diagnosis of the index tumour. Any second primary malignancy identified after 6 months can be classified as a metachronous tumour5. However, a metachronous tumour may have been a synchronous primary which was not identified at initial staging. This would depend on the screening strategy used within the department.

The detection of synchronous primary malignancies is of importance clinically as it has a significant effect on prognosis and dependent on the stage and site may affect the subsequent management6. This is important when counselling a patient with a new diagnosis of HNSCC and as part of informed consent that they know the full extent of the disease and the prognosis. Equally patients without any evidence of a synchronous primary tumour can be re-assured.

The most common site of second primary tumour outside of the head and neck is within the thorax. The incidence of
synchronous malignant tumours in the thorax is 4%. Higher rates (15% - 33%) of synchronous tumours and pulmonary metastases are seen in patients with more advanced (T3/T4) primary tumours, or where there is level IV nodal involvement.

**Evaluation of head and neck cancers**

The main aim when evaluating a newly diagnosed HNSCC is to assess the extent of the primary tumour and to identify pathological cervical lymphadenopathy, identify distant metastases and to detect a synchronous tumour. The accepted current practice is endoscopy with biopsy and imaging.

Published clinical guidelines recommend computerised tomography (CT) or magnetic resonance imaging (MRI) as part of the staging in confirmed head and neck malignancy. This should preferably be carried out prior to endoscopy; in theory to prevent upstaging of the tumour by oedema post-biopsy. The purpose of CT or MRI scan is to stage the local extent of the primary tumour, to determine the presence of cervical lymph nodes, to search for an occult primary and to identify distant metastases or synchronous primary.

Endoscopy and biopsy should also be carried out. Panendoscopy is only recommended for symptomatic patients or in those patients at high risk of a synchronous primary. Routine oesophagoscopy and bronchoscopy in the absence of specific symptoms has a low yield in detecting synchronous primary tumours. Endoscopy which is ‘symptom-directed’ appears to be an effective alternative to panendoscopy for the identification of synchronous primary tumours. When combined with a chest X-ray, symptom-directed endoscopy will detect most second primaries of the upper aerodigestive tract. The recommendations from the SIGN guidelines are that all patients with head and neck cancer should have direct pharyngolaryngoscopy and a chest X-ray with symptom-directed endoscopy where indicated. Panendoscopy has been described in the literature as having a detection rate of 1.5-3% for synchronous primary tumours in the upper aerodigestive tract. The rate is thought to be even lower in non-smoking patient groups with HNSCC.

The stage of the primary tumour affects the likelihood of finding a secondary tumour in the lung. CT or MRI has not been shown to provide an improvement in the accuracy of staging of the index site in T1 laryngeal tumours which are localised to the vocal cord. The sensitivity and specificity of CT scan for detecting synchronous tumours or pulmonary metastatic disease is 100% - 95% compared to 33% – 97% for chest radiograph. It is generally accepted within clinical practice that CT skull base to diaphragm should be performed for all patients with biopsy confirmed head and neck malignancy. MRI should be used in the staging of oral and oropharyngeal tumours as it has greater detection of superficial lesions and no artefact from dental amalgam. MRI should be used in addition to CT if there is an uncertainty of whether there is laryngeal cartilage invasion or involvement of skull base, cervical spine or orbit. Ultrasound guided fine needle aspirate (FNA) or core biopsy is recommended in the investigation of head and neck masses.

Ultrasound guided FNA and FDG-PET have a role in the investigation of the primary tumour in certain circumstances. When CT and MRI findings are equivocal with regards to neck node status ultrasound guided FNA or FDG-PET can be indicated. FDG-PET also has role in the investigation of metastatic cervical lymphadenopathy of unknown origin where CT an MRI have been unable to identify a primary site.

Many papers discuss the theory of targeted screening of those patients with a new diagnosis of HNSCC who are thought to be at a higher risk of having a synchronous primary. Such groups include those with positive nodal disease in the neck and advanced stage of primary HNSCC at presentation (stage III/IV). Other factors thought to place patients at low risk of synchronous primary are patients with HPV positive oropharyngeal HNSCC. The theory in this group of patients with virally mediated tumours, who are predominantly non-smokers, is that the remainder of the aerodigestive tracts will not be exposed to the same carcinogens and therefore the ‘field cancerisation’ theory cannot be applied. Studies have shown a lower incidence rate of second primary tumours in p16-positive patients with oropharyngeal HNSCC when compared to p16-negative patients. Panendoscopy and FDG-PET were used in detection of second primary tumours in this study and the differences in the two HPV status groups were statistically significant. Other factors, such as p53 mutations have been thought to be associated with a higher risk of synchronous primary but this has not been proven in the literature.

For synchronous lung malignant tumours bronchoscopy and biopsy or CT guided biopsy of lung lesion will be required, followed by appropriate staging and discussion at lung multidisciplinary team (MDT) meeting. The investigation of synchronous oesophageal tumours requires additional PET-CT staging and discussion at the relevant upper gastro-intestinal MDT.

Despite the routine use of FDG-PET in the initial staging of oesophageal malignancy and its use when small discrete lung nodules are of uncertain significance our current
guidelines advocate its use in the investigation of an occult primary where CT / MRI have been unhelpful in locating a primary index site or in the investigation of recurrent or residual disease of the head and neck.

A review of the literature has shown the benefits of FDG-PET in the initial investigation of HNSCC to help with the identification of a synchronous primary. Studies have shown FDG-PET significantly increases the detection rate of second primaries in comparison to standard investigations such as panendoscopy and CT scan\textsuperscript{12}. One small study of 68 patients found second simultaneous primary tumours in 18\% of patients with FDG-PET versus 7\% detection rate in the same cohort by routine investigation with clinical examination, CXR, ultrasound and CT scanning of the head and neck\textsuperscript{12}. This difference in detection rate of second primary tumours by FDG-PET was statistically significant (p=0.016)\textsuperscript{12}. Unfortunately panendoscopy was not routinely performed in this department and could therefore not be evaluated in this study\textsuperscript{12}.

The other smaller group of patients are those head and neck lesions that show up incidentally in FDG-PET investigation of for example oesophageal or lung primary lesions. If this is the case we revert back to our default protocol of endoscopy and biopsy and CT scan of skull base to diaphragm to stage the potential synchronous primary of the head and neck.

Management

Once the primary head and neck malignant tumour and the synchronous primary tumour have been staged and discussed at the appropriate MDT, management plans should be proposed. Depending on the staging and site a decision should be made with regards to whether surgical, oncology or palliative treatment would be most appropriate. Collaboration between the various MDTs is required. The two management plans are closely interlinked.

Obviously a metastatic status of one of the primary tumours would curtail radical/curative treatment of the other secondary. If however both primary malignancies are treatable with curative intent the next decision would be co-ordinating the timing of each treatment. The ideal scenario in this situation would be in the case of a laryngeal and proximal oesophageal lesion where a joint procedure could treat both primary sites.

One study of the management of patients with synchronous primary tumours observed that the treatment was dependent on the staging of each primary tumour. If both tumours were advanced often treatment was initiated with chemotherapy. If both tumours were in the early stage then often locoregional treatment could be extended to target both tumours in 30\% of cases. Where there was discrepancy in staging of both tumours, treatment priority was given to the more advanced tumour. Despite co-ordination with regards to treatment, 21\% of patients with synchronous primary tumours had interruption to definite treatment\textsuperscript{20}.

The presence of a synchronous primary tumour has a significant adverse effect on survival. Factors associated with adverse outcome in these patients were low body mass index (p=0.03) and advanced staged tumours (p=0.01)\textsuperscript{20}. In one study of 43 patients with synchronous primary tumours 71\% died with a median time to death 7.7 months. Three-year overall survival in this cohort was low at 33.9\% \textsuperscript{20}.

The emphasis on screening for patients with HNSCC should be in finding synchronous primary tumours at an early and potentially treatable stage. This is the theory behind the use of chromoendoscopy to detect early synchronous primary oesophageal carcinoma. Although the incidence of synchronous oesophageal primary in this study was low (1.5\%) and therefore this approach would only be viable in high risk populations \textsuperscript{21}.

One area of ongoing debate is whether a lung lesion detected by staging CT scan is a second primary or lung metastases. If the lesion is a large endobronchial lesion then it can be more readily assumed to be a second primary. However, if it is a small peripheral lesion then differentiating between a small lung second primary and a metastasis can be more challenging. Classical appearances such as spiculation of the lesion can be more indicative of a second primary. However, often these features are not present. If the lung/bronchial lesions are amenable to biopsy then histological characteristics can help differentiate between the two. Histologically, if it is an adenocarcinoma it can most likely be assumed to be a second primary of the lung. If the histology shows a squamous lesion then the diagnosis is uncertain but probably more likely to be metastatic disease. For indeterminate small nodules of the lung not amenable to biopsy often interval scanning to observe the evolution of the lesion and hence the diagnosis is recommended. This is acceptable if the patient has already had their primary HNSCC treated and the debate is between incidental lung nodules and metastases. If however a lung lesion is detected at the first presentation of HNSCC then there is a strong indication for an FDG-PET to determine the nature of the second lesion.

The presence of a synchronous primary requires good communication between MDT groups. This should ensure where possible that the investigation and management of
synchronous primary tumours does not significantly delay the management of the primary head and neck cancer. Although clearly the staging and proposed management of the second primary is likely to significantly influence the treatment offered for the primary head and neck tumour.

Conclusions

As survival from primary head and neck malignant tumours improves, morbidity and mortality from metastatic disease or second primary malignancy is likely to increase. Patient’s with HNSCC are at higher risk than other cancer groups of developing a second primary malignancy and it has been observed that the incidence of second malignant primary tumours steadily increases from the time from diagnosis of the index primary tumour in the head and neck. This influences our follow up and awareness that particularly after 4 years follow up the risk of mortality in our patient group is higher from a second primary rather than the risks from the index tumour itself. Given this influence of a second primary it is now time for PET-CT at the time of head and neck cancer diagnosis to be formally evaluated with respect to the detection of second primary malignancies.

References:

Assessment and management of adult laryngotracheal stenosis

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Abstract
During the 19th century the principle causes of airway stenoses were infections such as diphtheria, syphilis and tuberculosis. The discovery of antibiotics and the use of endotracheal tubes changed the pathophysiology of laryngotracheal stenosis. Whereas the vast majority of cases of airway stenosis in the paediatric population are related to intubation (95% +), while in adults this figure is > 50%. In adults a considerable proportion of cases of airway stenosis are related to systemic inflammatory disorders, as well as more obscure conditions such as idiopathic subglottic stenosis (ISS). The incidence of airway stenosis related to tracheostomies and orotracheal intubation is roughly similar but the sites and types of injuries sustained differ. Endoscopic assessment and initial management of adult airway stenosis is advised in nearly all cases. Two-thirds of cases of post-intubation laryngotracheal can be treated endoscopically with the remainder requiring open resection or laryngotracheal reconstruction procedures.

Key words
Stenosis, laryngotracheal, subglottis, trachea, dyspnoea, larynx, trachea, idiopathic, granulomatosis, sarcoidosis, tracheostomy, intubation.

Introduction
The larynx, trachea and bronchi form the conduit between the external environment and the lungs through which respiratory gases are transported and pulmonary secretions are expectorated. The narrowest site of the adult airway is the glottis whereas in the neonate it is the subglottis. The principle function of the larynx is to protect the airway from aspiration during swallowing, but the larynx is also involved with phonation and the Valsalva manoeuvre.

Adult airway stenosis
Until the end of the 19th century the principle causes of airway stenoses were infections such as diphtheria, syphilis and tuberculosis. Since the middle of the 20th Century antibiotics and the ability to maintain prolonged ventilation have made endotracheal intubation the most common cause of laryngotracheal injury. In the author’s personal series (Table I) about half of the cases of adult airway compromise were due to periods of ventilation on the Intensive Care Unit (ICU). This series has also shown that the incidence of airway narrowing is similar in patients who have had endotracheal ventilation only when compared to those that had an early tracheostomy. Even though it has been shown that there is no difference in morbidity or mortality when comparing early versus late tracheotomy1, it is more likely that prolonged endotracheal intubation will risk glottic stenosis and the repair of this is always a compromise between airway, voice and swallowing.

Table 1. Four hundred consecutive adult referrals with laryngotracheal stenosis

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>48.00%</td>
<td>Acquired laryngotracheal stenosis</td>
</tr>
<tr>
<td>34.75%</td>
<td>Subglottic stenosis</td>
</tr>
<tr>
<td>13.25%</td>
<td>Tracheal stenosis</td>
</tr>
<tr>
<td>14.75%</td>
<td>Bilateral vocal cord mobility impairment</td>
</tr>
<tr>
<td>8.75%</td>
<td>Nerve injury</td>
</tr>
<tr>
<td>4.75%</td>
<td>Scar/fixation</td>
</tr>
<tr>
<td>1.25%</td>
<td>Rheumatoid arthritis</td>
</tr>
<tr>
<td>11.25%</td>
<td>Wegener’s granulomatosis</td>
</tr>
<tr>
<td>9.75%</td>
<td>Idiopathic subglottic stenosis</td>
</tr>
<tr>
<td>5.50%</td>
<td>Supraglottic stenosis (2.5% sarcoid,3.0% other)</td>
</tr>
<tr>
<td>3.25%</td>
<td>Previous papillomatosis treatment</td>
</tr>
<tr>
<td>3.25%</td>
<td>Glottic web</td>
</tr>
<tr>
<td>2.00%</td>
<td>Tracheomalacia (1.25% relapsing polychondritis)</td>
</tr>
<tr>
<td>1.00%</td>
<td>Amyloidosis</td>
</tr>
<tr>
<td>0.75%</td>
<td>Vascular lesion</td>
</tr>
<tr>
<td>0.50%</td>
<td>Subglottic stenosis congenital</td>
</tr>
</tbody>
</table>
Paediatric airway stenosis

Paediatric airway stenosis nearly always involves the subglottis and is a well-researched area of surgery. Treatments in children include airway augmentation with rib grafts as well as tracheal and cricotracheal resection procedures. Adult laryngotracheal stenosis has been poorly researched and the surgical options included tracheostomy, tracheal resection or cricotracheal resection. Some surgeons continue to use primary cartilage grafts to augment the adult airway. There has been little appreciation of the fact that there is a high incidence of ischemic necrosis of primary rib graft in adult patients. Furthermore, the quality and quantity of rib cartilage that can be harvested diminishes with age.

Patient Assessment

The patient attending the airway clinic has in most cases already been diagnosed with airway stenosis and is experiencing a variable degree of dyspnoea. As a part of the history it is important to ask about the voice and swallowing but also coexisting medical conditions such as diabetes, vasculitis and other airway disorders such as chronic obstructive pulmonary disease and ‘true’ asthma. Obesity is associated with a poor outcome following airway surgery and the body mass index should be determined and if appropriate a dietetic referral made.

Clinical examination

Clinical examination should assess the degree of stridor and chest related recession. The chest and trachea should be auscultated. Flexible nasal endoscopy should be used to exactly determine and document any limitations in vocal cord movement, evidence of laryngopharyngeal reflux, pooling of hypopharyngeal secretions and appearance of the airway stenosis if visible. If there is a tracheostomy present then the endoscope should be passed through this to look at the lower airway.

If there is evidence of swallowing problems then the patient should be referred for videofluoroscopy to determine aspiration risk. Airway surgery in a patient with even micro-aspiration is unlikely to be successful.

Flow-volume loops:

Flow-volume loops are the mainstay of diagnosis and monitoring adult patients with laryngotracheal stenosis and should always be requested as part of respiratory function testing. The flow-volume loop test begins from total lung capacity as a maximum effort expiration of the forced vital capacity, which is then proceeded by a maximum effort inspiration back to total lung capacity. From a diagnostic perspective, flow-volume loops can distinguish between obstructive and restrictive lung diseases, can characterize airway obstruction as upper airway or lower airway, and can separate upper airway obstruction into fixed obstruction, variable extrathoracic obstruction, and variable intrathoracic obstruction (Figure 1). Flow-volume loops are highly sensitive to stenosis severity and can also be used to quantify treatment response.

Radiology imaging

Although computer tomography (CT) is excellent at determining the diameter of the normal trachea, if the axial image does not pass through the narrowest part of the stenosis, the severity of the stenosis can be underestimated. Serial scanning, to monitor treatment progress, is not advisable because of concerns related to radiation exposure. The most useful assessment tool is endoscopy under anaesthesia which allows one to determine the site, diameter and length of the stenosis. The four key prognostic factors are the nature of the underlying disease process, presence of acute fibroinflammatory tissue as opposed to mature fibrotic strictures, site of the stenosis (in particular whether the glottis is involved) and the vertical height of the lesion.

Grading of airway stenosis

Meyer and Cotton have developed a system of grading paediatric airway narrowing based on the surface area of the stenosis as a percentage of the normal airway:

- Grade I: 0-50%
- Grade II: 51-70%
- Grade III: 71-99%
- Grade IV: 100%

This system was initially developed for assessing the subglottis in children, but has since been expanded to encompass tracheal lesions in both children and adults. The Meyer-Cotton system allows for stratification of airway stenosis size, but there is considerable variation in resistance to airflow even within one grade of this...
scoring system. Flow physiology is a better guide to the need to intervene than precise knowledge of lesion cross-sectional anatomy.

**Surgery and Anaesthesia**

Virtually all patients undergo airway assessment under anaesthesia. This is performed using suspension laryngoscopy and high frequency jet ventilation. Suspension laryngoscopy allows the use of both optical rigid endoscopes and flexible bronchoscopes to access the airway. The advantages are that the patient is paralysed and the full spectrum of rigid instrumentation, dilators, lasers and stents can be inserted and used with relative ease. As the patient is most commonly ventilated using a supraglottic jetting technique, lasers can also be used with minimal risk of airway fires. Suspension laryngoscopy also allows the use of the operating microscope with the advantages of binocular vision, depth of field, superior axial illumination and two hands free for instrumentation. The carbon dioxide laser can be used with a “line-of-sight” technique through a micromanipulator attached to the microscope. Many otolaryngologists and thoracic surgeons still use the ventilating bronchoscope for tracheal or bronchial assessment and surgery.

**Use of airway stents**

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

Stents are usually made of an expanding metal mesh and they may be uncovered, partially covered or completely covered with plastic polymers or silicone. Other stents are made purely of silicone and the next generation of stents will be able to deliver drugs and others will be resorbable.

To a variable degree all stents are prone to migration and bio-fouling. They also encourage airway granulation and metal stents may fracture (Figure 2). They should therefore only be used long-term, for palliation, when surgery is not an option. Patients with airway stents should be prescribed daily saline nebulisers. Carbocysteine can be added in those patients where there is mucus plugging, and the prolonged use of low dose macrolide antibiotics may help with granulation tissue and bio-fouling.

**Post Intensive Care Laryngotracheal Stenosis**

The long-term incidence of post ICU airway stenosis is unknown and can only be approximated at between 1- 4% 8-11, a significant early injury is reported in 47% of patients in one series12. This is despite the usage of high volume, low pressure cuffs on endotracheal and tracheostomy tubes.

The risk factors for laryngotracheal stenosis following a period of ventilation on the ICU include: sizing of endotracheal tubes, excessive lateral cuff pressure due to poor cuff pressure monitoring, hypotension, local infection, gastroesophageal reflux, duration of intubation, use of steroids (other causes of compromised patient immunity), patient movement and agitation, tracheostomies and bilateral injuries to the posterior vocal cords. The majority of patients ventilated on ICUs do not appear to develop airway stenosis. Although there is no current research to support this, patients who tend to scar excessively following injury, may self select for airway stenosis.

The early phase of the post-intubation airway stenosis is characterized by mucosal ulceration and perichondritis followed by the formation of exophytic granulation tissue. As healing progresses, granulation tissue is gradually replaced with mature fibrotic tissue and the wound.
contracts giving rise to the classical picture of mature airway scar (Figure 3). It has been shown that inflammatory conditions in the airway do respond to intra-lesional steroids\textsuperscript{11}. Using suspension laryngoscopy and supraglottic jet ventilation, up to 3 mL of methylprednisolone acetate (40mg/ml) can be injected into the stenosis. Radial cuts are then made into the stenosis with the carbon dioxide laser (8–10 W continuous) delivered through the microscope using a line-of-sight technique. The lesion is then dilated using a pulmonary balloon dilator to the size of the adjacent normal airway. With more mature and fibrotic lesions, intralesional steroids are of limited value. In these cases radial cuts into the lesion are followed by balloon dilatation and topical mitomycin-C application may be considered. Endoscopic surgery is repeated every 3–4 weeks. Patients whose lesions prove recalcitrant to endoscopic therapy, and this usually became evident by the third procedure, should be treated with open laryngotracheal reconstruction or tracheal resection techniques. Where there is collapse and damage to the laryngotraheal cartilaginous support, open surgical techniques should be considered earlier, as endoscopic techniques are likely to fail (Figure 3). Figure 4 shows the overall success rate of the endoscopic approach to airway stenosis of 72%. It is highly relevant that in this series all patients with a body mass index of greater than 45 failed endoscopic airway surgery\textsuperscript{5}.

A less common variant of post-ventilation tracheal stenosis is seen in a small number of tracheostomy patients. This is caused by over-resection or subsequent pressure necrosis of anterior tracheal rings due to a tracheostomy. At decannulation, there is scarring and contracture at the stoma site which draws in the lateral ring remnants as a result of the wound contracture leading to a “Lambda-shaped” stenotic deformity and airway compromise. The lesion usually extends over 1–2 tracheal rings with normal proximal and distal trachea\textsuperscript{13}. The trachealis is not involved and there is usually a small anterior bridge not contributing to the stenosis (Figure 5, left). Tracheal resection and anastomosis has been recommended for this condition\textsuperscript{14}, but this is a major operation with associated morbidity and a small mortality rate.

The lesion can be treated using a CO\textsubscript{2} laser, delivering 8–10 W continuously, deployed through a micro-manipulator attached to the microscope using a ‘line-of-sight’ technique. The proximal and distal trachea is used as a guide to the limits of the resection and the collapsed cartilage is vaporised (Figure 5, centre). The resection can extend to the tracheal fascia if necessary and any bulging of the trachealis can also be reduced.
with the laser. A pulmonary balloon dilator may be used to expand the airway. The mucosa over the trachealis and the apex of the Lambda must be preserved because a circumferential injury with the laser will lead to further stenosis.

**Idiopathic Subglottic Stenosis**

Idiopathic subglottic stenosis (ISS) is a rare, slowly progressive, fibro-inflammatory process of unknown aetiology leading to narrowing of the airway in the subglottic region and usually involves the first and second tracheal rings. It occurs predominantly in women, post puberty, but has been reported in males 15 – 18. The diagnosis is one of exclusion and the patient must not have been intubated, received neck trauma or had a significant respiratory tract infection in the preceding two years. Patients must also be investigated for GERD, auto-immune disorders including granulomatosis with polyangitis (GPA) and have tissue sent for histology at each opportunity. Histology reveals a fibro-inflamatory process. It is not unusual for these patients to have been treated for asthma, when the cause of their airflow restriction could simply be determined using flow volume loop studies (Figure 1).

An endoscopic approach is recommended for the majority of patients. Most patients respond to intralesional methylprednisolone (up to 120mg), radial laser incisions and dilatation. Stenosis recurs usually over a period of 6 to 12 months at which time surgery can be repeated. Cricotracheal resection has been recommended\(^{17}\) but the high reported success rate has not been matched by other units\(^{18}\). Cricotracheal resection is not possible for lesions extending up to the glottis and when performed it removes part of the pitch elevation mechanism. The author’s approach to open ‘curative’ surgery differs from the orthodoxy of cricotracheal resection. A laryngofissure is performed to include the first two tracheal cartilages. Next a posterior cricoid split is also performed taking care not to enter the hypopharynx. The majority of the stenosed mucosa is removed and a piece of costal cartilage is placed in the posterior cricoid split to act as a ‘spacer’ (Figure 6).

A closed laryngeal stent, covered with a superficial skin graft (epidermal surface against stent), is held in place inside the larynx with a single, strong, monofilament suture. The laryngofissure is closed completely at the anterior commissure and above but left separated below this by a few millimeters to allow one sternohyoid muscle to be sewn in as a vascular transposition flap. A temporary tracheotomy needs to be fashioned as the stent obstructs the airway. At two weeks the stent is removed endoscopically and the patient is decannulated the next day\(^{19}\).

**Bilateral Vocal Cord Mobility Impairment**

The term bilateral vocal cord mobility impairment (BVCMI) best describes cases where there may be sub-optimal movement in both vocal folds as well as cases where there is no movement at all. There are three mechanisms of injury:

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

Bilateral recurrent laryngeal nerve injuries leave the vocal folds in the paramedian position and patients suffer with significant shortness of breath and stridor. They often end up with a tracheotomy in the acute situation. Various techniques have been described to manage this problem and these include laser to the posterior vocal fold or arytenoid (Figure 7) and suture lateralisation of the vocal folds. These all result in a compromise between voice airway and swallowing.

Various reinnervation operations have been described, for example anastomosing the ansa cervicalis or hypoglossal...
nerve to the recurrent laryngeal nerve or using muscle nerve pedicle flaps. A more promising technique has been developed by Professor Jean-Paul Marie in France who has been using the accessory phrenic nerve and anastomosing it to the posterior cricoarytenoid muscle. Other groups are looking at reanimating the human larynx with implantable electrical stimulation devices. With fixed cricoarytenoid joints the only surgical option is some form of laser to the posterior cord or arytenoid as described above (Figure 7).

Posterior glottic injuries can result in inter-arytenoid scar tissue, which in turn can lead to cricoarytenoid joint ankylosis, unless identified and treated early. The most common cause for this type of injury is endotracheal intubation on the Intensive Care Unit. Attempts at treating scar in the posterior glottis have included posterior laryngeal mucosal flaps, advanced into the post glottis, after division of the scar tissue. The author’s technique involves the open placement of a costal cartilage derived ‘spacer’ within a posterior cricoid split (Figure 6). This is usually resorbed within a few weeks but prevents scar tissue reforming.

Laryngotracheal Compromise due to Inflammatory Diseases
Granulomatosis with Polyangitis (GPA), formally called Wegener’s granulomatosis, is a multi-system inflammatory disease with an underlying vasculitis involving small and medium sized vessels. There is associated granuloma formation and necrosis. GPA classically involves the upper and lower respiratory tract, and the kidneys. The diagnosis of GPA is often made on clinical presentation when a patient has had the appropriate symptoms for a prolonged period of time. The presence of a positive ANCA (antineutrophil cytoplasmic antibody) test may aid in the diagnosis, but positivity is not conclusive and negative ANCA results are not sufficient to reject the diagnosis. It is important to appreciate that up to 20% of patients with untreated active GPA lack cANCA or may show positivity later on in the disease history. A definitive diagnosis of GPA can be made by a biopsy of suspicious lesions (demonstrating granulomatous inflammation) in conjunction with positive serological analysis.

Up to 23% of patients with GPA develop a subglottic stenosis. This subglottic inflammation and narrowing does not uniformly respond to systemic immune-suppressives and may persist despite adequate disease control in other organ systems (Figure 8).

Intra-lesional corticosteroid injections, radial lesionsal cuts, and dilatation will treat the majority of new stenoses involving the larynx, trachea and bronchi due to GPA. The use of tracheostomies and long-term stents can lead to further airway complications, which may prove difficult to treat.

Sarcoidosis:
Sarcoidosis is a non-caseating granulomatous condition of unknown aetiology. Although there is no cure, corticosteroids may control the rate of disease progression. The larynx is involved in 1-5% of cases. The supraglottic larynx tends to be affected more often than the subglottis. The laryngeal lesion is usually a pale pink, edematous swelling that can pedunculate into the airway and produce stridor (Figure 9). Intralesional steroids and CO2 laser debulking of laryngeal lesions can be effective in restoring the airway.

The Future
In the adult patient 4 to 6 cm of trachea can be resected with primary anastomosis. Longer lengths of tracheal damage, failed resections and extensive tracheomalacia have so far no easy solution other than palliation with stents or long-term tracheostomies. Tissue engineering for tracheal replacement holds promise. Similarly laryngeal transplantation may be the solution to restoring
the airway where this organ is damaged beyond repair. The other area of research with potential for future treatments is biotechnology. Biocompatible and bio-integrating scaffolds that mimic the mechanical properties of tracheal cartilage could be used to provide shape to muscle flaps for use as tracheal replacements. Bio-integrating stents could be an even simpler solution to the management of airway stenosis. Until these technologies are proven and widely available prevention of laryngotracheal airway compromise is essential. Not just the early recognition and treatment of airway diseases but an understanding of the risk factors for airway injury in the Intensive Care Unit. More appropriate sizing of ventilation tubes and monitoring cuff pressures may reduce the incidence of subglottic and tracheal stenosis, and the early change to tracheostomies in patients destined for prolonged ventilation will reduce the incidence of glottis stenosis.

References:
What is the future of targeted therapy in head and neck cancer?

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Abstract
Advances of our knowledge of genomics and cancer signaling in head and neck cancer has increased the opportunities for the discovery of novel molecular targets to be incorporated into future treatment therapies. Single agents have been tested in clinical trials with disappointing results. The most common substances are small molecules and antibodies. Further targets comprise angiogenesis, apoptosis or cancer stem cell-related targets, metabolic targets, PI3K/Akt/mTOR pathway inhibition and gene therapy amongst others. Introduction of gene therapy that restores loss of function mutations or to introduce DNA that encodes a therapeutic protein is under investigation. Key problems are the delivery of genes into tumor cells which might be overcome by targeted viral vectors in future. Therapeutic vaccines are in development for HPV-related HNSCC, however, clinical efficacy and appropriate immunological responses have not been demonstrated yet. Targeting the PI3K-PTEN-AKT signaling pathway also seems promising.

Established targets need to be combined and novel biological agents within future research projects that hit multiple targets will be tested. Patient selection will be improved with the help of new biomarkers.

Key words
Head and neck cancer, human papilloma virus, targeted therapy.


Introduction
Despite advances in diagnosis and treatment, mortality rates remained high for head and neck squamous cell carcinomas (HNSCC) over the last decades, making this disease a serious problem worldwide. About 650,000 newly diagnosed cases per year are estimated and almost 50% of patients will die their disease. The main subgroups of HNSCC are either related to alcohol and tobacco consumption or to infections by high risk human papilloma viruses (HPV). While it is anticipated that the incidence rates for HNSCC to decline due to a reduction of alcohol and tobacco abuse in the western world, the incidence rates for HPV-associated HNSCC are rising in general with statistics on incidence varying greatly among nations ranging from 30 to 40% for Germany, 40 to 80% for the USA and more than 90% for Scandinavia. In regard to primary tumor location the probability of an HPV-association can be expected in decreasing order for the different sub-sites as follows: oropharynx, larynx/hypopharynx, oral cavity. Over the past years it became clearer resulting from the work of molecular and genetic analysis, that HNSCC associated with HPV and HNSCC related to alcohol and tobacco consumption are distinct diseases with differences in carcinogenesis which has significant impact on treatment response and prognosis that should influence therapeutic management and differing outcomes in the future.

Heterogeneity
The key issue of translational medicine is to overcome the burden of heterogeneity of clinical samples, which is usually absent in a basic science experimental setup. Reasons for heterogeneity are complex and may be divided into endogenous (e.g. genetic variations) or exogenous factors (e.g. uptake of carcinogenic substances). While endogenous factors largely depend on genetic or epigenetic background and may therefore be useful to determine a certain risk or predisposition to develop carcinoma, exogenous factors largely act randomly and may be more or less harmful for certain subgroups of individuals, depending on endogenous factors and probably also on additional exogenous factors. It has been reported, that at least HPV status and tobacco consumption are independent prognostic factors by determining differential molecular profiles of the cancer and therefore are responsible for varying therapy response. By using cDNA microarrays for example four groups of HNSCC (EGFR-pathway signature, mesenchymal-enriched subtype, normal epithelium-like subtype, and subtype with high levels of antioxidant enzymes) have been defined and have distinct gene expression patterns correlating statistically significantly to disease free
survival of patients. These finding has been confirmed by analyzing FFPE samples afterwards. In conventional comparative genomic hybridization (CGH) experiments fewer genetic alterations and amplifications were found for HPV-related oral squamous cell carcinoma (OSCC) with some alterations (e.g. deletions at chromosome 3p, 5q, 9p 15q and 18q amplifications at region 11q13) being significantly prevalent for HPV unrelated oropharyngeal squamous cell carcinoma (OSCC). This has recently been approved by genome wide approaches. In general, HPV-related HNSCC show less frequent genetic alteration like mutations, translocations or gains and losses. Genes of important tumor suppressor proteins like TP53 or CDKN2A are rarely mutated in HPV-associated HNSCC. However, certain pathways which are important for carcinogenesis in general are modulated in HPV-associated HNSCC as well. Unlike HPV-negative HNSCC, for example TP53 or Rb is silenced not by mutations, but rather by down regulating protein activity via the action of viral oncoproteins (mainly HPV-E6 and -E7 oncoproteins).

Heterogeneity between different tumors is complemented by heterogeneity within one single tumor, which is related to the term “field carcinogenesis”. It is assumed that pre-neoplastic processes may occur at diverse sites of an area and each individually may develop depending on de- or accelerated cellular programs or other stimuli. Accumulation of diverse mutations in a step wise process, which finally leading to carcinogenesis, may be typical for the mucosa of the upper aerodigestive tract being damaged by tobacco and alcohol usage and may occur at different sites simultaneously. Multicentric tumor growth induction by HPV has been reported, however, field effects are uncommon in HPV-related HNSCC.

**Targeted therapy**

Rapidly dividing tumor cells are targets of traditional chemotherapy, which is a systemic approach and limited by considerable side effects and overlooking of slowly dividing tumor cells which are considered to be cancer stem cells. Radiotherapy targets the tumor itself, but is rather systemic not targeting any certain cell type or signaling pathway. Genetic mutations driving carcinogenesis, named oncogenes, may serve as promising targets. Unfortunately, in HNSCC, the majority of genetic damage is related to tumor suppressors, which are difficult to compensate. This drawback may sometimes be resolved by targeting downstream factors of the “lacking target”, but generally different methods have to be applied to restore such loss of function, which is important for carcinogenesis. Targeted therapies are systemic and selective, promising to have fewer side effects and aimed

<table>
<thead>
<tr>
<th>Table 1: Selected targeted therapies in Head and Neck cancer</th>
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<tr>
<td><strong>Target</strong></td>
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<tr>
<td>-------------------------------------------------------------</td>
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<tr>
<td><strong>Small molecule</strong></td>
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<tr>
<td>Imatinib (Glivec)</td>
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<tr>
<td>Erlotinib (Tarceva)</td>
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<tr>
<td>Bortezomib (Velcade)</td>
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<tr>
<td><strong>Monoclonal antibody</strong></td>
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<tr>
<td>Cetuximab (Erbitux)</td>
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<tr>
<td>Panitumumab (Vectibix)</td>
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<tr>
<td>Bevacizumab (Avastin)</td>
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<tr>
<td>Nimotuzumab (Theraloc)</td>
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<td>human mini antibody F16SIP</td>
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at being effective at resting / dormant tumor cells. Additionally, cellular targets, as well as potential inhibitors and chemical modification methods are abundant.

**Therapeutic Approaches**

Different therapeutic approaches may be applicable to achieve targeted therapy. The most common substance classes are “small molecules” and antibodies. Examples of both have been well established in clinical practice or are being studies intensely under current clinical trials (Table 1).

Small molecules are defined as molecule of low molecular weight, typically below 500 Daltons and 200-300 times smaller than their “large” counterparts (proteins and antibodies). Unlike small molecule drugs which are produced synthetically or are obtained through biosynthetic pathways (e.g. fermentation). Small molecules can be grouped according to the molecule-type into natural products, oligonucleotides, peptides, biologicals and chemicals, the last two representing about 75% of drugs currently in preclinical/clinical development and about 2,000 small molecule drugs are available on the market covering innumerable clinical scenarios.

Antibodies are unable to pass through the cellular membrane; however, therapeutic antibodies can recognize cellular surface antigens and may stimulate the immune system to eliminate labeled cells or to prevent tumor cells from growing by blocking required growth receptors. Tumor cells may display antigens uncommon to their originating cell type, the surrounding tissue or the developmental state of the organism and therefore be recognized / targeted for elimination. Antibodies are perfect for biotechnological modification to either reduce immune complex formation (increasing serum half life) or to enhance immune cell recruitment. Additional features may be fused to antibodies to deliver for example therapeutic drugs or (cytotoxic) enzymes in combination with systemic administration of prodrugs (antibody-directed enzyme prodrug therapy) into close proximity to the targeted cancer cell. Trastuzumab-Emtansine consists of a monoclonal antibody targeting human epidermal growth factor receptor 2 (HER2)-positive breast cancer cells and the potent cytotoxic agent mertansine.

**Cellular Targets**

The diversity of cellular targets is huge; however it’s a challenge to identify the most appropriate target for each specific disease. Since tumors and HNSCC in particular are heterogenic, it is important to establish reliable biomarkers and invent an adequate classification systems in order to identify suitable targets. There are several subclasses of potential points of action like receptor or metabolic targets, targets in angiogenesis, apoptosis or cancer stem cell-related targets. The established targeted receptor in head and neck oncology is the epidermal growth factor receptor (EGFR) which is frequently overexpressed in HNSCC samples. Effectiveness of blocking of EGFR with specific antibodies (Cetuximab (Erbitux®)) has been demonstrated. Other applications for EGFR antibodies are currently under clinical investigation (Table 2).

It is well known that tumor cells possess a distinct metabolic phenotype that supports rapid proliferation and disease progression. This altered phenotype provides unique opportunities for pharmacologic manipulation e.g. using small molecules. Metabolic targets can be affected by competitive and noncompetitive inhibitory mechanisms and the best studied compounds are 2-deoxy-d-glucose, 3-bromopyruvate, and lonidamine. PI3K/Akt/mTOR inhibition has been addressed in reducing HNSCC tumorigenicity while Rapamycin was successfully used in HNSCC animal models to inhibit tumorigenicity. However, it is not easy to demonstrate a metabolic effect in such case, since altered pathways for example like mTOR mostly have broad cellular implications. Further promising cellular targets are related to angiogenesis, apoptosis and cancer stem cells properties. To inhibit angiogenesis by targeting VEGF for example has been demonstrated by means of antisense-mRNA in vitro for HNSCC and other tumor cell lines.

**Gene Therapy**

The introduction of therapeutic genes is a promising approach for cancer therapy. Unlike approaches mentioned above it is also possible to restore loss of function mutations for example by reintroducing the respective wild-type gene. Another form of gene therapy is to introduce DNA that encodes a therapeutic protein drug or a prodrug acting in combination with a substrate applied systemically (Gene-Directed Enzyme Prodrug Therapy).

The delivery through intratumoral injection of therapeutic genes coded by viral and nonviral vectors are currently applied in gene therapy approaches. Viral vectors have been shown to be efficient in transducing tumor cells, however, certain problems concerning toxicity and safety, e.g. mutagenesis and unexpected immune responses have still to be solved. In comparison to viral gene delivery safety is improved for nonviral gene delivery, but this requires physical methods like electroporation or ultrasonography for transfection which are rather inefficient and may cause tissue damage. A new method for target gene transfection is optical transfection and in particular laser-mediated gene transfection. In a recent study targeted gene transfer by using laser-induced stress waves was demonstrated for...
HNSCC cells, which might be an example for nonviral gene therapy in HNSCC in future.

An interesting variant of gene therapy is Gene-Directed Enzyme Prodrug Therapy. Here, a systemically applied substrate is converted to a cytotoxic product by an enzyme, which is selectively introduced an expressed by tumor cells by means of gene therapy. The limitation of this approach is, that by disruption of the transfected tumor cell the information for this targeted killing is also lost and thus for efficient tumor killing almost 100% of tumor cells have to be transfected, which may hardly be achieved. For high grade tumors a novel gene-based product (Cerepro®) is already applied, in addition to standard surgery and radio-/chemotherapy. By adenoviral transfection a thymidine kinase is delivered and expressed into the surrounding healthy brain tissue left following surgery, and after applying the prodrug ganciclovir a substance toxic for dividing cell, is produced leaving resting cell unaffected. This toxic substance may also be produced in healthy cells and spread via gap-junctions to kill nearby tumor cell which try to divide (bystander effect). It may be possible that similar approaches also be applicable for HNSCC in future, however translation into clinical practice still requires further investigations.

**Alternatives for HPV-related HNSCC**

Limitations on the development of current prophylactic HPV vaccines demonstrates a pressing need for novel approaches are necessary to the eradication of HPV-related neoplasia and suggest that the development of therapeutic vaccines, even if prophylactic vaccine programs might be successful in the future. The HPV-encoded early proteins, the E6 and E7 oncoproteins, form ideal targets for therapeutic HPV vaccines, since they are consistently expressed in HPV-associated cancers.

### Table 2: Current clinical trials including Cetuximab (selection)

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Study design</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eribulin Mesylate and Cetuximab</td>
<td>Dose finding study</td>
<td>Dose escalation of eribulin mesylate a fully synthetic ketone analogue a potent mitotic inhibitor inducing apoptosis</td>
</tr>
<tr>
<td>Erbitux or Cisplatin</td>
<td>Pharmacogenetics for selection</td>
<td>Genotyping of three genes involved in DNA nucleotide excision repair (ERCC1, ERCC2, and XRCC1) - Patients with 3 to 8 variants will receive cisplatin. Patients with 2 or fewer variants receive cetuximab.</td>
</tr>
<tr>
<td>E7050 and Cetuximab</td>
<td>Phase Ib/II Study</td>
<td>E7050 (Met kinase inhibitor) given orally at 200, 300, or 400 mg once daily</td>
</tr>
<tr>
<td>BYL719 and Cetuximab</td>
<td>Phase Ib/II Study</td>
<td>BYL719: oral alpha-specific PI3K inhibitor</td>
</tr>
<tr>
<td>Cetuximab and Tregs Depletion</td>
<td>feasibility study</td>
<td>Potentiation of Cetuximab by Tregs Depletion With Metronomic Cyclophosphamide is examined</td>
</tr>
<tr>
<td>Biomarkers and Cetuximab</td>
<td>observational</td>
<td>PTEN determination by gene expression, microarrays and other markers to predict the outcome</td>
</tr>
</tbody>
</table>

### Table 3: Clinical vaccination trials targeting HPV induced lesions

<table>
<thead>
<tr>
<th>Target</th>
<th>Vector</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>L1, E7</td>
<td>Recombinant fusion proteins assembled into Virus-like particles (VLP) Hsp (SGN-00101) a fusion protein consisting of a heat shock protein (Hsp) from Mycobacterium bovis and HPV16</td>
<td>28</td>
</tr>
<tr>
<td>E7</td>
<td>E7</td>
<td>29</td>
</tr>
<tr>
<td>E6, E7</td>
<td>(TA-HPV) a recombinant vaccinia virus expressing modified human papillomavirus (HPV)-16 and HPV-18 E6 and E7 genes</td>
<td>30</td>
</tr>
<tr>
<td>E6, E7</td>
<td>Cocktailed synthetic peptide</td>
<td>31</td>
</tr>
<tr>
<td>E7</td>
<td>Recombinant Listeria Monocytogenes(Lm)Based Vaccine Virus</td>
<td>NCT01598792</td>
</tr>
<tr>
<td>p16</td>
<td>Immunization With a p16INK4a Peptide Combined With MONTANIDE ISA-51 VG</td>
<td>NCT01462838</td>
</tr>
</tbody>
</table>
Therapeutic HPV vaccines for HPV-related HNSCC might include live vector-based, peptide or protein-based, nucleic acid-based, and cell-based vaccines targeting the HPV E6 and/or E7 antigens. The approach of immunization with E6 and/or E7 of HPV 16 and 18 predominantly, and the generation of antigen-specific cytotoxic lymphocytes for HPV associated cancer has been tested with a wide array of potential vaccine delivery systems (Table 3).

To date, definitive clinical efficacy and appropriate immunological responses have never been demonstrated for cancers, although promising results have been reported in patients with vulvar intraepithelial neoplasia. Some of the tested therapeutic vaccines elicited systemic cellular immunity after intramuscular or subcutaneous injection, but none of the trials have assessed local cellular immune responses to vaccine antigen. Vaccination strategies involving intramuscular or subcutaneous injection of E6/E7-based antigens might be more promising in the future. One innovative approach is a DNA vaccine that is administered into the dermis by means of gene gun to deliver DNA directly into dendritic cells for priming antigen-specific T cells in mice. Further promising future targets in HPV-related HNSCC consist of gene silencing with siRNA targeting E6/E7, that has been applied in cell lines and targeting the PI3K-PTEN-AKT signaling pathway since HPV-related HNSCC show extra copies of chromosome 3q in up to two-thirds of cases, including the 3q26 gene locus, harbouring the PI3K gene.

Future outlook

A plethora of new biological agents will be developed in the near future. The focus of research in HNSCC will be on inhibitors that are capable of hitting multiple targets. An alternative approach is to combine different substances to overcome resistant tumor cells that frequently escape any therapeutic effect. Third, patient selection with the help of novel biomarkers will be crucial for a more reliable prediction of any therapy response. One problem of current phase II trials is the selection of patients with recurrent cancers. These patients have tumor cells that are more likely to harbor multifactor resistance and are unlikely to respond to new agents. Translational research in the future will also depend on the availability of tumor biopsies before and after treatment. New imaging modalities will be used in future to monitor anti-angiogenic agents. There is a need for better tumor modelling (cell lines, animal models, ex-vivo cultures) to understand target inhibition in humans. Chip technology decoding the transcriptome and epigenome as well as large-scale study of metabolic and signaling pathways of head and neck cancer cells by means of proteomics will certainly lead to the identification of novel candidate targets. HPV related cancers are promising candidates for the future development of successful targeted therapy.

Conclusion

Presently targeted therapy is being used as an adjuvant therapy in the treatment of head and neck cancer alongside classical treatments, and continued research in this field will result in the future being one of the mainstay treatment. The translation of in-vitro findings to patient management is a major challenge. HPV-related cancers might be used as a prototype since less frequent DNA mutations are present where viral oncoproteins could be the ideal targets. The combination of multiple targets and improved patient selection with the use of novel biomarkers to predict efficacy will be crucial in advancement of effective targeted therapies the future.

References:

Advances in the surgical management of hyperparathyroidism

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Abstract
Due to advances in clinical laboratory science, radiographic techniques and medical technology, the management of parathyroid diseases has changed dramatically over the last two decades. The development of focused, minimal invasive parathyroidectomy techniques has allowed patients with hyperparathyroidism to have their disease addressed safely and effectively, while enjoying a number of the benefits of minimally invasive surgery including less pain, reduced dissection, fewer or no drains, ambulatory care, faster recovery and smaller, more cosmetically pleasing scars.

Key words
Minimally invasive parathyroid surgery, parathyroidectomy, hyperparathyroidism.


Introduction
Due to advances in clinical laboratory science, radiographic techniques and medical technology, the management of parathyroid diseases has changed dramatically over the last two decades. The development of focused, minimal invasive parathyroidectomy techniques has allowed patients with hyperparathyroidism to have their disease addressed safely and effectively, while enjoying a number of the benefits of minimally invasive surgery including less pain, reduced dissection, fewer or no drains, ambulatory care, faster recovery and smaller, more cosmetically pleasing scars.¹² When first introduced, there was widespread skepticism regarding the application of minimally invasive techniques in parathyroid surgery. However, the safety and benefits of these techniques have become increasingly apparent and have therefore led to the rapid expansion of their use.

Rationale
The previous traditional approach to the surgical management of patients with primary hyperparathyroidism is bilateral neck surgery with four-gland exploration.³ This is effective for the treatment of both adenomatous and hyperplastic pathology. In the setting of a single or possible double adenoma, one or two glands could be excised. In the case of hyperplastic disease, either a subtotal or total parathyroidectomy with re-implantation of a portion of one gland can be performed. Four-gland exploration remains the appropriate procedure for patients with suspected hyperplasia (including those with renal hyperparathyroidism, multiple endocrine neoplasia or other syndromic hyperparathyroidism).

While bilateral exploration performed by an experienced surgeon has an excellent cure rate, in the vast majority of patients with primary hyperparathyroidism a single adenomatous gland is the cause of the hypercalcemia. Only, approximately 15% of primary hyperparathyroidism is due to multi-glandular pathology (multiple adenomas or 4-gland hyperplasia). (See Figure 1) In patients with single gland disease dissecting and excising only the one gland, results in sharply reduced tissue trauma and risk of potential complications compared with bilateral exploration.⁴ This is the rationale for focused, or minimally invasive, parathyroidectomy.

Figure 1: The important structures in the lateral thyroid region in a patient with multi-gland hyperplasia. Reprinted with permission Randolph G. Surgery of the thyroid and parathyroid glands. Second ed. Philadelphia: Saunders; 2013.
Technology
Several technological advances, starting with the introduction of localizing radiologic studies in the 1970s, have allowed for the development of focused parathyroidectomy. With the current radiologic techniques, most adenomas can be localized prior to surgery and targeted for removal.

Radionuclide imaging of the parathyroid glands was introduced in the late 1970s. Until the early 1990s radionuclide imaging utilized two imaging agents, which had different uptake characteristics by the thyroid and parathyroid glands. Subtracting the uptake of one agent from the other provided imaging of the hyperfunctional parathyroid tissue. In 1992, however, Taillefer and colleagues described the use of Technetium-99m sestamibi (99mTc-sestamibi) as a single agent in a dual-phase technique. Both thyroid and parathyroid tissue take up 99mTc-sestamibi. However, hyperfunctional parathyroid tissue retains 99mTc-sestamibi for longer than normal thyroid or parathyroid glands. Two images are taken, the first 10 to 15 minutes after injection of the 99mTc-sestamibi and the second 1.5 to 3 hours after the first. Taking advantage of the differential washout rates, the first

Figure 2: Results of a dual-phase 99mTc-sestamibi is shown. An apparent right inferior parathyroid adenoma is prominently seen in the delayed image on the right.

Figure 3: Combined SPECT/CT imaging can provide precise 3D localization of parathyroid adenomas. A right inferior adenoma is shown.
image is subtracted from the second. This highlights the prolonged uptake by the hyperfunctional parathyroid tissue. (See Figure 2) Dual-phase 99mTc-sestamibi is highly specific and sensitive for identification of single gland adenomas (90 percent or better). Cases of double adenomas and ectopically located glands are also effectively assessed by 99mTc-sestamibi imaging. Four gland hyperplasia is less accurately identified by this imaging technique. By combining 99mTc-sestamibi imaging with single-photon emission computed tomography (SPECT) greater 3-dimensional localization can be achieved. (See Figure 3)

High resolution ultrasonography (US) aids in localizing parathyroid adenomas in primary hyperparathyroidism. When used by an experienced operator, US has a high sensitivity and specificity for diagnosis of adenomas. (See Figure 4) It can be particularly useful in patients with concurrent thyroid nodules or possible intrathyroidal parathyroid adenomas. The anatomical details provided by US complement the physiologic findings seen on radionuclide imaging. Typically adenomas are identified as uniform hypoechoic ovoid to teardrop shaped lesions in typical locations with a clear single arterial blood supply often demonstrable on Doppler.

Inexpensive, high-resolution ultrasound, which does not use ionizing radiation, can be easily repeated by physicians in their offices. The quality and ease of use of current US machines has also spawned surgeon performed scans, putting imaging of the anatomy directly into the hands of the surgeons.

The other critical innovation, which has allowed focused parathyroidectomy to thrive, was the introduction of intra-operative parathyroid hormone (IOPTH) assays, which allow for the rapid assessment of surgical completeness and cure. Numerous algorithms for IOPTH use have been reported. While the exact protocol for the use of IOPTH assays remains debated, there is general consensus that their use reduces the need for unnecessary and time-consuming neck exploration. The utility of IOPTH may be more limited in cases of patients with positive and concordant ultrasonographic and sestamibi scan findings.

Benefits
A number of different focused parathyroidectomy techniques have emerged. While these techniques differ in their technical details they all are directed at dissecting and removing the pathologic gland only. The performance of focused parathyroidectomy allows patients to be treated as effectively as with bilateral exploration (over 90% cure rate) while realizing the benefits of a minimally invasive approach including less pain, faster recovery times, ambulatory care and smaller scars. But focused parathyroidectomy is also safer than classical parathyroidectomy. As focused parathyroid surgery limits the amount of dissection performed, the risk of injury to the laryngeal nerve is less than in conventional parathyroidectomy and the rate of both transient and permanent hypocalcemia is also reduced.

Embryology & Anatomy
Knowledge of the embryologic development and resulting anatomic positioning of the parathyroid glands is essential in managing patients with parathyroid disease. The inferior parathyroid glands and thymus gland originate from the third branchial pouches and arches respectively. By descending in concert with the thymus gland, these parathyroid glands move caudally in the neck to a position inferior to the pair of glands derived from the fourth pharyngeal pouches. Thus, the superior parathyroid glands are fourth pouch derivatives, while the inferior glands are from the third pouches.

Several embryologic factors can make localization of the parathyroid glands challenging. The superior pair of glands typically remains intimately associated with the posterolateral aspect of the mid to superior segment of the thyroid gland. The inferior parathyroid glands most often are located near the inferior poles of the thyroid. The lengthy migration of the inferior parathyroid glands during embryologic development is associated with a higher risk of aberrantly located glands. Ectopic glands, present in 15 to 20 percent of patients, can be located at any position along their developmental course of descent. The inferior glands when ectopic may retain a relationship with the thymus with which they are embryological related. Glands have been identified from the angle of the mandible to the level of the aortic arch. Ectopic positioning of the superior glands is less...
common as they have a more limited migratory course. Due to their embryologic co-development, intrathyroidal and intrathymic positioning should always be considered when confronted with ectopic parathyroid glands.

A second embryologic confounder of parathyroid localization is the significant incidence of supernumerary glands. Approximately 2 to 5 percent of patients have five or more glands. A similar percentage of patients have been reported to have fewer than four glands.

Typically, the inferior thyroid artery supplies both the superior and inferior parathyroid glands. Alternatively, an anastomotic branch between the inferior and superior thyroid arteries may supply the superior glands. In a coronal plane, the superior glands generally are more posterior than the inferior glands. Consequently, the superior glands tend to be deep to the recurrent laryngeal nerve (RLN), while the inferior glands are superficial to the nerve. (See Figure 5)

**Techniques**

Although dissection is limited to just the presumed pathologic gland, the techniques typically employed for conventional parathyroid surgery are used to perform focused parathyroidectomy. There are a number of focused parathyroidectomy techniques that are both minimal incision and minimally invasive. Minimally invasive non-endoscopic parathyroidectomy (MINEP), the lateral approach, radioguided parathyroidectomy and minimally invasive video-assisted parathyroidectomy (MIVAP) are briefly discussed.

**Pre-operative**

Prior to surgery, appropriate localizing studies should be performed. Many surgeons obtain 2 studies, often sestamibi and ultrasound scans. The combination of these modalities improves the overall sensitivity compared with either technique alone.

The value of pre-operative assessment of laryngeal function before thyroid surgery has become widely recognized. While for parathyroid surgery this is not as widely accepted, we advise pre-operative evaluation, accomplished with either indirect mirror laryngoscopy or fiberoptic laryngoscopy, in all patients undergoing parathyroid surgery in accordance with the recently published American Academy of Otolaryngology guidelines for this optimization at the time of thyroidectomy.

While not performed in many institutions, post-operative assessment we feel is essential for optimal modern neural outcome postsurgical determination.

**MINEP**

MINEP utilizes a small incision and limits dissection in the quadrant of the neck in which the suspected gland has been localized. Incisions can be made as small as 2.5 cm. No subplatysmal flaps are elevated. The midline raphe of the strap muscles is divided and attention is turned to the quadrant of the expected pathologic gland. The thyroid gland is retracted medially and the strap muscles laterally. After the abnormal gland is identified it is skeletonized and the pedicle is isolated and divided. Following excision of the gland, intraoperative PTH levels are obtained to confirm biochemical cure. Some feel post resection IOPTH testing is not necessary if the patient presents with positive and concordant ultrasonographic and sestamibi scanning.

**Lateral Approach**

The lateral approach, accesses the pathologic gland in a manner that limits the amount of dissection of the strap muscles and thyroid gland that is necessary. Additionally, many authors argue that there is improved healing of laterally placed cervical incisions compared to those centrally placed. Finally, coming from a lateral orientation,
posteriorly located adenomas may be more easily accessed\textsuperscript{18}.

The incision is placed directly over the medial border of the sternocleidomastoid (SCM) muscle. The sub-platysmal plane can be developed with blunt dissection. After the medial margin of the SCM is exposed together with the lateral border of the strap muscles, the SCM is retracted laterally. The space lateral and deep to the strap muscles is developed revealing the lateral border of the thyroid gland. This is then retracted medially. At this point the structures deep to the thyroid gland, including the recurrent laryngeal nerve and the parathyroid glands, are visualized. At this point the adenoma can be identified and excised with the nerve often in view.

**Minimally Invasive Radioguided Parathyroidectomy**

In some centers, radioguidance is used for parathyroidectomy\textsuperscript{19}. This technique requires the administration of technetium-99m sestamibi pre-operatively. Localization studies are utilized for guidance to the approximate position of the adenoma. Prior to making the incision, a baseline assessment of background radioactivity is measured by placing a gamma probe over the thyroid isthmus. After a small incision is made in the midline of the neck, a gamma probe is inserted into the wound and is used to direct dissection towards the adenoma. Glands identified by the surgeon can then be assessed in vivo for radioactivity over the baseline count. If appearing to be consistent with a diseased gland, the vascular pedicle can be divided and the specimen is excised. Ex vivo counts of the excised gland are taken with the tissue balanced on the tip of the probe to ensure no background radioactivity is picked up from the patient. (See Figure 6) Counts greater than 20\% over background are thought to represent pathologic parathyroid tissue, and confirm the presence of parathyroid tissue within the specimen\textsuperscript{20}. Intraoperative PTH levels are also often used in these cases.

**MIVAP**

In contrast to radio-guided surgery or the lateral approach, which provide limited exposure of the cervical anatomy, MIVAP is performed with excellent visualization of the neck structures, and utilizes an anatomical orientation and approach that is similar to classical parathyroidectomy\textsuperscript{21}. Therefore, the learning curve for surgeons familiar with traditional parathyroidectomy and endoscopic surgery is minimized.

In the operating room the operating table is rotated 180\°. The surgeon stands at the patient’s right side with one assistant across the table and a second assistant positioned at the head of the patient. Monitors for the endoscopic portion of the case are placed accordingly\textsuperscript{22}.

The incision, as small as 1.5 centimeter, is made, and carried through the subcutaneous tissues. No subplatysmal flaps are elevated. The strap muscles are separated in the

**Figure 6:** In radioguided parathyroidectomy, after the presumed adenoma is excised, radioactivity counts in the gland are measured. Counts 20\% percent over background levels are thought to represent pathologic parathyroid tissue.

**Figure 7:** The view of a left sided parathyroid adenoma is seen during MIVAP. The thyroid gland is retracted to the left and the strap muscles to the right.
midline from the sternal notch to thyroid notch, and are bluntly elevated off of the thyroid gland ipsilateral to the adenoma and retracted laterally. A 5-mm 30˚ laparoscope is introduced into the wound and held by the first assistant. Using the endoscopic view, blunt dissection allows identification and mobilization of the adenoma. (See Figure 7) The vascular pedicle (usually comprised of a single vessel) is ligated with either vascular clips or monopolar cautery.

Conclusion
For many patients with hyperparathyroidism, focused parathyroid surgery is an ideal option. The excellent results and manifold benefits provided by the different focused approaches have led to their widespread adoption.

References:
When compared to ligation and electrocoagulation the use of the Harmonic Focus® led to additional superior clinical outcomes such as:

- lower mean post-operative pain rating\(^1\)\(^2\)
- reduced post-operative blood loss and volume of drainage fluid\(^1\)\(^2\)
- smaller number of ligatures\(^2\)
- lower rate of transient hypocalcemia\(^1\)

The Harmonic Focus® was also associated with a significant reduction in operating time in each analysis when compared to LigaSure Precise™, Harmonic ACE® and Clamp-and-tie technique\(^1\)\(^4\)

References:

LigaSure™ is a trademark of Covidien.
Retrosternal goitre: contemporary challenges and controversies

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Abstract
Retrosternal goitre (RSG) presents many challenges to the surgeon and its true incidence is dependant on the definition used. A detailed clinical evaluation will identify symptomatic disease due to regional compressive effects in the majority of patients. Slow, progressive growth is the typical course and the incidence of malignancy does not appear to be increased relative to cervical goitre. Newly proposed classification systems better define the extent and anatomy of the retrosternal component. Treatment is generally surgical and evaluation of goitre depth and shape by computed tomography scanning can identify which patients are likely to require an extracervical approach. Goitre descent relative to the aortic arch is a key radiological feature. Meticulous operative technique with optimal exposure and early identification of parathyroid glands and recurrent laryngeal nerves can improve surgical outcomes. Tracheomalacia in RSG is a rare occurrence.

Key words
retrosternal; substernal; goitre; thyroidectomy.


Introduction
Retrosternal goitre (from Latin guttur, throat) was first described by Haller1 in 1749 and it was not until 1820 that Klein accomplished its first successful removal2. Currently it comprises between 2-19% of all thyroidectomies performed3. Proposed causative factors include negative intrathoracic pressure generated from respiration, traction related to deglutition, gravitational forces from the enlarged gland, and anatomical structures (vertebral bodies, strap muscles, thyroid cartilage) encumbering its growth in other directions4. This review will describe current controversies pertaining to RSG definition, surgical candidacy and morbidity as well as highlight the challenges involved in the operative approach and technique.

Clinical Evaluation
The presentation of RSG may be as an incidental finding on chest x-ray or cross sectional imaging, or as an asymptomatic or symptomatic extension of a cervical goitre. Symptomatic presentation will relate to regional compressive effects and/or altered gland function. The former may include dyspnoea, dysphagia, dysphonia and presence of globus (perception of lump). Dysphonia is quite commonly volunteered by the patient (up to 21%4) and is most often unrelated to any nerve paralysis. Positional variability of symptoms is a key feature, which are frequently reported as being induced or exacerbated in association with extreme neck extension or flexion, with raised arms, or when supine. Accordingly, nocturnal symptoms should be inquired upon, both from patient and partner. Less common, features of superior vena cava compression or Horner’s syndrome secondary to sympathetic chain compression may occur. Hyperthyroidism (10-20% of patients) may be provoked by radiological contrast medium or iodine containing medication such as amiodarone.

The airway compromise in RSG is sometimes misdiagnosed as chronic asthma or chronic obstructive pulmonary disease5. Flow volume loop studies, whilst superfluous and lacking sensitivity in the workup of most thyroid lesions6, may assist in this scenario by discriminating between fixed large calibre upper airway obstruction (blunted inspiratory and expiratory loop) and small calibre distal airway obstruction (predominantly expiratory loop deficit).

On physical examination a suspicion of RSG is determined by the inability to identify the lower edge of a thyroid mass. Important clinical features in the assessment of a patient should include a history of previous thyroid surgery, venous distension on the anterior chest wall or neck, and signs of airway compromise. In 20-30% of cases, palpation of the neck reveals little or no evidence of a cervical goitre7. Pemberton’s sign seeks to provoke obstructive features by forcing the thyroid into the thoracic inlet and is positive when the patient, on holding their arms up vertically for 60 seconds, develops dilated neck veins, facial plethora, cyanosis, dyspnoea or stridor.
Asymptomatic Retrosternal Goitres

Escalating diagnostic imaging of the neck and chest has led to increased detection of incidental RSG. Management of the patient with asymptomatic RSG remains contentious with many adhering to a strict recommendation for surgery. Hardy cautions that many patients labelled as ‘asymptomatic’ actually elicit symptoms on direct questioning that do improve following surgery. Serpell similarly determined a low 16.6% rate of truly asymptomatic RSG. Furthermore, there appears to be a poor association between radiological findings and symptoms. Deferring surgery until the emergence of symptoms risks catastrophic acute airway complications from haemorrhage or acute laryngeal oedema secondary to pressure effects in up to 5-11% of patients.

An increased potential for malignancy has been heavily touted to dictate surgical intervention for RSG. However, this was not borne out in the excellent evidence based review by White that revealed equivalent malignancy rates to cervical goitres. Rios demonstrated a protective effect of RSG compared to cervical goitre - 5.7% vs 10.7% malignancy - the majority were papillary microcarcinomas (62%) of debatable biological significance. Likewise, Serpell found a low (2.5%) incidence of malignancy. Risk factors for malignancy in RSG include a family history of thyroid cancer, history of neck irradiation and recurrent goitre. Balasubramanian highlights that RSG is not a biologically distinct entity from cervical goitre but merely a variant on account of its anatomy thus portending not a biologically distinct entity from cervical goitre but merely a variant on account of its anatomy thus portending no increased risk of malignancy. Definitive exclusion of malignancy is often problematic as a consequence of the inaccessibility of a RSG to ultrasound (secondary to skeletal artefact) and fine needle biopsy.

The natural history of RSG is typified by slow, progressive growth after presentation in the 5th or 6th decade of life. Volume increases of up to 10-20% per year can be expected and have been used to justify a recommendation for surgery. Surgical candidacy is strengthened by a history of rapid goitre growth, large goitres (>5cm) causing cosmetic concerns, tracheal compression on computed tomography (CT) scan and evidence of hyperthyroidism, which may be subclinical. The lack of efficacious alternative treatments for RSG enhance the argument towards early surgical intervention. Thyroxine suppression therapy is generally ineffective in large nodular goitres. Radioactive iodine therapy may have a role in patients with surgical contraindications, producing a modest reduction in goitre volume (up to 30% reduction in both cervical and mediastinal components). Recent evidence suggests an enhanced response utilizing a recombinant human thyrotropin (rhTSH) pre stimulation protocol.

Definitions of RSG

Various terms for RSG are utilized in the literature including substernal goitre, goitre plongeant (French, plunging), intrathoracic goitre and wandering goitre. Inconsistent definitions have hampered accurate scientific appraisal and consequently published rates of RSG vary between 0.2% and 45% of all goitres encountered. The least restrictive definition, verifiable clinically, is when examination of the non-hyperextended neck has a portion of goitre that remains permanently retrosternal. The definition promulgated by de Souza and Smith - at least 50% of the goitre to be retrosternal - has been most widely adopted in the literature.

RSG can be broadly categorized into the rare primary intrathoracic goitre, which denotes absence of connection to a cervical goitre, or the more prevalent secondary RSG, where a cervical goitre extends into the mediastinum.

Subsequent classification systems have endeavoured to anatomically segregate RSG to better inform surgical management decisions. Huins proposed that referencing goitre descent to an intrathoracic landmark such as the aortic arch is not only easily established radiologically but determines the surgical approach. In his scheme, grade 1 includes goitres above the upper border of the aortic arch and requires a cervical approach; grade 2 represents goitres from aortic arch to pericardium and usually requires manubriotomy alone; grade 3 goitres extend below the right atrium and demand full sternotomy.

The classification system recently proffered by Randolph incorporates goitre compartment, trajectory and anatomical relations. Type 1, accounting for 85% of RSG, extends into the anterior mediastinum, anterior to the great vessels, trachea and recurrent laryngeal nerves (RLNs). These are more common on the left side due to more posterior positioning of the arch at this site. Type 2 RSG extends into the posterior mediastinum, thereby placing the RLN in a precarious position draped on its anterior aspect. These goitres may be purely ipsilateral (2A) or possess contralateral extensions (‘crossover glands’ – 2B) that often require thoracotomy. Type 3 RSG are the rare isolated mediastinal goitres (primary intrathoracic, ectopic or aberrant mediastinal goitre), comprising 0.2-1% of all RSGs, lacking connection to the thyroid gland in the neck. Their vascular supply is solely mediastinal in origin, directly from aorta, internal mammary vessels, thyrocervical or brachiocephalic trunks.

CT Prediction of the Need for Extracervical Approach at Thyroidectomy

Thyroidectomy for retrosternal goitre via a cervicotomy is achievable in up to 98% of cases, although in rare cases...
an extracervical approach may be required (manubriotomy, median sternotomy, posterolateral thoracotomy). Planning of such cases is crucial and may require preoperative liaison with thoracic surgeons, specialist equipment and the possible need for high dependency unit care. Delivering informed consent to patients requiring extracervical approaches is clearly essential. CT will reveal the extent of mediastinal descent and characterize goitre shape and its relationship to adjacent structures; it thus enables the surgeon to predict the likelihood of a successful thyroidectomy from a cervical approach (see Table 1).

### Table 1: Features predictive of the need for an extracervical approach

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>Factors predicting extracervical approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flati et al²³</td>
<td>2005</td>
<td>‘Iceberg-shaped’ RSG, greater than 70% of goitre in mediastinum</td>
</tr>
<tr>
<td>Randolph et al⁵</td>
<td>2013</td>
<td>Diameter of mediastinal nodule greater than thoracic inlet</td>
</tr>
<tr>
<td>Cohen²⁴</td>
<td>2009</td>
<td>Posterior extension, descent below aortic arch, malignancy, ectopic mediastinal goitre</td>
</tr>
<tr>
<td>De Perrot et al²⁵</td>
<td>2007</td>
<td>Malignancy, ectopic mediastinal goitre, revision goitre surgery</td>
</tr>
<tr>
<td>Grainger et al²⁶</td>
<td>2005</td>
<td>Descent below aortic arch</td>
</tr>
<tr>
<td>Casella et al²⁷</td>
<td>2010</td>
<td>Descent below aortic arch, goitre duration greater than 160 months</td>
</tr>
</tbody>
</table>

The aortic arch has emerged as a pivotal radiological landmark when establishing the surgical strategy. Grainger demonstrated that extension to the aortic arch singularly predicted the need for sternotomy, performed in 12% of cases in that study. The weight of the resected gland did not influence surgical approach. Interestingly, neither tracheal involvement nor major vessel displacement correlated with the need for sternotomy as stand alone features. Casella similarly distilled two factors informative of the surgical approach: goitre depth below the aortic arch and goitre duration >160 months³⁹. CT estimation of RSG size was not predictive.

**Operative Strategies**

Pre- and post-operative direct laryngoscopy is imperative. Transoral intubation is usually accomplished however an awake fibroptic transnasal technique may occasionally be required in a more compromised or deviated trachea. The patient should be draped to permit extracervical access if necessary. Positioning the patient in reverse Trendelenberg reduces venous dilatation. A generous incision should be employed from the outset. Maintenance of a bloodless operative field is pivotal to operative success.

Division of the strap muscles is not mandatory but one should not hesitate to perform this if exposure if limited; section of the cranial head of sternohyoid alone is often advantageous. The carotid sheath should be sought early as a key landmark and the gutter between it and the thyroid developed from base of skull down to the inferior extent of the gland. Early identification of the superior parathyroid glands and the RLNs is advisable prior to tackling the mediastinal dissection. The inferior parathyroid glands are often devascularised and may require autotransplantation. The inferior cornu of the thyroid cartilage is a useful landmark for RLN entry into the larynx from where it may be traced caudally. The usual anatomy of the RLN may well be distorted by the goitre, especially those tracking posteriorly into the mediastinum - the nerve, splayed anteriorly on the gland, is vulnerable.

**Surgical tips include:**

- Early mobilisation of the upper border of the isthmus and upper pole of the thyroid lobe to just above the inferior cornu of the larynx
- Division of the thyroid isthmus
- Mobilisation of the infero-medial aspect of the thyroid from the trachea
- Using an assistant’s finger to pull the cricoid cartilage in a cephalad direction

At this point gentle traction and successive upward mobilization of the thyroid will nearly always effect delivery of the mediastinal component into the neck. Rough handling manoeuvres to achieve this result in RLN neuropraxic injury. Judicious index finger sweeping in a strictly extracapsular plane facilitates extraction. In patients with bilateral disease, removal of the more normal lobe first may assist by augmenting the available working space. When there is a large dead space drains may be used to minimize seroma formation.

Studies investigating the surgical morbidity for RSG relative to cervical goitre have yielded conflicting results. A recent large Italian multicentre study looking at 1055 patients with RSG found a significantly higher overall morbidity rate associated with surgery for RSG (35% vs 23.7%)³⁵. Transient and permanent RLN paralysis, transient and permanent hypoparathyroidism and haemorrhagic complication rates were all significantly increased. Studies by Sancho³⁶ and
Pieracci similarly demonstrate increased morbidity in association with RSG surgery. Low complication rates are feasible, however, as evidenced in the study by Serpell where no cases of permanent RLN injury or permanent hypoparathyroidism were observed in a series of 199 patients. Raffaei also determined a non-significant difference in morbidity rates between RSG and cervical goitre.

**Tracheomalacia**

The question of tracheomalacia may cause considerable perturbation from both anaesthetic and surgical viewpoints. Inconsistent definitions range from a general softening and floppiness of the trachea, which may be indented by gentle digital pressure, to obvious tracheal collapse. High-grade compression for greater than 5 years appears to predispose to the tracheal ring destruction which may manifest as acute airway compromise postoperatively. Some groups report incidences of up to 10% whilst others remain sceptical of its existence (and report 0% incidence) on suspicion that previously reported cases have represented undiagnosed bilateral vocal cord palsy.

**Conclusions**

The management of RSG is surgical in the majority of cases. Evaluation of goitre descent and shape by CT allows one to determine whether a cervical or extracervical approach may be required. Appropriate preparation and operative technique facilitates surgery with improved morbidity.

**References:**

Changing practice in the management of advanced hypopharyngeal cancer

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Abstract
Squamous cell carcinoma of the hypopharynx is a unique clinical entity amongst head neck cancers as the majority of patients have an advanced stage at presentation in association with multiple co-morbidities. The survival rates associated with this group of patients are less than half that of laryngeal cancer, despite the anatomical locations being just a few millimetres apart. Carcinoma of the hypopharynx is rare, accounting for 3-5% of all head neck cancers. Approximately 360 new cases are registered annually in England. The traditional treatment for operable hypopharyngeal cancer incorporates a total laryngectomy, partial / full circumference pharyngectomy and surgical reconstruction. Of those patients who make a suitable recovery from surgery, the majority demonstrate poor pathologic parameters and undergo adjuvant radiotherapy. The option to treat advanced hypopharyngeal cancer by primary chemoradiotherapy has become increasingly popular (without a firm evidence base) following the improved survival and functional results from studies assessing advanced laryngeal cancer. The story is explained, with comments on survival and functional outcomes associated with each treatment option.

Key words
Hypopharynx; squamous cell carcinoma; treatment; functional outcome; laryngopharyngectomy; chemoradiotherapy.


Introduction
The hypopharynx is divided into three sub-sites, the pyriform fossae, postcricoid area and posterior pharyngeal wall. In common with other head and neck cancer sites, primary hypopharyngeal cancer cells arise from mucosal epithelium, the result is that more than 95% are squamous cell carcinomas (SCC). The most frequent site involved by SCC is the pyriform fossae (65-85%), with the posterior pharyngeal wall and postcricoid area making up the remaining 10-20% and 5-15% respectively. Early stage cancers classically remain asymptomatic or may masquerade as globus pharyngeus. Local advanced disease (stage III-IV) can be associated with symptoms of pain and dysphagia in 70-85% of patients1-6. In the largest epidemiological study of patients with SCC hypopharynx, ~50% of the patients presented with a metastatic neck node6. The same study reported nodal disease to be more common if the primary originated from the pyriform fossa region. Some patients may have airway narrowing with stridor, or present with acute airway obstruction, while others may present in a cachectic state due to chronic dysphagia. Five-year survival is reported in the range 15-45% and the factors that contribute to this poor outcome include:

1) High rates of regional metastasis (60-80%);
2) High rates of distant metastasis (chest, liver or bone ~10-30%);
3) Extensive submucosal spread of tumour not detected by the surgical team (histological studies suggest this can range from 10-20mm at the superior margin and up to 30 mm for the inferior margin)7,8.

Search Strategy:
A systematic literature search was conducted of MEDLINE (1966 to August 2013), CINAHL, EMBASE, Cochrane Central Register of Clinical Trials, clinicaltrials.gov, and Google Scholar without language restriction for studies including combined key terms and exploded Medical Subject Headings of the terms: [hypopharynx] AND [squamous cell carcinoma] OR [treatment] OR [functional outcome] OR [laryngopharyngectomy] OR [chemoradiotherapy]. The retrieved articles also had their references scanned for any additional information that may have been missed. Institutional review board approval was not necessary because all data were retrieved from previous published sources.
Current treatment choices:
As noted previously, up to 85% of patients present at an advanced stage of disease which contributes significantly to the high rate of non-operative / palliative management (~25%). In the recent past, non-operative interventions were usually reserved for patients presenting with distant metastases, or when extensive local or cervical nodal disease involved the carotid artery +/- pre-vertebral fascia. Local recurrence rates following surgery have been reported to be similar between patients who have negative histological margins and those with positive margins - highlighting the need for adjuvant radiotherapy or radiochemotherapy treatment where this may be possible. There exist two surgical options for the treatment of advanced hypopharyngeal cancer: total laryngo-pharyngectomy or partial laryngectomy with pharyngectomy +/- unilateral or bilateral neck dissection. This form of surgical treatment inevitably results in significant speech and swallowing disability. As a result of this concept of “radical mutilating surgery” there has developed a global trend towards organ preservation as a primary treatment (preservation of larynx and pharynx) by combining the effects of radiotherapy with chemotherapy (CRT) as has been shown the case for advanced laryngeal cancer. However, unlike laryngeal cancer, there is paucity of data regarding functional outcomes (especially voice and swallowing) following the non-surgical treatment of advanced hypopharyngeal cancers. It is important to understand that organ preservation and function of an organ do not necessarily go hand in hand.9 Current treatment options available for advanced hypopharyngeal cancer include CRT alone with the option of surgical salvage in primary operable disease, primary surgery followed by chemoradiotherapy, or CRT alone when the primary disease is considered inoperable. In the modern head and neck cancer treatment environment, the decision making pathway for each patient should be conducted through a multidisciplinary clinical and supportive team.

Primary surgery:
The scope of surgical excision is to excise the tumour with microscopic clearance. As noted above, because of the extensive submucosal extension of these tumours, superior margins should be 2cm and inferior margins 3cm.

a) Total laryngectomy with partial pharyngectomy (conservation surgery):
This procedure is indicated for small tumours (T1 – T2) of the pyriform sinus and in patients with poor pulmonary function. Resection of one pyriform fossa results in a partial defect of the pharynx between the oropharynx and the cervical oesophagus and reconstruction of the pharyngeal lumen is required to maintain a functioning swallowing conduit. Since the 1970s, the pectoralis myocutaneous flap has been widely used for reconstruction of such defects as an on-lay patch pharyngoplasty technique, especially for severely malnourished and elderly patients (short anaesthetic and speedy surgery)10,11. The use of a free-tissue transfer flaps are generally not indicated for this defect, as the functional results reported with either technique are similar12.

b) Total Laryngo-pharyngectomy:
This procedure is indicated for the treatment of defects involving more than two thirds of the circumference of the hypopharynx. Such defects are likely to result after excision of large tumours located in the postericoid region and the posterior pharyngeal wall. It is also indicated for tumours that extend into the cervical oesophagus, in which case, a pharyngo-laryno-oesophagectomy is likely to be necessary for complete excision. Reconstruction is most commonly in the form of gastric pull-up procedure, which has the advantage of resulting in a single enteral Anastomosis, which is located in the neck. In the majority of such cases, post-operative radiotherapy is required. Reported five-year survival rates range between 40 – 50%.

Flap reconstructive options:
The ideal outcome for any reconstructive procedure should incorporate low patient functional morbidity and a low operative mortality, a low resultant post-operative fistula and stricture rate, as well as a rapid restoration of “normal” swallowing and speech function (Table 1).

1) Pedicled myocutaneous flaps (e.g. pectoralis major, latissimus dorsi):
These flaps are not indicated for circumferential hypopharyngeal defects as the pharyngocutaneous fistula and stricture rate are higher than those obtained by the use of a free-tissue transfer flaps12.

2) Fasciocutaneous free flaps (e.g. radial forearm or anterolateral thig):
These flaps are increasingly used to replace the previously popular use of intestinal flaps (e.g. jejunum, or colon) as they have higher surgical reliability and are less technically challenging. The functional outcomes, mainly swallowing, are also reported to be better when compared to the use of the free jejunal flap. Clark et al13 published a retrospective review of 65 patients undergoing free flap reconstruction for circumferential pharyngectomies (the majority of which were jejunal free flaps which had undergone radiotherapy), they reported a 15% pharyngeal stricture and 16% permanent gastrostomy rate. Surgical voice restoration employing the tracheoesophageal puncture technique was only achieved in 44% of patients13.
3) Gastric pull-up:
This reconstruction technique is reserved for circumferential defects that extend to involve the oesophagus or go below the manubrium. The advantage of this surgical technique is that there is only one enteral anastomosis, thus there is decreased risk of post-operative mediastinitis and carotid blowout associated with a fistula. However, a higher mortality has been associated with the gastric pull-up technique (now reduced significantly with the advent of laparoscopic surgery)\textsuperscript{14}.

Management of the neck:
A high rate of occult lymph node neck metastasis (~20%) can be associated with hypopharyngeal malignancy. Primary drainage is to levels II – IV, VI and the paratracheal / retropharyngeal nodes\textsuperscript{21}. Various studies have shown that nodal metastasis to levels I and IIb have very low incidence, hence dissection of levels II-IV with preservation of level IIb may be justified in patients with no evidence (palpable or imaged) of cervical lymphadenopathy\textsuperscript{22}. In patients with clinically positive nodal status, modified radical neck dissection with preservation of the internal jugular vein, or accessory nerve should be the goal, with radical neck dissection being less often necessary\textsuperscript{23}. Surgery is reserved as the best option for patients with N3 disease (>6cm diameter) due to the limited efficacy of radiotherapy in this scenario.

Radiotherapy:
The use of conventional radiotherapy for hypopharyngeal cancer requires a higher dose of radiation than intensity modulated radiotherapy (IMRT) as the target/tumour volume is higher/larger. This higher dose results in higher likelihood of fibrosis and resultant stricture formation of the pharyngeal constrictors and upper oesophageal sphincter\textsuperscript{24}. Intensity modulated radiotherapy is postulated to reduce this effect on muscular structures and thus preserve function but so far this benefit has not been demonstrated in the paucity of studies produced\textsuperscript{9}. Hypopharyngeal carcinoma requires a larger delivery dose of radiation compared to other subsites within the head and neck which may support the utility of surgical resection with radiotherapy reserved as adjuvant treatment.

Two studies available in the literature, which compare survival for advanced stage hypopharyngeal cancers, have demonstrated that primary surgery followed by radiotherapy is superior to radiotherapy followed by salvage surgery\textsuperscript{25, 26}.

Induction chemotherapy (ICT):
The first landmark study to report on larynx preservation strategy, was published in 1994 by the Department of Veterans Affairs Laryngeal Cancer Study Group. Patients with stage III-IV laryngeal cancer were randomly assigned to receive two cycles of induction chemotherapy (cisplatin and 5-fluorouracil). Responders to this initial treatment proceeded to a third cycle of induction chemotherapy followed by radiotherapy. Non-responders were offered total laryngectomy. Two-year survival rates between the two arms were similar (~68%) with two thirds of the patients successfully preserving their larynx. The group that was treated by chemoradiotherapy had more local recurrences and the surgically treated group of patients had more distant metastases\textsuperscript{25}. As there were no patients with primary hypopharyngeal carcinoma included in this study, the results may not be an appropriate substitute to guide non-surgical intervention in this review.

A study conducted by the European Organization for Research and Treatment of Cancer (EORTC), one of the

<table>
<thead>
<tr>
<th>Reconstruction method</th>
<th>Study</th>
<th>Year</th>
<th>Number of patients</th>
<th>Mortality%</th>
<th>Morbidity%</th>
<th>Fistula%</th>
<th>Oral diet%</th>
<th>Speech%</th>
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<tr>
<td>Gastric pull-up</td>
<td>Triboulet et al\textsuperscript{15}</td>
<td>2001</td>
<td>127</td>
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<td>Disa et al\textsuperscript{16}</td>
<td>2003</td>
<td>90</td>
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<td>10</td>
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<td>Sarukawa et al\textsuperscript{17}</td>
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<td>201</td>
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<td>56</td>
<td>9</td>
<td>85</td>
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<td>Radial forearm free flap</td>
<td>Scharpf et al\textsuperscript{18}</td>
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<td>2005</td>
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<td>Lewin et al\textsuperscript{20}</td>
<td>2006</td>
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<td>50</td>
<td>8</td>
<td>81</td>
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few randomized phase III trials on hypopharyngeal cancer, compared the results of initial surgical against nonsurgical treatment. The first arm consisted of induction chemotherapy (cisplatin + 5-fluouracil [PF]) followed by radiotherapy and the second arm involved primary surgery with adjuvant radiotherapy. The disease-free survival rate at 5 years was similar with 25% for the induction chemotherapy group and 27% for the surgical group. No difference was found in local or regional recurrence. The organ preservation rate (with a confirmed functional larynx) was 35%26.

Concurrent chemo-radiotherapy (CCRT):
An update of 93 randomised trials and 17,346 patients demonstrated a survival and loco-regional control benefit for CCRT (utilising cisplatin +/- 5-fluorouracil) compared with radiotherapy alone for treating cancer of larynx, oropharynx and hypopharynx27.

CCRT is increasingly becoming the standard therapy for advanced stage hypopharyngeal cancer in many centres because of the comparable survival rates compared to surgical management and the fact that the organ is preserved. Studies which assess percutaneous gastrostomy tube (PEG), tracheostomy dependence rate and long-term toxicity are increasingly published. These studies are all retrospective reviews and as a result it is difficult to capture information about the length and severity of dysphagia, patient nutrition status, skin desquamation, haematological toxicity and associated treatment delays28. Adverse effects should be recorded by using standard terminology where grade 3 toxicity is severe, grade 4 is life threatening and grade 5 fatal29. Radiotherapy restricts the movement of the base of the tongue, the pharyngeal muscles and the opening of the upper oesophageal sphincter. This results in a residual food residue within the pharynx that can divert to the airway causing aspiration. The only way to monitor this is by videofluoroscopy. Alternatively, another indicator would be the number of aspiration pneumonia episodes.

In a recent study of 243 patients treated with CCRT, PEG dependence was 47.7% at 6 months following treatment and the median PEG duration was 9 months. Tracheostomy was required in 10.3% of the patients in this study and 4.5% were tracheostomy dependent a year after treatment9. In another study of 73 patients, 26% and 3% had grade 3 and 4 dysphagia six months after completion of treatment30. In another retrospective study of 27 patients treated with CCRT (utilising intensity modulated radiotherapy), 63% of patients developed acute grade 3 dysphagia and seven patients (26%) needed tracheostomy during or within 3 months after CCRT, and only two of them could be successfully decannulated31. Staar et al reported 51% of patients to be PEG dependent at 2 years after accelerated fractionation radiotherapy and chemotherapy32.

Table 2: Gastrostomy and tracheostomy results in hypopharyngeal carcinoma

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Number of patients</th>
<th>Gastrostomy dependence %</th>
<th>Tracheostomy dependence %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tulunay-Ugur et al9</td>
<td>2012</td>
<td>243</td>
<td>47.7*</td>
<td>4.5**</td>
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<td>Kereweer et al30</td>
<td>2012</td>
<td>73</td>
<td>26†</td>
<td>-</td>
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<tr>
<td>Liu et al31</td>
<td>2010</td>
<td>27</td>
<td>63†</td>
<td>18.5††</td>
</tr>
<tr>
<td>Staar et al32</td>
<td>2001</td>
<td>62</td>
<td>51††</td>
<td>-</td>
</tr>
</tbody>
</table>

* = Six months after completion of treatment; ** = Twelve months after completion of treatment; † = Unknown time period; †† = Twenty four months after completion of treatment;

There is paucity of evidence regarding voice and speech outcomes after CCRT. This indicates the fact that speech is considered a secondary outcome and that after organ preservation the preservation of function is taken for granted. CCRT effects on voice and speech seem to peak at 10-week post-treatment but level off at the 1-year time point. However, at the latter assessment point, most patients still perceive their voice as different from baseline33.

Conclusion:
There is increased popularity of organ preservation strategies (CCRT) in an attempt to preserve the speech and swallowing. Only recently, we are becoming aware of the fact that sparing of the organ does not necessarily mean normal function or better quality of life. It must be also remembered that the same studies, which describe larynx preservation protocols, have enrolled a mixed population of patients with laryngeal and hypopharyngeal cancer. Although these two types of tumours are very close anatomically, the natural history of the disease is very different. So results from laryngeal cancer studies should not be assumed to apply to hypopharyngeal cancer. Prospective randomized trials with pre- and post-treatment evaluation of function are required. These trials should be specific for hypopharyngeal cancer, to date no trial has been reported which has compared CCRT directly with laryngopharyngectomy.

To summarise our view, despite the progressively declining use of primary surgical resection, this modality of treatment should remain an option in select patient groups.
Patients with small tumours may be treated by conservation surgery (endoscopic laser excision or open partial laryngopharyngeal surgery) followed by postoperative radiotherapy when indicated. Patients with advanced tumours that impair laryngeal and/or pharyngeal function (vocal cord palsy or stenosing dysphagia) may also be treated by a primary laryngopharyngectomy with good results.

References:

Transoral Robotic Surgery (TORS): An overview of the literature, current national guidelines and the clinical applications in oropharyngeal surgery


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Abstract
The incidence of oropharyngeal squamous cell carcinoma (OPSCC) in Denmark and in the Western World has been on the rise during the last 30 years. Transoral robotic surgery (TORS), a novel minimally invasive method for the treatment of OPSCC show encouraging results when compared to primary chemoradiotherapy and traditional surgery. Nineteen TORS published studies were identified and reviewed. The outcomes of TORS treatment to date seem excellent, both oncologic, and patient pharyngeal function. A greater focus is required on the evaluation of the swallowing related outcomes, especially in relation to Quality of Life (QoL). To solve this a risk stratification model based on HPV status could be used as a prognostic parameter to evaluate the applicability of TORS.

Key words
TORS, Chemoradiotherapy, Human Papilloma Virus, Swallowing, Quality of Life


Introduction
The incidence of oropharyngeal squamous cell carcinoma (OPSCC) in Denmark and in the Western World has been on the rise during the last 30 years. While the laryngeal cancer incidence has remained stable in Denmark, the incidence of OPSCC has doubled some five times between 1977 to 2007, for both men and women. In Denmark (2011), a total of 471 cases were diagnosed with pharyngeal cancer according to the Danish Cancer Registry, of these, 21 had cancer of the nasopharynx, 330 of the oropharynx (mainly tonsil and posterior tongue) and 120 of the hypopharynx, indicating that OPSCC constitutes 70% of all pharyngeal cancers. Tobacco and alcohol are strong etiological risk factors in the development of OPSCC, and their effect is not only additive but also synergistic as a recent review has shown. However, one cause to account for the recent increase of OPSCC is the association with Human Papilloma Virus (HPV) a sexually transmitted disease. In 2009, HPV (type16) was recognized as a “new” etiologic factor in the development of OPSCC by the International Agency for Cancer Research. In Scandinavia, a recent study from Sweden has shown a nearly two-fold increase in the age-standardized incidence of HPV positive (+) tonsillar cancers per decade from 1970-2006, while the incidence of HPV negative (-) tonsillar cancers has decreased. They noted a significant continuous increase in the proportion of HPV + tonsillar cancers rising from 23% in 1970s to a remarkable 93% in 2006-2007. To date there has been no HPV studies performed in head and neck cancers in Denmark.

The primary treatment of OPSCC in accordance with the current Danish National Head and Neck Treatment Guidelines is primary radiotherapy (RT) and in most cases combined with chemoradiotherapy (CT). So far no trials have been reported comparing primary surgery approaching both T and N site with or without post-operative RT + CT of OPSCC versus primary radiotherapy with or without chemotherapy in terms of survival and function. During the recent decades, trans oral laser microsurgery (TLM) has been advocated as an alternative surgical approach for certain head and neck sites such as oropharyngeal cancers (tonsil and base of tongue), because it allows better visualisation, and greater manipulation of the surgical instruments.

Recently, these newer surgical techniques (TLM) have reported that there is an improvement in patient overall outcome results, especially in the large tertiary head and neck centres in the USA. In 2004 a trans oral robotic surgery (TORS) research programme using the da Vinci...
Surgical System (Intuitive Surgical, Sunnyvale, CA) was developed. In 2009, the U.S. Food and Drug Administration (FDA) approved TORS to be used as primary treatment of T1 and T2 (early stage) OPSCC (tonsil and BOT) and for T1 and T2 (early stage) laryngeal cancer. In 2007 a new radical tonsillectomy technique was described, which was tested on patients with advanced tonsillar carcinoma (Table 1). This study demonstrated that the surgeon had the ability to achieve a primary tumour free excision margins and allowed a sufficient surgical access for cancer resection resulting in acceptable early patient’s post-operative morbidity. The use of a similar TORS technique was used for BOT tumours, and similar results could were reported, similar to that as for the radical tonsillectomy.

This study sought to assess the clinical and functional outcome of TORS, as reported in the literature, by addressing the indications and putative advantages of primary treatment of OPSCC using TORS with/without CRT compared with the traditional primary CRT.

**Material and methods**

Literature search was performed using the medical database PubMed search engine addressing the following keywords: oropharyngeal squamous cell carcinoma, tonsil cancer, base of tongue cancer, human papilloma virus, laser, laser microsurgery, radiotherapy, chemotherapy, functional outcomes, oncologic outcomes, Quality of Life. Articles published in English have been included.

**Results**

As a consequence of this newly developed surgical device and techniques for OPSCC was first reported in 2004, the reported clinical outcomes following treatment using TORS are short-term, with between one and three year survival analysis as well as the reporting on the functional results. In 2011, A review of the use of TORS usage in head and neck cancers identified 45 publications, they found that TORS accounted for the largest number of publications i.e. no. =17 and its usage was in the management of OPSCC, 85% of these cases.

**Surgical advantages - TORS**

Some of the advantages of TORS are improved visualisation and accessibility, thereby avoiding complex surgical approaches (mandibulotomy) as compared to traditional open transcervical surgery. TORS allows better manoeuvrability of the surgical instruments, they being able to angle the “wrists” of the robotic arms and with computerisation technology also removes the surgical “tremor”. The TORS approach permits “en bloc resection” compared to TLM where a trans-tumour “piece meal resection” is commonly performed in the larger tumours. This technology therefore improves the likely ability to achieve complete surgical excision with negative tumour margins. This achievement of negative tumour margin surgery which is important determinant as to whether adjuvant therapy is indicated.

The da Vinci System’s ergonomic design allows surgeons to operate from a comfortable and individually adjustable

<table>
<thead>
<tr>
<th>Authors</th>
<th>Patients N</th>
<th>Tumour site (%)</th>
<th>HPV+ (%)</th>
<th>T1+T2 (%)</th>
<th>N0+N1 (%)</th>
<th>Stage 3+4 (%)</th>
<th>Post OP RT/CRT (%)</th>
<th>PEG (%) mean follow up (months=mat)</th>
<th>LR (%) mean follow up (year=mat)</th>
<th>RFS (%) mean follow up (year=mat)</th>
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<td>Tonsil 100</td>
<td>NS</td>
<td>78</td>
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<td>89</td>
<td>4</td>
<td>6 m</td>
<td>NS</td>
<td>NS</td>
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<td>45</td>
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<td>73</td>
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<td>87</td>
<td>18 RT / 56 CRT</td>
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<td>NS</td>
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<td>62</td>
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<td>80</td>
<td>NS</td>
<td>NS</td>
<td>41 RT / 20 CRT</td>
<td>17; 12 m</td>
<td>NS</td>
<td>NS</td>
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<td>73</td>
<td>63 RT</td>
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<td>3; 2 y</td>
<td>86.5; 2 y</td>
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<tr>
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<td>NS</td>
<td>74</td>
<td>53</td>
<td>100</td>
<td>57 CRT</td>
<td>2.4; 12 m</td>
<td>2; 2 y</td>
<td>NS</td>
<td>82; 2 y</td>
<td>90; 2 y</td>
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<td>NS</td>
<td>HPV+ 75</td>
<td>HS</td>
<td>93</td>
<td>HPv+18</td>
<td>100</td>
<td>NS</td>
<td>NS</td>
<td>HPv+ 14</td>
<td>HPv- 43</td>
<td>3 y</td>
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</table>
seating position at a work console some distance from the patient.

**Surgical disadvantages - TORS**

Naturally with every new technology there are several factors are apparent, such as the cost of purchasing the robot, ~ 2 million euros, along with the high service charges, the need for specialised instruments, the need for a permanent physical location for the extended equipment essentials; the console, the patient cart and videorack, as well as the expense necessary for nursing, medical and technician staff training and their accreditation. The lack of tactile feedback for the operator is reported to be an important disadvantage.

**Feasibility studies**

The first feasibility study, using a radical tonsillectomy technique with TORS based on 27 patients operated on with tonsil cancer showed an excellent access leading to a radical tumour resection with acceptable treatment morbidity (Table 1).

Another feasibility study using 45 patients and measured three factors of the surgeons ability to; 1) to expose the tumour and complete the planned surgical procedure with TORS, 2) to document the per- and post-operative complications and 3) to record the total procedural time, including the operating time. It was reported that the ability to setting up the equipment / expose the tumour and the ability to complete the planned surgery was mainly influenced by the appropriate patient selection and the experience of the surgeon. The average operating surgical time for completing a TORS radical tonsillectomy (T1-T2 tumours) was 24.5 minutes. Weinstein et al. have stated that performing a pre-operative panendoscopy was of mandatory importance and the only accurate way of selecting suitable patients to TORS.

**Survival analysis, oncologic and functional results with TORS**

Table 1 tabulates the tumour characteristics, the use postoperative adjuvant CRT, the need for percutaneous endoscopic gastrostomy (PEG) placement and the patients survival data recorded among the largest TORS studies. One study found no early local or regional recurrences among 27 patients with advanced OPSCC. Swallowing without the use of PEG, at minimum six months follow-up, was possible in (26/27) 96% of patients. Chemotherapy was not given in (12/27) 44% of the patients who had achieved a negative tumour free resection margin.

A two-year survival analysis, aimed for the first time to publish survival data based on 89 patients following TORS. Tumours were stage III or IV and mainly located in oropharynx (77/89) 87%. The overall two-year recurrence free survival rate was 86%. Among the 82 patients who underwent TORS as primary treatment (52/82) 63% underwent postsurgical radiation therapy. Eleven (13%) patients developed recurrence of their primary tumour. Regarding their functional outcomes, all patients (100%) had their PEG removed within two years.

Another study reported on 47 patients undergoing primary TORS for advanced oropharyngeal stage III and IV tumours and found local, regional and distant recurrences in one, two and four patients respectively. Overall survival rates were 96 % (45/47) at one year, and 82 % (27/33) at two years. Disease-specific survival was 98 % (45/46) at one year, and 90 % (27/30) at two years. The high rate of negative surgical margins 98 % (46/47) allowed deintensification therapy for 5 patients (not being treated with pre-treatment planned CRT). PEG dependency rate was at 2%, at minimum follow-up of 12 months.

One of the more promising studies published evaluates the local disease control in 30 patients, more than 50 % having advanced stage tumour, all patients has primary tumour TORS followed by a staged neck dissection for positive nodal disease, without postoperative adjuvant chemoradiotherapy. At a mean time follow up of 2.7 years, the overall survival was 100 % with local, regional and distant disease control in 97% (29/30), 90% (27/30) and 100% (30/30) patients respectively, and all patients were on “normal diet”, no patients had a PEG.

To our knowledge, only three studies with oncologic and functional outcomes stratified their patients based on the HPV status of their primary OPSCC. One study assessed these outcomes in 66 patients following primary TORS alone or in combination with adjuvant therapy. Three year local, regional and distant control rates were 97% (64/66), 94% (62/66) and 98.4 % (65/66) respectively. When comparing HPV+ and HPV- patients, they found three years disease-specific survival at 98 % and 89 %, respectively. Recurrence-free survival was 96 % and 83 % respectively for HPV+ vs. HPV- patients. Only 5 % of the patients were PEG dependent, mean follow up three years. Another study have recently assessed the oncologic outcomes in 323 patients with stage III or IV OPSCC and known HPV status in a retrospective analysis. HPV+ patients had significantly better three-year overall survival rates (82 % vs. 57 %) and had a 58 % reduction in the risk of death compared to HPV- patients. Loco-regional relapse at three years was significantly lower for HPV+ patients (14 %) vs. HPV+ patients (35 %).
There are few publications regarding the functional outcomes such as swallowing and quality of life (QoL) data in patients with OPSCC following TORS23. Preliminary studies have showed better long-term functional status compared to RT alone, with reduced treatment morbidity and decreased length of hospitalization. Table 2 summarizes studies that had evaluated and reported on swallowing-related QoL among patients treated with TORS and/or combined with CRT.

One study measured the functional assessment of swallowing in 45 OPSCC patients by using the Functional Outcome Swallowing Scale (FOSS) score17. Twenty-two patients (49%) had a PEG temporary placed during the surgical tumour excision procedure, and the PEG were removed by latest 12.5 mean days after their placements. Following the PEG removal, the swallowing function improved with 40 patients (89%) able to resume an oral diet within four weeks postoperatively. They found associations between PEG and advanced T and primary tumour site. Another study aimed to assess PEG dependency in 29 patients with OPSCC undergoing TORS and compared four groups; primary T1/2 (8/29), primary T1/2 + CRT (9/29), primary T3/4 + CRT (5/29) and salvage therapy (7/29) 24. They evaluated their patients by T-stage of primary tumour because above mentioned studies found this to be an independent predictor of PEG. No patients with early disease without CRT required PEG at 12-months follow up.

Iseli et al aimed to evaluate factors associated with worse swallowing outcomes in a study group of 62 patients prospectively enrolled in a TORS trial25. They measured the swallowing-related QoL using MD Anderson Dysphagia Inventory (MDADI). The results showed 1) 17 % of the patients retained a PEG at 12-months follow up, and 2) post-operative PEG and poor swallowing were significantly associated with pre-operative tube requirement, higher T stage, age>60 years and oropharyngeal tumour site.

Leonhardt et al. assessed the QoL and function of 32 patients with OPSCC after 12 months following TORS measured by two questionnaires; the Performance Status Scale for Head and Neck Cancer Patients (PSS) and Short Form-8 Health Survey (SF-8)23. The patients were divided and analysed separately in 3 groups; surgery alone, surgery + RT, and surgery + CRT. They demonstrated that when TORS was used as a primary surgical approach alone, it had minimal and temporary effects on speech at six- and 12-months follow up. TORS plus RT had significantly fewer detrimental effects on the QoL compared to TORS + CRT.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Patients N</th>
<th>Tumour location (%)</th>
<th>Tumour characteristics (%)</th>
<th>Questionnaire</th>
<th>Pre-treatment scores (completed by N patients)</th>
<th>Post-treatment scores, (completed by N patients) - mean follow up, months=</th>
<th>Correlations</th>
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<tr>
<td>Moore et al 2009</td>
<td>45</td>
<td>BOT 58 Tonsil 42</td>
<td>T1+2: 73 N0+1: 31 Stage III+IV: 87</td>
<td>FOSS</td>
<td>BOT patients: FOSS=1 (18) FOSS= 2 (4) FOSS=3 (4) Tonsil patients: FOSS=1 (18) FOSS= 2 (1)</td>
<td>BOT patients: FOSS=1 (18) FOSS= 2 (4) FOSS=3 (4) Tonsil patients: FOSS=1 (19)</td>
<td>NS NS</td>
</tr>
<tr>
<td>Iseli et al 2009</td>
<td>62</td>
<td>Oral cavity 11 Oropharynx 61 Larynx 22 Hypopharynx 6</td>
<td>T1+2: 80 N0+1: NS Stage III+IV: NS</td>
<td>MDADI</td>
<td>75 (49)</td>
<td>NS 65 (49) NS NS NS</td>
<td>Retained enterogastric feeding, age&gt;60, advanced T-stage, laryngeal site, postoperative complications</td>
</tr>
</tbody>
</table>

BOT: Base of tongue, NS: not specified, MDADI: MD Anderson Dysphagia Inventory, FOSS: Functional Outcome Swallowing Scale, PSS: Performance Status Scale for Head and Neck Cancer Patients, SF-8: Short Form-8 Health Survey

1) FOSS scores were recorded at 4 weeks postoperatively if patients were undergoing surgical therapy only or at 3 months after completing adjuvant therapy.
2) The correlations between swallowing and clinical factors <0.001 6- and 12 months follow up compared to baseline
3) Group 1: TORS alone / Group 2: TORS + postoperative radiotherapy / Group 3: TORS + postoperative chemoradiotherapy (scores rounded)
Discussion
Since 2005, 19 TORS published studies and differing clinical treatment plans have been published on the management of OPSCC patients. Though many authors demand the need for higher level of evidence as in randomized trials, it may not be entirely necessary to understand and evaluate the beneficial outcomes of the minimal invasive surgical procedure, TORS, in OPSCC treatment. The majority of the authors state that TORS “seems to be associated” with less co-morbidity and toxicity than CRT and that the long-term functional outcomes are “near normal”. This could indicate that a lower level of evidence such as in observational studies, could suffice in this matter, compared to what is achieved by randomized control trials. However, a study protocol for a randomized phase II trial in Canada (ORATOR) has recently been proposed and published26. Their aim is to assess the outcome of early-stage OPSCC i.e. RT vs. TORS as a primary treatment. The trial is designed to provide a definitive QoL comparison between the two groups, and to inform the design of an eventual phase III trial for survival outcomes.

Weinstein et al have shown encouraging results using TORS as a single modality treatment without CRT21. Compared to current guidelines, the advantages may be that it improves local control rates, en-bloc resection and thereby faster and accurate pathologic processing and identification of significant poor prognostic parameters and tumour location. This supports the fact that TORS can be implemented as a new deintensification treatment modality, combined with more precise and reduced dose of adjuvant RT. This reduces the overall co-morbidity and the short- and long-term swallowing related outcomes.

A higher focus has turned towards HPV status and the association with OPSCC; a potential crucial clinical factor. Patients with HPV associated tumours compared to smoking and alcohol related HPV- patients are younger with tumours presenting at a higher stage, often due to large metastatic cystic lymph nodes and showing overall better survival rates and prognosis when treated with RT, concomitant CRT or surgery alone4,14,27. Ang et al suggest that a combination of tumour HPV status, pack-years of tobacco smoking, and cancer stage may be used to classify patients as having a low, intermediate or high risk of death14. A few studies have been incapable of presenting the same results and found no differences in oncologic outcome based on HPV status alone28.

A good prognosis seems more pronounced in HPV+ patients with p16 overexpression than in patients who are p16 negative. Most noteworthy is the fact that HPV is the most important prognostic factor in head and neck squamous cell carcinoma27. Today, no formal treatment guidelines exist based on HPV status. Two studies have emphasized the possible of deintensification of adjuvant therapy in HPV+ patients. Weinstein et al found it reasonable to consider a primary TORS approach as a means of therapeutic deintensification in an HPV+ patient1,20.

Applying TORS as a primary treatment modality ensured better TNM staging and preliminary studies show equal tumour and nodal control to CRT with lower patient morbidity. In case of salvage TORS is still possible, but due to fibrosis and changed anatomy from either surgery or radiation it is more complicated and often require local reconstruction especially after CRT where healing time is prolonged. The standard regarding N site handling is selective neck dissection (SND). This is performed either ipsilaterally in case of lateral tumours that do not reach the midline or bilateral in case of midline tumour. The National Comprehensive Cancer Network guidelines (www.NCCN.org) suggest removal of level II - IV for isolated OPSCC, which is followed by most centres. Postoperative CRT treatment is based on final TNM classification and the presence of adverse pathological features (e.g. resection-margin status)29,30.

The harder endpoints as mortality and survival analysis following TORS has been of greater focus since the early application of the procedure and have shown promising early results with three year analysis at best so far. But we have to keep in mind that one of the main reasons why TORS might be superior compared to primary CRT is due to i.e. a minimal invasive procedure with lesser complex surgical excision thereby improving the postoperative health-related and especially swallowing-related QoL. As our results imply, most if not all TORS patients post-treatment do not require a PEG.

So far, FOSS, MDADI, PSS and SF-8 questionnaires have been used in recent swallowing related QoL studies. There is no unanimously agreement upon a first choice questionnaire when assessing functional status and QoL in patients with OPSCC. No studies differentiate whether the questionnaires are better suited for surgery and/or CRT studies that evaluate the impact on swallowing function. The MDADI is the first validated and reliable self-administered questionnaire designed specifically for evaluating the impact of dysphagia on the QOL of patients with head and neck cancer31. The FOSS is successful for staging various adult patients with dysphagia into clinically useful, overall performance categories and has been applied to different specialties32. The SF-8 is an 8- item
version of the well-validated Short Form-36, providing summary scores that measure general health-related QoL across 8 health dimensions\textsuperscript{23}. The PSS is a validated instrument designed to evaluate the performance of patients in areas of function that are most likely affected by head and neck cancer and its treatment\textsuperscript{23}. Thus the above mentioned questionnaires are all suitable for assessing swallowing related QoL but the use of too many different questionnaires complicates the ability to compare results between studies. As radiotherapy treatment has acute side effects such as mucositis, edema, xerostomia, and dysphagia and more delayed effects such as fibrosis, stricture, mucosal atrophy, and thick secretion, all of which impact on the swallowing function, co-morbidity resulting in a higher symptom burden and lower QoL\textsuperscript{25,26}. Combining RT with chemotherapy will only add up the toxicity effects and compromise the swallowing function even more.

Many of the functional outcome studies have found comparable results when investigating factors associated with swallowing outcome. This means that information about age, tumour-location, T-stage, and pre-operative transnasal tube dependency can help us predict the swallowing-related QoL in patients with OPSCC. But it is important to keep in mind that these studies have their limitations and cannot be generalized, as they are not randomized, include limited and selected cases with short follow-up periods.

It is widely recognized in the TORS literature and by the FDA that the indications for TORS comprise benign lesions and T1-T2 malignancies in the oral cavity, pharynx and larynx. As many authors have implied, pre-operative case selection is very important and necessary for assessing the surgical exposure of the tumour\textsuperscript{17,21,23}.

Significant trismus, which is often pronounced in case of salvage surgery post RT, is among of one of the factors contributing to limited per oral visualisation.

As mentioned above with the importance of QoL and the fact that TORS seems to reduce co-morbidity and swallowing related QoL, it might be criticised that the majority of the TORS literature does not assess and compare the QoL pre and postoperative. Pre-operative QoL could be evaluated e.g. before surgery and postoperatively would be recommended every third/fourth month in the first two years and then every six months for three years according to our National Danish Guidelines\textsuperscript{8}.

**Conclusion**

Promising clinical results in the treatment of OPSCC based on consecutive case series have been shown when assessing TORS as a primary treatment modality alone compared to primary CRT. The oncologic results are comparable to previous trans oral surgical techniques and CRT. The majority of the authors state that TORS seems to be associated with less co-morbidity and toxicity than CRT and the long-term functional outcomes are promising. A risk stratification model based on HPV status and expression types might result in a withdrawal of the planned post-operative adjuvant therapy (deintensification) with TORS alone or combined with reduced post-operative dosage or treatment fields of radiotherapy.

**References:**
Evaluation and management of cervical nodal disease after chemoradiotherapy in head & neck cancers

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Abstract
Despite the recent advancements in the treatment of squamous cell carcinoma of the head and neck, there has been little impact on the overall survival. Presence of metastatic cervical lymphadenopathy continues to be the most important negative prognostic factor. Since the introduction of nonsurgical organ preservation protocols, there has been a particular interest and debate over the management of the neck after obtaining a complete response with chemoradiation protocols. This is particularly true for advanced stage neck disease (N2, N3), in which case a clinical response correlates poorly with a pathologic response.

More recent refinements in imaging and functional studies have had a substantial role to play in the evaluation of the neck, and helping to decide which and the extent of the neck needs to be addressed surgically. Finally, the transition of a comprehensive complete cervical lymphadenectomy, i.e. radical neck dissection, to excision of the more selective group of lymph nodes and preservation of the un-involved non-lymphatic structures of the neck, has also emerged as an area of refinement. The aim of this manuscript is to review the evidence related to these controversies in an attempt to establish a reasonable approach in the evaluation and management of the neck after chemoradiation treatment strategies.

Key words
Squamous cell carcinoma, head and neck cancer, primary chemoradiotherapy treatment, persistent post-treatment neck disease, evaluation, management, selective neck dissection.

Introduction
Despite the advancements in organ preservation protocols, the overall life expectancy after treatment of a head and neck cancer has remained essentially unaltered. There are two main goals of treatment: eradicating disease and preserving vital organ function. In case of advanced neck disease, the “past practice” was of a planned neck dissection after treatment with an organ preservation protocols was the standard of care. However, given the short and long term complications of chemoradiotherapy (CRT), salvage surgical resections not only come with a certain level of difficulty, especially for the novice work-hour restriction by-product, but the patient also suffers from potentially significant post-operative complications resulting in delayed recovery. The role of CRT in the treatment strategies for head and neck squamous cell carcinoma (HN SCC) has been well established since the Veterans Affairs laryngeal cancer study group1. This laid the foundation to an entirely different approach towards the treatment of HN SCC. Numerous clinical trials and studies have since reported to establish that the concomitant use of chemotherapy along with radiation therapy as an effective and accepted protocol in a multimodality approach towards treatment of head and neck squamous cell carcinoma2-4. These treatment strategies have been successful in controlling disease at the primary site as well as in the regional lymph nodes of the neck, particularly true for early nodal disease (N0, N1). In such cases, where there is a complete clinical response (CCR) in the neck, addressing the neck surgically after treatment seems superfluous and could be deferred. Furthermore, the argument against salvage neck dissection for clinical partial response (CPR) seems rather weak and hardly creates a controversy.

However, there is substantial debate in the management of advanced nodal disease (N2, N3), where despite achieving...
an apparent complete response, there may be a 5-20% risk of harboring residual active disease. The decision to perform a post treatment neck dissection remains debated. This decision to a great extent is dependent on Institutional preference. It is also affected by reports related to the increased risk of complications resulting from neck dissection in the post-radiated neck\textsuperscript{5,6}.

Although there is no proven method of predicting regional recurrence after CCR, the approach towards the post-treatment neck may involve clinical observation alone versus reliance on imaging studies (Ultrasound, CT, MRI or PET-CT); or the use of salvage neck dissection as a standard approach for advanced pre-treatment staged neck disease. For patients initially staged N2 or greater, irrespective of the clinical response and for patients with N1 disease with CPR, dissection of levels I through V was perhaps the most accepted surgical strategy in the pre-PET era. Proponents of a salvage neck dissection debate that perhaps the most accepted surgical strategy in the pre-PET era. Proponents of a salvage neck dissection debate that clinical examination is unreliable in identifying less than complete response to CCRT and formal pathologic evaluation is the most definitive way of discovering residual disease. There is however evidence to the contrary that observation may be a suitable approach after CRT therapy for complete responders\textsuperscript{7}. There is evidence from several trials that support observation as a reasonable option for complete clinical response to CRT therapy. The Trans-Tasman Radiation Oncology Group 11 performed a prospective trial of definitive CRT therapy for patients with N2-N3 disease associated with head and neck squamous cell carcinoma. Patients in this trial who had obtained a complete clinical and radiological response had a zero incidence of neck failure without a planned neck dissection.

Although there is lack of prospective randomized data, but some of the prognostic factors that help select high risk patients to address the neck after CCRT, include the advanced pre-treatment neck stage, HPV negative tumors, advanced age, high T stage and tumors of the hypopharynx.

**Assessment of Treatment Response:**

The entire premise in the controversy of addressing the neck following CRT, is dependent on accurately assessing the treatment response. It is especially crucial if the treatment strategy involves observation of complete responders. There is evidence to suggest that clinical examination alone may not be sufficient to accurately rule out residual or recurrent disease in the neck. Clinical examination combined with a contrast-enhanced CT scan has a negative predictive value of approximately 95% when evaluating treatment response following CRT\textsuperscript{12}. A study from the Cleveland clinic reviewed 109 patients treated with CRT\textsuperscript{13}. Neck dissection was performed in all patients with CPR and in 32 of 65 patients with CRT. Clinical examination alone was found to be a weak predictor of pathologic response with 25% of CRT and 39% of CPR patients demonstrating pathologic evidence of residual disease on neck dissection. This may have been due to a lack of routine imaging for evaluation of treatment response at that time. In this cohort, there was no statistically significant difference in the nodal failure rate between patients who underwent a salvage neck dissection and those who were observed. No survival benefit from neck dissection was seen.

The role of FDG-PET scan as an adjunct to CT scan for the assessment of disease response continues to develop. PET-CT has now been reported to be of value as an adjunct to clinical examination. The negative predictive value of PET-CT has been reported to be between 97 and 100%. Some institutions rely heavily on post-treatment imaging studies to guide neck treatment while others have found these studies to be inconsistent predictors of pathologic response as PET-CT may have higher false-positive rate of up to 20-43\%\textsuperscript{14}. Another study assessed the use of clinical examination, CT and PET and based on their low sensitivity and positive predictive value, concluded that no single modality or combination of modalities was ideal in accurately identifying those patients that would benefit from a neck dissection\textsuperscript{13}. The relationship of pretreatment FDG and outcomes showed high substance uptake value (SUV) to be related to significantly worse disease free survival and node progression free survival\textsuperscript{15}. Patients with an SUV of >6.0, who underwent neck dissection had a better node progression free survival (p=0.04) than those that did not undergo neck dissection.

Despite the shortcomings, functional imaging has greatly improved disease response evaluation and with continued advancements, will further its role in evaluating treatment response. Patients who have a complete metabolic response at 12 weeks despite showing residual regressing mass, have a significantly low risk of subsequent regional failure. Such patients are closely observed clinically and radiologically with a repeat CT or PET-CT in another 12 weeks and as long as the PET-CT is negative, clinical observation is continued. If there is however, clinical or PET evidence of progression of neck disease, then neck dissection is mandated.

**Timing of Neck Dissection:**

The timing of salvage neck dissection is crucial. Data suggests that there is no increased risk of regional recurrence or even distant metastases if neck dissection is delayed for several weeks after chemo-radiation therapy. The tumoricidal effect of radiation therapy continues well
beyond 6 - 8 weeks after completion of treatment. Additionally the acute toxic effects of treatments last for 6 -10 weeks in that the soft tissue fibrosis and other chronic effects set in after this timeframe. Hence it is reasonable to plan the salvage neck dissection 2 - 3 months after completion of CCRT. At the Cleveland Clinic, We a PET-CT would be routinely obtained at 3 months following treatments and neck dissection scheduled thereafter, based on the results. If bilateral neck dissections are necessary and if both the internal jugular veins have to be ligated, then a staged neck dissection is performed with a 4 to 6 week interval. The side with more significant disease volume is addressed first.

This fact also seems debatable in the present setting where less ‘radical’ approaches are employed to address the neck without compromising disease control. The use of selective neck dissection not only limits the morbidity of shoulder dysfunction, and excessive fibrosis of neck, but also prevents carotid exposure from wound breakdown with appropriately selected incisions and preservation of the sternocleidomastoid muscle. The fact that Internal jugular vein is also routinely preserved, unless involved with disease, significantly reduces post-operative edema and avoidance the need for a tracheostomy to prevent the need for emergency airway stabilisation secondary to RT edema of the upper airway.

**Type of Neck Dissection:**

Historically, a complete cervical lymphadenectomy involving levels I-V has been advocated when addressing the neck after CRT. Many institutions favored a radical or modified radical neck dissection as a salvage operation for treated N+ neck. However there is emerging data to suggest that selective neck dissection (SND) may be equally effective in clearing residual neck disease. SND results in low morbidity and improved quality of life for the patient. Several studies support selective neck dissection to have equivalent results with comprehensive neck dissection related to regional control and disease-free and overall survival. For oropharyngeal and hypopharyngeal carcinomas, dissection of levels II, III and IV is found to be sufficient in eradicating and controlling neck metastases.

The role of selective and superselective neck dissection (SSND) with removal of only the affected groups of lymph nodes has shown promising results with no significant difference in regional recurrence based on the type of neck dissection performed. SND has been shown to be an effective and oncologically safe procedure even for N2 or greater neck disease. SND would effectively remove residual disease in the vast majority of cases in the original levels plus one distal level. Although a more comprehensive neck dissection is usually performed with greater (N3) pretreatment nodal disease, data from this study suggests that the residual neck disease is typically found within the original positive levels, or the next distal level. Hence dissection of the clinically involved nodal levels and one adjacent nodal level appear to be sufficient in controlling the disease. In addition to the oncologic outcomes, the potential radical effects of the more comprehensive neck dissections are also avoided by a more selective lymphadenectomy.

In an attempt to reduce the long term consequences on quality of life measures following a comprehensive neck dissection, the concept of SSND is becoming increasingly acceptable following reports where SND or SSND, appear to be as effective as a comprehensive neck dissection in preventing regional recurrence. Obviously, if the adjacent non-lymphatic structures cannot be separated from the lymphatic tissue, a more comprehensive neck dissection is still required. In contrast to the concept of SSND, the number of nodes dissected has also been shown to be of importance. The ratio of positive nodes to the total number of nodes dissected is gaining interest in head and neck cancers. A nodal yield of less than 18 has been shown to have a significant impact on the overall survival in comparison to higher yields (5-yr OS of 51% vs 74%; p=0.0009).

**Conclusions**

The management of nodal disease in the neck following CRT can no longer be considered a planned procedure. Should these patients be observed clinically or should they undergo salvage neck dissection after achieving a complete clinical response to CRT, continues to be a controversial topic. The studies referenced are some of the many that have looked at the different variables employed to decide on whether to operate or not. For early stage neck disease (N0, N1), the risk of neck recurrence after CRT is rare and clinical observation is a safe option, given patient compliance with surveillance. In case of advanced staged neck disease, and in particular N2 disease, for the clinical complete responders, taking into account the presence of poor prognostic indicators of advanced neck disease and primary tumor are important considerations. The use of PET-CT is also helpful in identifying those that may be harboring residual disease and would eventually require neck dissection.

The timing of these radiologic studies is also of significance to reduce the chances of false positivity. Additionally, the timing of the salvage procedure is of great consequence.
given the post treatment fibrosis and increased risk of complications after such treatments. A post treatment PET at 12 weeks seems reasonable and neck dissection around the same time or, sooner in case of less than a partial clinical response, seems best from the surgeon standpoint.

Finally, the use of SND and SSND to eradicate the primary echelon lymph nodes and the next level down, seems to be oncologically safe and effective. The role of modified and radical neck dissection appears to be limited to only those still resectable cases where the primary treatment modalities have been unsuccessful in eradicating or slowing the progression of disease.

References:

Is Recurrent Respiratory Papillomatosis a primary immunodeficiency, or is it all about the virus, or could it be both?

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Introduction
Patients with Recurrent Respiratory Papillomatosis (RRP) are burdened by chronic infection with HPV 6 or 11, manifesting as non-regressing papilloma within their airway. The immune system is likely to play an important role in preventing papilloma from developing and subsequently causing regression. An important question is why patients with RRP develop severe disease to HPV but are not susceptible to other infective organisms common to patients with immunodeficiency.

Methods
We conducted quantitative analysis of immune cells in patients with RRP and age-matched controls. Furthermore, we compared their ability to mount functional immune responses to HPV, influenza A M1 protein, and to direct activation of their T-cells by Phytohaemagglutinin (PHA), IL-2 and anti-CD3 antibody. We also analysed the virus life-cycle and local immune response.

Results
Patients with RRP have a normal complement of immune cells; nonetheless, patients with severe disease are less able to effect lymphocyte proliferation in response to both IL-2 and direct activation of their T-cell receptor when compared to healthy controls. This is independent of antigen presentation. Furthermore, patients with severe RRP secrete significantly lower concentrations of the cytokines IFN-γ, IL-10, and IL-6 in response to HPV 6 and 11 E6 peptides compared to controls; whilst on the other hand, their functional immune response to influenza A M1 is normal.

Discussion
The ability of lymphocytes to proliferate is the hallmark of a normal immune response. RRP may result from the combination of patients having a sub-optimal proliferative response and the mechanisms developed by the virus to evade immune detection.

Is there survival benefit from life-long follow-up after treatment for differentiated thyroid cancer?

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Introduction
Differentiated thyroid cancer (DTC) in the young (<45 years) confers a favourable prognosis following optimal initial treatment. However, the current international guidelines (from the British, European and American Thyroid Associations) advocate life-long follow-up for DTC. This strategy of life-long follow-up for everyone is not evidence-based.

Methods
A systematic review of the literature was conducted. The Cochrane Controlled Trials Register, Medline and EMBASE were searched from 1966 onwards. A total of 137 studies were retrieved. Based on design, number of patients and origin (high volume/specialised centres and national registries) 7 papers were identified that provided the best evidence to answer the question.
Expression of total vascular endothelial growth factor (VEGF) and inhibitory isoforms of VEGF in head and neck squamous cell carcinoma

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Introduction
Angiogenesis, of which vascular endothelial growth factor (VEGF) is a potent stimulator, is a prerequisite for tumour survival, progression, and distant metastasis. Alternative splicing, however, results in a family of highly anti-angiogenic endogenous sister isoforms of VEGF (VEGFxxxb), not yet investigated in head and neck squamous cell carcinoma (HNSCC). We evaluated, therefore, whether VEGF isoform expression was altered in HNSCC with respect to several clinicopathological outcomes.

Methods
Using a tissue microarray 187 HNSCCs (87 larynx, 73 oropharynx, 27 hypopharynx) were studied. Tumour sections were assessed by immunohistochemistry with total VEGF (panVEGF) and VEGFxxxb-specific antibodies, and were scored by 2 assessors (blinded) for staining intensity (0–3) and proportion (0–4). Scores were compared against clinicopathological parameters using multivariate statistical analysis.

Results
PanVEGF and VEGFxxxb staining was observed in the vast majority of samples. No meaningful significant differences were observed in panVEGF, VEGFxxxb, or expression ratio (VEGFxxxb:panVEGF) with respect to T stage, vascular invasion, presence or absence of lymph node metastasis, N stage, or extra-capsular spread (ECS). This remained the case when tumour subsites were analysed independently and also when HPV positive tumours were excluded from analysis.

Conclusions
Neither total VEGF nor anti-angiogenic isoform expression predicts primary tumour stage, vascular invasion, lymph node metastasis or ECS in HNSCC. It appears, therefore, that VEGF isoform expression is unhelpful in predicting loco-regional disease burden. Further investigation of correlations with
Free Radical Scavengers to Mitigate Noise-Induced Hearing Loss: Is there a role for Red Bull?

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Abstract
Exposure to acoustic trauma causes an increase in metabolic activity in the inner ear, resulting in free radical production. Free radicals such as nitric oxide (NO•) can cause cellular damage, which in turn can cause apoptosis and necrosis. For this animal study, we tested the effect of taurine, a potent NO• scavenger, to mitigate noise-induced hearing loss (NIHL). Male CBA mice aged 4-10 weeks were randomised into six groups treated with 0.9% saline (control) or taurine (50, 100, 200, 300 or 400 mg/kg) via daily IP injections over 14 days (7 days before and after acoustic trauma). Acoustic trauma was 8-24 kHz banded noise at 110 dB SPL for 2 hrs. Auditory brainstem responses (ABR) were tested at 8, 16 and 24 kHz, and collected one week before, one week after, and one month after acoustic trauma to represent pretreatment thresholds, temporary threshold shifts (TTS), and permanent threshold shifts (PTS), respectively. Our results show that taurine significantly attenuated the effects of noise trauma as shown by ABR threshold shifts when compared to saline controls in all groups (P<0.05 at 8, 16 kHz for TTS and 8, 16, 24 kHz for PTS). Thresholds shifts were on average 13.2 dB better in all taurine treated mice compared to the saline control group. Taurine improves hair cell survival for both inner and outer hair cells when compared to controls using cytocochleogram analysis. Our future studies will investigate taurine as a potential therapeutic agent to prevent and/or treat NIHL.

Ultrasound in Otolaryngology – A Pilot Questionnaire to Otolaryngologists

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Introduction
Ultrasound is often the primary investigation for lumps in the neck. Around the world otolaryngologists perform their own ultrasounds in clinic and training includes ultrasound competencies. This questionnaire looks at the current state of ultrasound provision, the potential use of ultrasound by otolaryngologists and opinions about ultrasound competencies in the trainee curriculum in the UK.

Method
The questionnaire was hosted by SurveyMonkey® and was made up of 10 questions. An email with a link to the questionnaire was sent to otolaryngology trainees in (17) and otolaryngology consultants with an interest in Head and Neck (9).

Results
Six consultants (67%) and 11 trainees (65%) answered the questions. Sixty percent of respondents had a rapid access neck lump clinic in their hospital, ultrasound guided fine needle aspirates were more commonly performed by radiologists (88%). Thirteen respondents (76%) would like to be trained to use ultrasound. Ultrasound would be most useful in the assessment of acute neck lumps and guiding fine needle aspirations. Time, cost and radiology department resistance were seen as obstacles to introducing ultrasound performed by otolaryngologists.

Discussion
There is a climate amongst otolaryngologists with an interest in head and neck to start to use ultrasound in the acute and out patient setting. There are training costs and time barriers to introducing this, nonetheless there are otolaryngologists in this country who use ultrasound in their clinical practice successfully. This questionnaire will be sent to members of ENTUK and the AOT and qualitative analysis will be undertaken.
Antifibrinolytic agent tranexamic acid for nasal haemorrhage (epistaxis)

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Background
Nosebleeds most commonly affect children and the elderly. The majority are managed at home, with more severe cases requiring medical intervention. Tranexamic acid helps reduce blood loss by preventing clot breakdown (fibrinolysis) and is used in many haemorrhagic conditions. It may have a role in the management of epistaxis as an adjunct to standard medical treatments.

Objectives
To determine the effectiveness of tranexamic acid compared with placebo or no additional intervention in the management of patients with epistaxis.

Selection criteria
Randomised controlled trials comparing the use of tranexamic acid with placebo in the control of epistaxis.

Results
Three trials comprising 232 participants were included, two studying oral and one topical tranexamic acid. For the primary outcome measure the studies showed there were fewer episodes of bleeding in those treated with tranexamic acid (odds ratio 0.52, 95% confidence interval 0.30 to 0.90; three studies; 225 participants; P = 0.02). For the secondary outcomes the two inpatient studies found a reduction in hospitalisation time in the treatment group compared to the control group, which could have significant healthcare cost implications for these patients. There were no adverse events or side effects noted in any study.

Authors' conclusions
The three studies in this review have shown a significant reduction in rebleeding rate following spontaneous epistaxis when tranexamic acid is used in addition to standard techniques. New trials would inform us as to the effectiveness of tranexamic acid in light of recent advances in the types of standard intervention available.

Nasal packing: One side or both. A study of intra-nasal pressure comparing unilateral and bilateral Rapid Rhino® pack insertion and effects on the patients’ level of discomfort.

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METHODS
12 healthy volunteers were recruited according to strict criteria. Rapid Rhino® 5.5cm anterior packs were inserted bilaterally following topical nasal preparation with co-phenylcaine. The first pack was inflated to a predetermined pressure. The contra-lateral pack was inflated to match, and any intra-nasal pressure change on the first side was measured. The subject’s level of discomfort was scored on a visual analogue scale. This procedure was repeated at incremental pressures.

RESULTS
Higher ipsilateral intra-nasal pressures are achieved when additional contralateral nasal packs are inflated. This change in ipsilateral intra-nasal pressure is greater at higher total inflation pressures.

At higher pressures, the subjects reported lower mean pain scores when bilateral packs were used compared to unilateral. This effect was only statistically significant at intra-nasal pressures of 140mmHg and above, (Wilcoxon Signed-Rank Test, p<0.02).

CONCLUSIONS
Our results support the use of bilateral nasal pack inflation when unilateral packing at low to medium pressures has failed to control epistaxis. In addition, bilateral pack inflation may be better tolerated than unilateral inflation when higher intra-nasal pressures are required.
Laryngeal Mask Airways and the Use of a Boyle-Davis Gag: Is There A Learning Curve?  
A Prospective Analysis of Surgical Technique in ENT Surgery

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OBJECTIVES
Our study was to identify whether the experience of the operating surgeon was relevant to the frequency of the Laryngeal Mask Airway (LMA) kinking causing airway obstruction or subsequent change to an Endotracheal tube (ETT) during ENT surgery.

METHODS
Data was prospectively collected for all patients (N=186) undergoing a procedure with the use of a Boyle-Davis gag and LMA, over 18 months. Information was gathered regarding patient demographics (Age, Mallampati Grade), grade of surgeon, grade of anaesthetist securing the airway, LMA size inserted, and any intra-operative adjustments needed.

RESULTS
There was an overall intra-operative airway intervention rate of 21%. The experience of the surgeon affected the rate of intra-operative airway interventions encountered. This experience was reflected by the significantly lower rate of airway complications (ie. 10%) seen when Associate Specialists perform these types of procedures compared to other grades of surgeon, (Fisher Exact Test, 2-tailed, p-value 0.04). A significant complication rate of 50% was seen with ‘Core Surgical’ trainees compared to other grades of surgeon, (Fisher Exact Test, 2-Tailed Test, p-value of 0.002).

Grade of anaesthetist had no significant effect. The patient demographics, (Age, ASA and Mallampati scores), made no significant difference to the intra-operative airway intervention rates, (p-values of 0.95, 0.78 and 0.18 respectively, Paired T-Test and Mann-Whitney U Tests).

CONCLUSIONS
This study supports the theory that there is a ‘learning curve’ associated with the use of LMA’s, and specific focus on teaching these techniques to ENT trainees needs to be emphasised for safe airway management and effective perioperative conditions.
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