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Volume 1 Number 1

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# JOURNAL OF ENT MASTERCLASS®

## Volume 1 Issue 1 December 2008


## Contents

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Rice D. H.; Cone-Wesson,B., "Intraoperative recurrent laryngeal nerve monitoring," *Otolaryngology Head Neck Surgery,* Sept. 1991, p 372-375.

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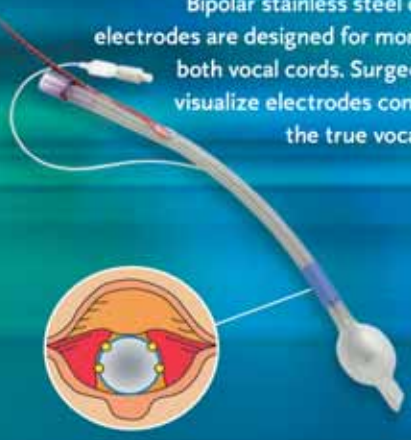

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**Editorial Comment: Journal of ENT Masterclass® Volume 1 Issue 1.**

Welcome to Volume 1 Issue 1 of Journal of ENT Masterclass®!

This project has arisen from the ENT Masterclasses that have been organised and so well supported and attended by Shahed Quraishi and his Doncaster team since inaugurated January 2005. Not only has there been Otolaryngology Masterclasses, but site specific Masterclasses, as well as Nursing Masterclasses. Initially it was agreed that the attendees would be given a "locked CD" of the presentations given on the day – but with time and reflection it was considered that most of these were filed away for posterity and never looked at nor used at any future date! With that in mind and then enthusiasm of Shahed the concept of a Journal based on the concept of "Current Opinions" on specific topics would be more relevant and more useful for the audience to which the Masterclasses are directed – trainees and those presenting for higher examinations and qualifications.

Over the past year, with consultation and topic selection, more than 20 articles were commissioned. Without exception, everybody was willing and produced their manuscript "on time" and returned their corrections to the editor, ensuring that this first issue could be delivered on time for the January Meeting 2009. Not only have we relied upon the local and national experts, but we are grateful to European experts for their efforts and time – Professors Ferlito and Rinaldo, Udine, Italy and Professor Remacle from Belgium.

We, the Editorial Board, would welcome suggestions of further topics for future issues of The Masterclass Journal. Should you be willing, able to and deliver on time please make contact with Mr Quraishi before end of March 2009 so that topic approval, delivery time-table and suitability of chapter contents be agreed – as we wish to prevent disappointment or rejection when the work has been completed!

We would like to thank Mr Nigel Clifton OBE, Chief Executive of Doncaster & Bassetlaw NHS Foundation Trust, for his willing support not only the post-graduate facilities, but his encouragement and persistence that Doncaster was the right place for this course! Also, our thanks go to the local medical and nursing staff of the Head and Neck Service at Doncaster for their continued support. And not least, much thanks to the pharmaceutical and trade representatives, and their companies, for their support and contributions to reducing the "cost burden" for this publication.

We continued to be indebted to the many lecturers who have "volunteered" their time, energy and efforts – all for free, and frequently at weekends with its inconvenience to families and other arrangements! Many thanks to all who have contributed to the success of the previous ENT Masterclass and to many future Masterclasses!

We remain in everybody's debt for the success of this project!

**Professor Patrick J Bradley**, MBA FRCS,
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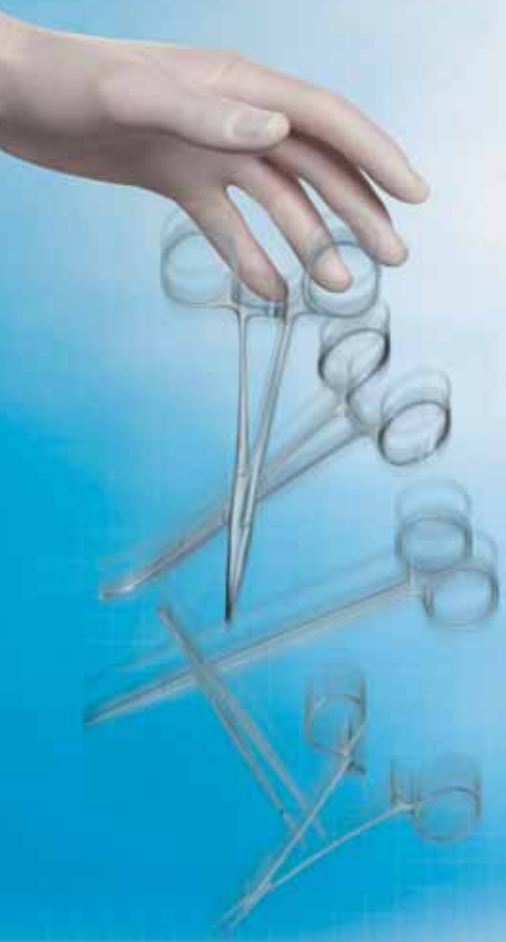

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# Management of Neck Lumps in Children

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## Introduction

Children commonly present to ENT with neck lumps. The vast majority will represent benign, self limiting pathology such as reactive lymphadenopathy. The challenge for the clinician is to identify those patients with conditions which require further investigation and management. Thorough history taking and examination are key, together with a familiarity with the range of congenital and acquired pathology encountered. The aim of this paper is to review the aetiology, investigation and appropriate management of neck lumps in children with a focus on recent literature.

## Persistent Cervical Lymphadenopathy

Palpable cervical lymphadenopathy is very common in otherwise-well children, with studies suggesting rates between 17-62%[1]. The difficulty is selecting from this population which children need further investigation to exclude significant pathology, and there is a dearth of published studies to guide us.

The majority of patients will ultimately be given a diagnosis of reactive lymphadenopathy, with lymphoma the most common malignancy in this age group. Open excisional biopsy remains the gold standard for obtaining tissue for histology in children, but the proportion of biopsies that show malignancy is very low and surgery carries risks[2]. This leads to a reluctance to proceed with surgery, and children are often subjected to repeated clinical review instead. While this may seem reasonable, the evidence suggests that the prevalence of malignancy is *lower* in patients who have lymphadenopathy for a longer period of time[3,4] and prolonged review leads to delayed diagnosis in the minority who actually do have serious pathology. A decision about surgery needs to be made as soon as is practical to avoid these problems.

Small (1cm or less), mobile, soft nodes are of low suspicion, and nodes which fluctuate in size are almost certainly reactive. These children should be reassured and discharged with instructions to return if things change. Large nodes (3cm, and possibly even 2cm[3,4]) should be excised urgently, as should all supraclavicular nodes[1]. For the remainder, chest Xray, blood count and ultrasound should be arranged. Ultrasound is cheap and can be performed without anaesthesia or sedation. Its results show promise in identifying malignancy[5]. Serology for toxoplasma, bartonella, cytomegalovirus and Epstein-Barr virus may identify the pathology and avoid biopsy in 10% [4].

FNAC is less accurate for lymphoid diagnoses (reactive nodes, lymphoma) than for carcinoma, making it less useful than in adults. Many children would require anaesthesia for FNAC, but this is difficult to justify when up to 20% of samples in children are inadequate for diagnosis.

## Atypical Mycobacterial Lymphadenitis

Non-tuberculous mycobacteria are widely prevalent in soil and are therefore prone to ingestion by toddlers. The mycobacteria travel to the first echelon nodes (parotid and submandibular) and cause persistent cervical lymphadenopathy. The presentation is typically that of a pre-school child with a subacute history (2-6 weeks) of a discrete neck mass and no systemic upset or fever. There is no response to standard antibiotics. Left untreated the child develops violet skin discolouration, cold subcutaneous abscess formation **(Fig 1)**, skin breakdown with discharge

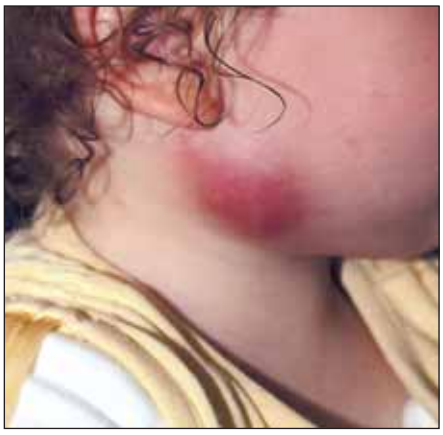

**Figure 1:** *Large abscess involving upper deep cervical nodes and parotid tail in a systemically-well 4-year-old girl with atypical mycobacterial infection.*

and eventually healing with scarring, all over the course of months to years. The diagnosis is clinical. Needle aspiration can lead to skin breakdown and culture is only positive in less than half of cases. Incision and drainage must be avoided as healing is protracted and scarring is unsightly. The treatment of choice remains complete surgical excision, which often requires a supraomohyoid neck dissection and partial superficial parotidectomy[6]. Prolonged antibiotic treatment (most commonly with clarithromycin and rifabutin) has been shown to produce a response in up to two thirds of cases but adverse effects are common and a large proportion of children still progress to surgery[7]. Cosmetic results are best if the disease is excised before skin breakdown occurs.

## Thyroglossal Duct Cysts

Thyroglossal duct cyst (TGDC) is the most common midline neck swelling in children, and can present as a painless mass, and infected mass or a draining sinus. Classically the mass is said to move on tongue protrusion but this sign can be unreliable in this age group. The mass is found around the hyoid in 60% of cases, suprahyoid in 24%, suprasternal in 13% and intralingual in 2%[8].

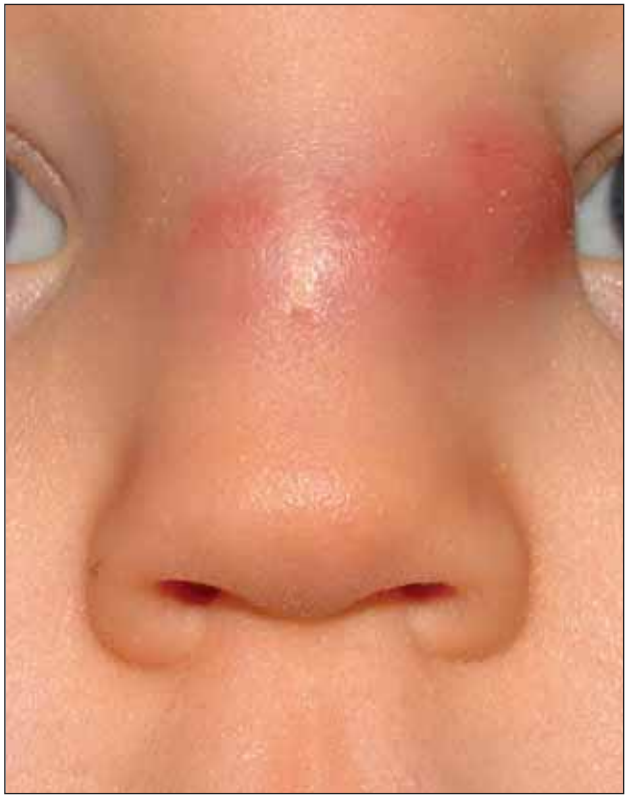

**Figure 2:** *Infected midline nasal dermoid cyst. Note the punctum on the nasal dorsum. The sinus tract extended to a large cyst deep to the glabella which was adherent to the dura. The lesion was subsequently removed via an external rhinoplasty approach.*

Ultrasound is the only investigation required, to confirm the presence of a thyroid gland prior to excision. The incidence of absent thyroid is not clear, nor is how to proceed if the finding were to be confirmed, however this has remained standard practice[8,9].

Management of TGDCs is surgical excision of the cyst and its associated tract. The tract can be seen histologically to branch widely[10], and any attempt to dissect out the tract is doomed to failure. A wide dissection in normal tissue should be performed to include a central strip of strap muscle and pretracheal fascia, plus the central portion of the hyoid and a block of tongue base. Such an operation carries a much lower recurrence rate than after traditional "Sistrunk" operations where the tract is dissected[11].

A significant number of dermoid cysts will be discovered intraoperatively. Simple excision is probably adequate if the mass is superficial to the straps, but if there is any doubt then surgery should proceed as for a TGDC.

## Dermoid Cysts

The most common head and neck dermoids are periorbital (at either end of the eyebrow), postauricular and submental[12]. Intracranial extension is rare in these sites but an MRI scan is not unreasonable. A sinus tract and punctum is also rare, and the infection risk is low. Surgical excision is straightforward and not urgent.

Nasal dermoids are different. They tend to present as a swelling over the nose with an associated punctum which can lie anywhere from the nasal dorsum to the philtrum of the upper lip. The presence of a hair protruding from such a punctum is pathognomonic. Intracranial extension is common and the cysts are often multiple, so imaging is mandatory. The sinus tract provides a route for bacterial entry and infection is common **(Fig 2)**. Infection can lead to skin loss and scarring, so excision should be performed as soon as possible to prevent this. Many approaches have been used but external rhinoplasty[13] provides excellent access and cosmesis, even for some with intracranial extension.

## Salivary Masses

90% of salivary neoplasms in children arise in the parotid gland. Under the age of 10 years, haemangiomas **(Fig 3)** and lipomas are common whereas over the age of 10 years lesions are more likely to be epithelial in origin. In adults the chance of a salivary gland mass being malignant varies inversely with the size of the gland in question. The same is not true for such lesions in children, where 50% of parotid lesions, 66% of submandibular lesions and 15% of sublingual gland lesions are malignant[14].

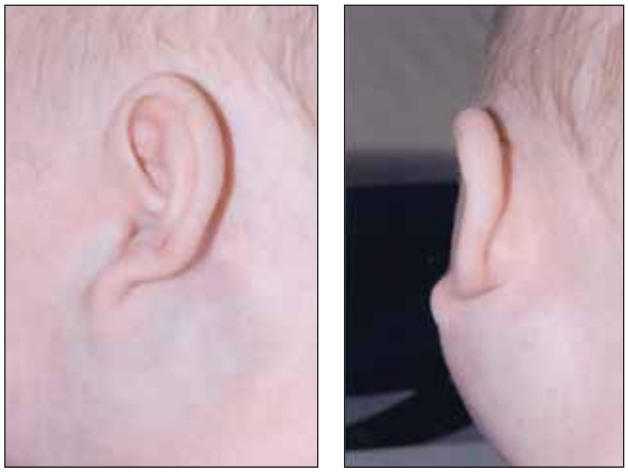

**Figure 3:** *An infant with a parotid haemangioma. The appearance is typical. No investigations are required. The lesion may take 2 to 3 years to resolve completely.*

Investigation with FNAC raises the same concerns with compliance and interpretation as for cervical lymphadenopathy. If FNAC findings fit the clinical picture they can be helpful, but they should not be relied upon for an accurate diagnosis.

Ultrasound imaging allows assessment of the solid or cystic nature of a mass as well as its relation to surrounding vascular structures. MRI can be used for further assessment of the nature and extent of a tumour and can outline its relationship with the facial nerve.

The aim of surgery should be a complete excision with preservation of the facial nerve if not involved. Involvement of the neck is uncommon except in high grade lesions, and so unless there is evidence of neck disease, there is no role for elective neck dissection.

Complications of parotid surgery seem to be more common in children than in adults, with a 9.5% permanent facial pareses rate and a 1.7% total palsy rate[15]. The recurrence rate after superficial parotidectomy for pleomorphic salivary adenoma also is reported to be higher in children than adults[16].

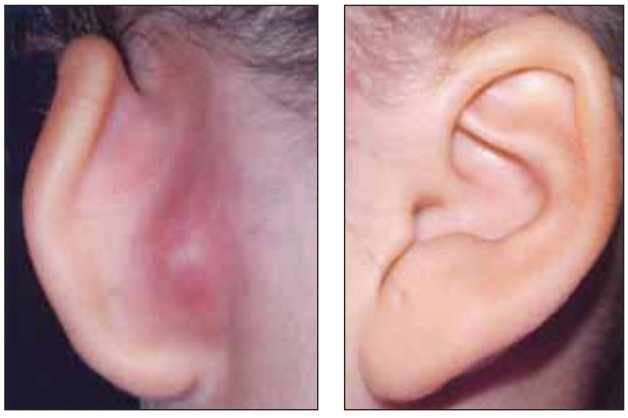

**Figure 4:** *First branchial cleft anomaly presenting as infected postauricular swelling and a punctum on the lobule.*

## Thyroid Masses

Children rarely present with a thyroid mass, and for those that do thyroid cancer must be considered. Most present as a mass in the neck, with dysphagia or hoarseness rare presenting features. Eighty percent of thyroid cancers are papillary, 20% are follicular. The disease process differs from that in adults. Metastasis to the neck is more common, with a recent study of 75 patients reporting metastasis to the central neck compartment in 80% of cases[17]. Distant metastasis occurs at around 5% to the lung, bones or brain. Hemithyroidectomy for malignancy is related to a higher local recurrence rate than total thyroidectomy with post operative iodine. Despite the aggressive nature of the disease, outcomes in children treated with total thyroidectomy, central or modified radical neck dissection depending on nodal status and post operative radioiodine, are excellent with 10 year and 20 year survival rates of 99% and 97% respectively.

## Branchial Abnormalities

Anomalies of the branchial clefts result in a sinus opening onto skin, while anomalies of the pharyngeal pouches open onto mucosa. True congenital fistulae are rare.

First branchial cleft anomalies are very rare and present as a mass or infection around the ear with a sinus opening visible in the ear canal, around the ear or adjacent to the angle of the mandible **(Fig 4).** There may be a cartilaginous duplication of the ear canal, and the lesion is often intimately related to the facial nerve[18]. Imaging provides limited information. Treatment is by complete surgical excision, which is most safely done using a parotidectomy approach with facial nerve monitoring.

Second cleft anomalies are the most common and present as a sinus opening along the anterior border of sternomastoid **(Fig 5).** The only imaging that is required is an ultrasound of the renal tract if branchio-oto-renal syndrome is suspected (second cleft sinuses in association with pre-auricular sinuses). The tract follows a predictable course upwards, between interal and external carotid arteries towards the tonsil, and surgical excision is straighforward. The risk of recurrence is greater following infection[19].

Third and fourth pharyngeal pouch anomalies present as recurrent infection around the left thyroid lobe. A tract from the piriform fossa may be identified on barium

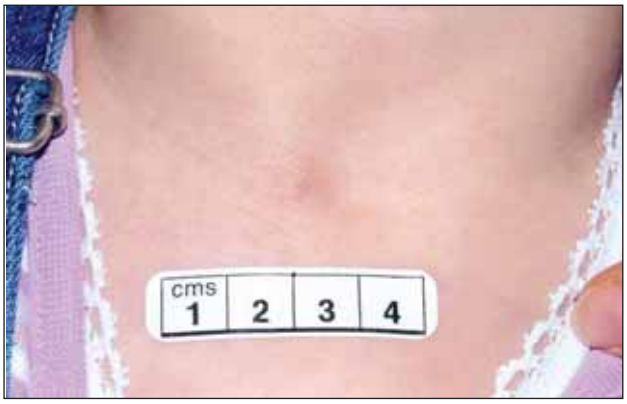


**Figure 5:** *Typical appearance of a second branchial cleft sinus*

swallow or on endoscopy **(Fig 6).** Open excision requires dissection of the trache-oesophageal groove and may require hemi-thyroidectomy to ensure complete excision and prevent damage to the recurrent laryngeal nerve. Recent case series report the use of endoscopic cautery to the tract in the piriform fossa as an alternative to an open surgical procedure[20,21]. This does not remove the anomaly but isolates it from the aerodigestive tract which may in turn prevent symptomatic infections. Long term results are unknown as is the risk to the superior laryngeal nerve which is immediately adjacent to the tract.

## Teratomas

These embryonal neoplasms arise in totipotent germ cells and affect the cervical region 1 in 20,000 to 1 in 40,000 live births. They contain sells from all 3 germ cell layers. They may contain mature and immature cells. They are usually large and can give rise to complications as a result of compression of surrounding structures[22]. Airway obstruction secondary to tracheal compression can result in perinatal mortality. Antenatal diagnosis may allow for a planned delivery with immediate intubation or tracheostomy on placental support.

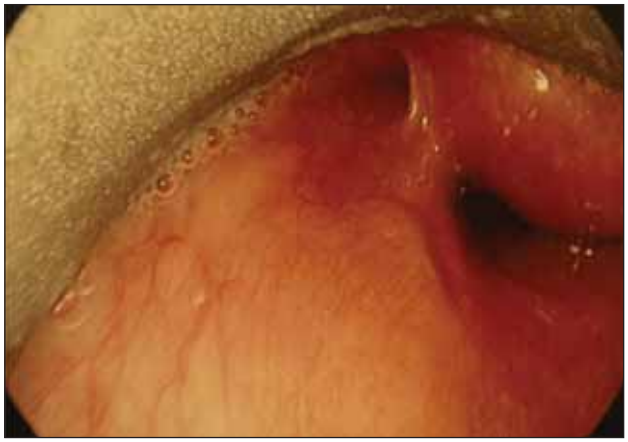

**Figure 6:** *Endoscopic view into the left piriform fossa showing the opening of a fourth pharyngeal pouch sinus. Cricopharyngeus is to the right of the picture.*

## Vascular Anomalies

The complex group of congenital vascular lesions has been somewhat simplified by a classification system which splits them into vascular malformations and haemangiomas[23].

Vascular malformations are present at birth, enlarge with the child and have neither a stage of proliferative nor of involution. This group includes capillary malformations (port wine stains), venous malformations, arteriovenous malformations (AVMs of lung or brain) and lymphatic malformations (lymphangiomas or cystic hygromas). Of these, only lymphatic malformations commonly present to ENT. Diagnosis of lymphatic malformation tends to be straightforward, examination showing an ill defined neck mass which is soft, compressible and may transilluminate. Imaging is essential in planning treatment. Lesions below the hyoid tend to be macrocystic in nature and reasonably well circumscribed. Treatment is by surgical excision or OK432 injections. Surgery can be challenging but complete excision should be possible without damage to important structures[24]. Injections of OK432 (a low virulent strain of streptococcus pyogenes treated with benzylpenicillin potassium and bleomycin) may need to be repeated a few times to achieve resolution, but a recent systematic review of sclerotherapy reported response rates as high as 87.5% with only 12.5% of patients requiring salvage surgery[25]. Major complications were reported with a rate of 3%, so injection therapy is not entirley benign and surgery remains the first line treatment for infrahyoid lesions **(Fig 7).** Suprahyoid lesions, however, tend to be microcystic and infiltrative in nature, often involving mucosal surfaces. Complete excision is rarely possible and the cysts are usually too small for effective injection therapy. Repeated lasering of mucosal surfaces may control bleeding and discomfort.

Haemangiomas, on the other hand, are benign tumours of vascular endothelium which tend to present shortly after birth and undergo a proliferative stage over the first 12 months, followed by a gradual involution over subsequent years. Fifty percent involute by age 5 years and 70% by 7 years. They can be sub-classified into superficial lesions

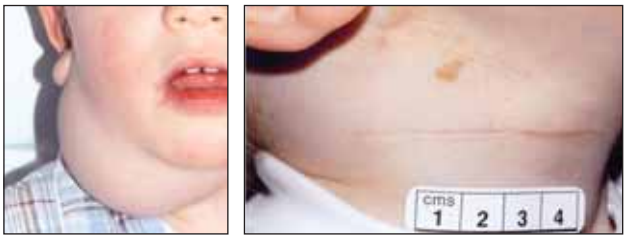


**Figure 7:** *Child with large macrocystic lymphatic malformation in the right submandibular region, before and after complete resection.*

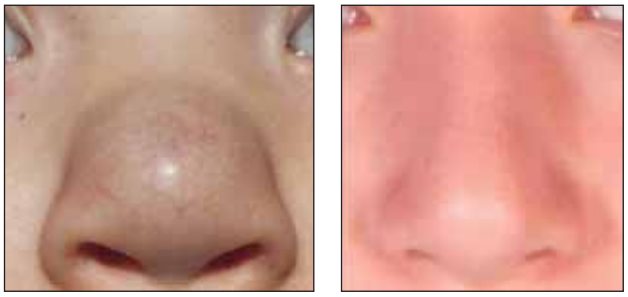

**Figure 8:** *Nasal tip haemangioma at age 6 months (left) and age 8 years (same child, right) showing complete resolution with no treatment.*

involving the papillary dermis, and deep lesions involving the reticular dermis and expanding into the subcutaneous fat. Treatment is required to prevent functional deficits (vision, breathing) and complications of lesions such as ulceration and bleeding. Treatment options include corticosteroids (systemic or intralesional), interferon, vincristine, laser treatment or surgical excision. The ideal treatment varies by site: for subglottic lesions, surgical excision is now the treatment of choice[26], whereas vincristine is finding a place for extensive subcutaneous lesions. In the absence of functional problems, the best management is to wait for spontaneous resolution **(Fig 8)**.

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# Paediatric Hearing impairment in the United Kingdom: Screening and statistics

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## ABSTRACT
Newborn hearing screening has been demonstrated to be a cost effective mechanism for the identification of children with permanent hearing loss, allowing early intervention and optimising long term outcomes. The screening programme in the United Kingdom (UK) aims to identify those with bilateral loss of at least 40dB (average 0.5, 1, 2 & 4 kHz). Current figures suggest that the yield from screening is around 1:1000 children screened, which is consistent with the known incidence. Areas of ongoing interest include the use of automated auditory brainstem response as a routine screening tool in the UK, identification of those children who develop hearing impairment after screening, mechanisms for ensuring minimisation of children lost to follow-up, and the diagnosis of auditory dyssynchrony / auditory neuropathy.

## KEY WORDS
Newborn, neonatal, hearing, screening.

The incidence of permanent childhood hearing loss (PCHL) of at least 40dB (average 0.5, 1, 2 & 4 kHz) in the better hearing ear is thought to be around 1:1000 in infants[1]. In the UK this equates to an estimated 840 children born yearly with moderate to profound deafness. One of the most important factors in treatment is early intervention to minimise the impact of hearing impairment on development[2,3]. Hearing screening in the United Kingdom (UK) was previously undertaken using the health-visitor distraction test between 6 and 12 months of age with a median age of detection of hearing loss between 12 and 20 months. Screening in this way was felt to have a sensitivity of around 40%, and 20% of children were never screened. With a median detection age of 26 months and subsequent six month delay to treatment, health visitor distraction screening did not allow early intervention[4].

Targeted hearing screening has been used in many areas to screen those children at greater risk of hearing loss from a variety of aetiological factors (e.g. prematurity, a prolonged stay on NICU, severe jaundice, use of ototoxic antibiotics, family history, and craniofacial abnormalities). The concept of universal neonatal hearing screening is based on the Rhode Island hearing study,[5] which used transient evoked otoacoustic emissions to screen 18,000 children. Of these children, 11 were subsequently found to have a hearing loss of > 40dB bilaterally; five of the children identified as having a hearing loss would not have been identified by targeted screening.

Any screening programme has to be justified in terms of incidence and impact of the disease being screened for,

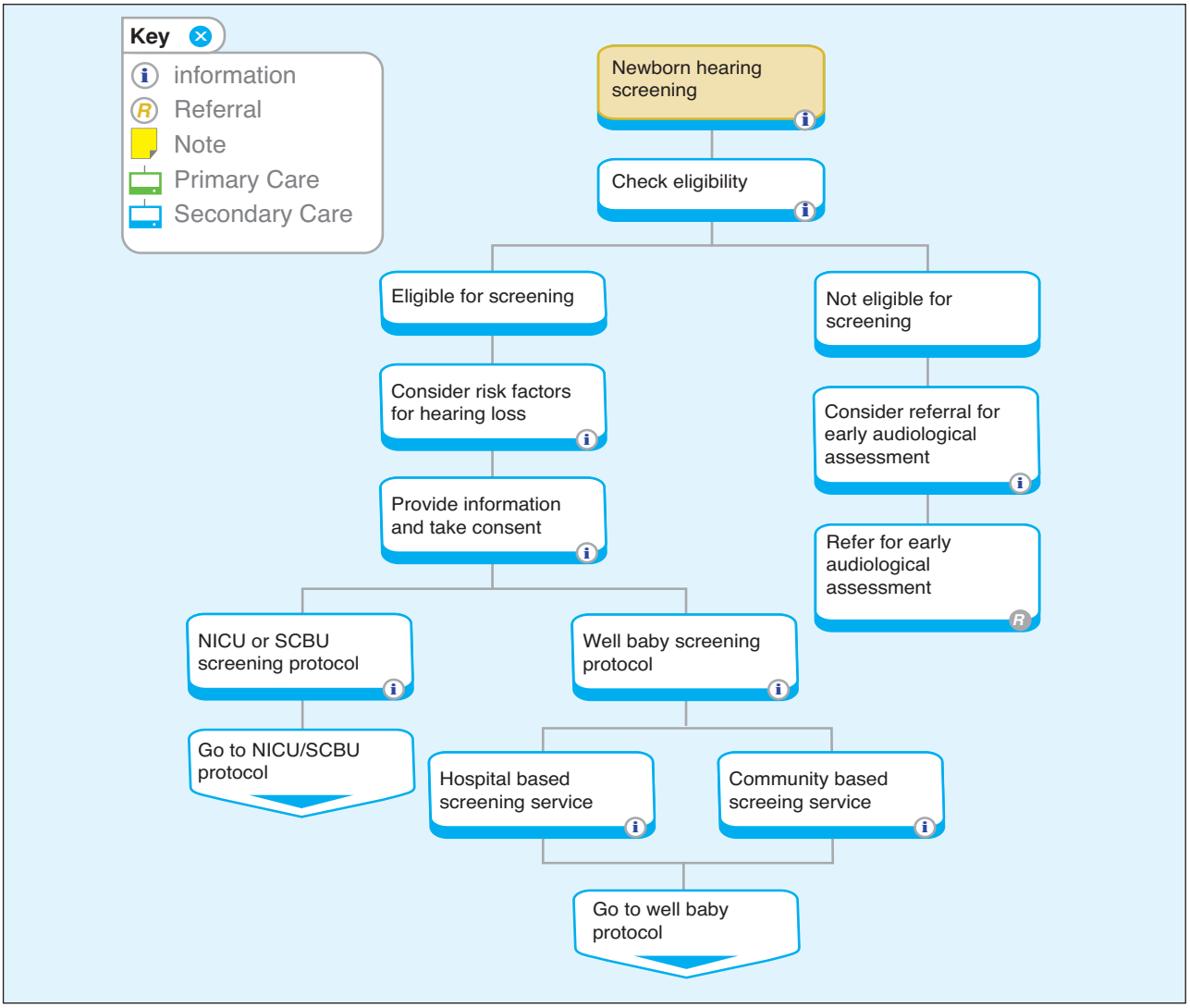


*Figure 1A. NHSP Care pathways for "well babies" (reproduced with permission from http://hearing.screening.nhs.uk/.)*

potential interventions available, and specificity and sensitivity of the screening test. Hearing impairment can be shown to impact on long-term socio-economic outcome and quality of life[6-9]. It is suggested that early identification and intervention results in the best long-term outcome2,3 with screening of newborn children shown to be both cost-effective and efficient[10-11]. A systematic review by Davis *et al*.[12] supported the introduction of what is now called the Newborn Hearing-Screening Programme (NHSP) in the UK. This was introduced in 2001 at a number of first phase sites with the aim of full coverage by 2005. The screening programme aims to identify children with PCHL of at least 40dB (average 0.5, 1, 2 & 4 kHz) in the better hearing ear.

There are two different screening protocols used in the NHSP (http://hearing.screening.nhs.uk); one for well babies and one for those that have spent more than 48 hours on the neonatal intensive care unit (see Figures 1 and 2). The "well-baby" screening protocol can be hospital or community-based and is carried out by health visitors or screeners specifically employed to perform hearing screening. The initial screening test is an automated transient evoked otoacoustic emission test (AOAE). Otoacoustic emisions are sounds generated in the outer hair cells of the cochlear which can be recorded in the ear canal. A probe is inserted into the infant's external ear canal and an acoustic stimulus, consisting of broadband clicks is applied to the ear through the probe, which also records sound. In the presence of normal or near-normal hearing (0–30 dBHL), an amplified version of the original stimulus will be recorded after an interval of 5ms, lasting about 15ms. This sound is produced by intact outer hair cells, and absence suggests the outer hair cells are abnormal, indicating cochlear hearing loss.

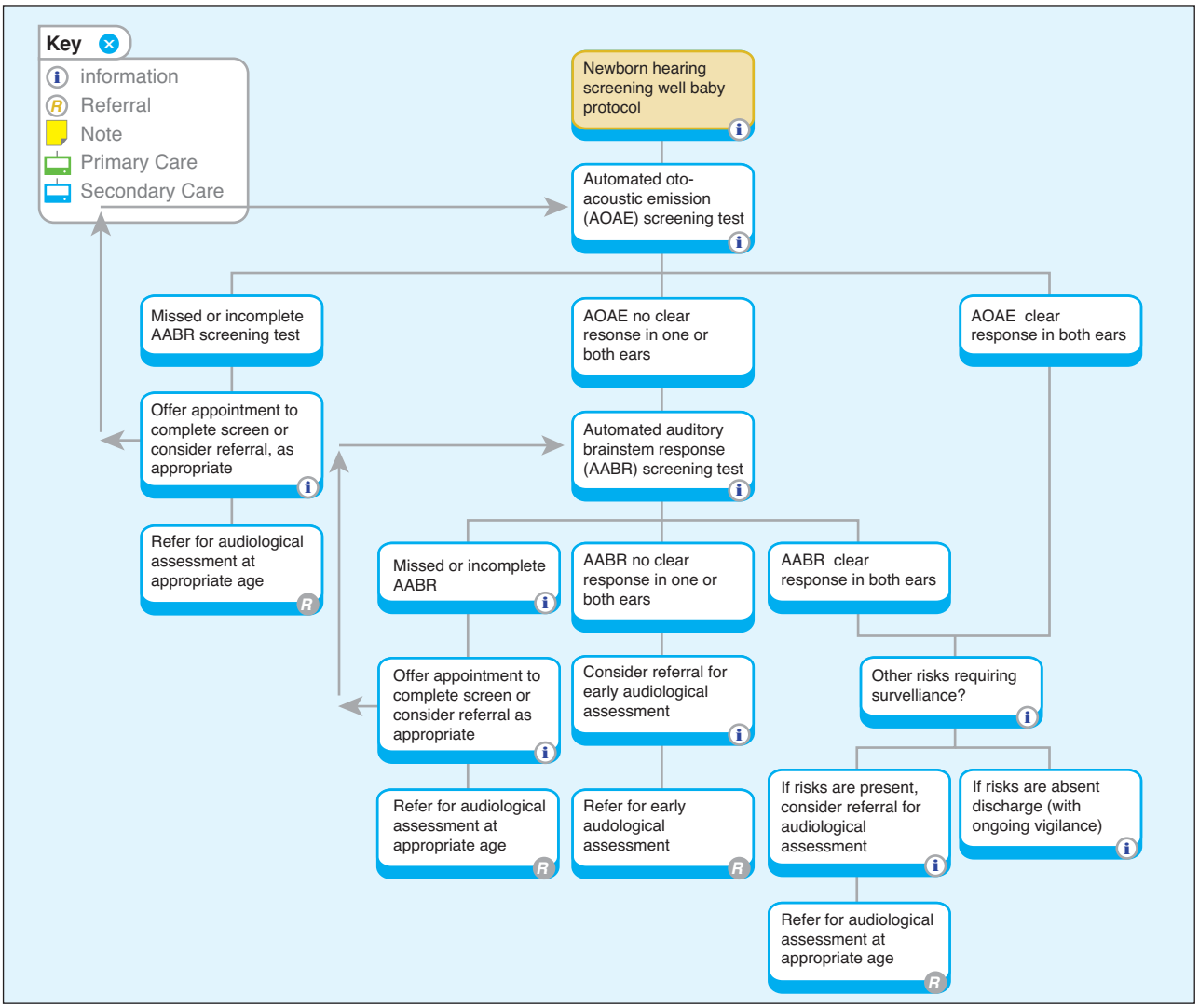


*Figure 1B. NHSP Care pathways for "well babies" (reproduced with permission from http://hearing.screening.nhs.uk/.)*

If there is no clear response to the initial test, a second AOAE test is undertaken. If there is no clear response on this test, an automated auditory brainstem evoked response test (AABR) is carried out. AABR is based on the brainstem electrical waveform response to auditory stimulation, which is measured by surface electrodes. Waveform peaks occur within 10-milliseconds of stimulus and are labelled I-VII. Recording electrodes are placed on the mastoid, forehead and neck. The stimulus currently used is a click generated by an electrical pulse of 100$\mu$s duration, at a high rate to minimise test time (usually greater than 30 clicks per second). The level of the click stimulus is usually 35 to 50dBnHL. The presence or absence of a response in the recorded waveform is determined objectively by the automated ABR machine using an algorithm based on mathematical techniques. The machine will conclude a 'pass' if a response is present. If the AABR results in "no clear response" repeat AABR is again undertaken; if no clear response persists in one or both ears on repeat testing, the newborn is referred to audiology for early audiological assessment.

Hearing screening including AABR should be completed by five weeks of age. The use of a two step, two stage screen with repeat AOAES followed by AABR where needed, allows the management of referrals for diagnostic testing to an acceptable level. A number of studies have reported significantly lower yield rates (and therefore presumably fewer false positives) with AABR (either as a primary or secondary screening modality) than AOAE and fewer referrals from repeat screening of those with no clear response from the initial screen[13,14].

A second protocol applies to newborn babies in the neonatal intensive care unit or special care baby unit (NICU or SCBU). Because these babies are at greater risk

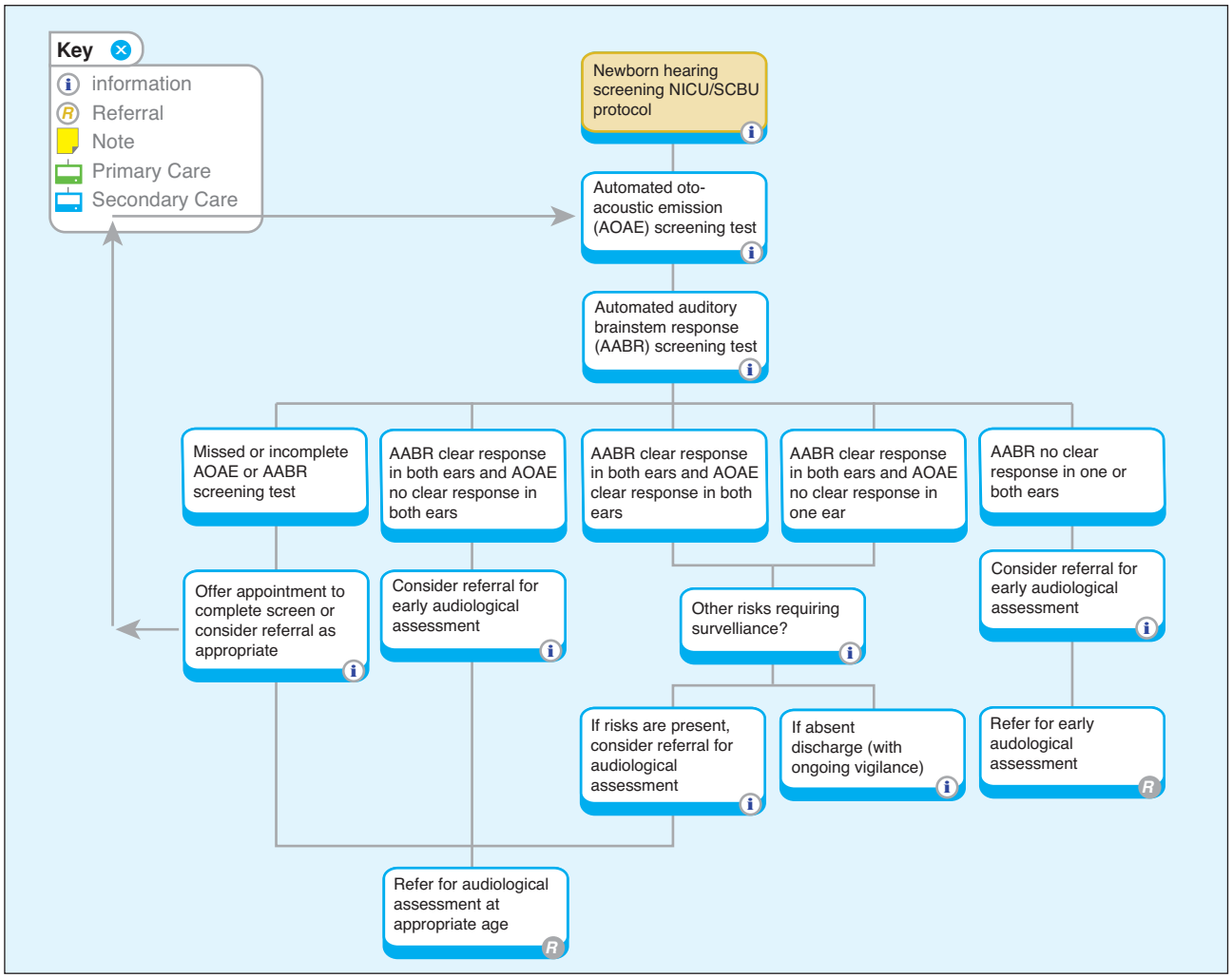


*Figure 2. NHSP Care pathway for "NICU / SCBU babies" (reproduced with permission from http://hearing.screening.nhs.uk/.)*

of problems affecting the hearing pathway beyond the cochlear hair cells, both the AOAE and AABR are performed on both ears, whatever the response to AOAEs. Screening is not performed on babies less than 34 weeks gestational age but where possible should be completed by 44 weeks gestational age. For further detail see http://hearing.screening.nhs.uk/.

Following referral for full audiological assessment, subsequent bilateral permanent hearing loss ≥40dB will be confirmed in approximately 1:1000 screened children.? However, it should be borne in mind that the presence of OAEs does not definitively confirm hearing, only the function of the outer hair cells. One of the questions to be addressed relates to the identification of false negatives from the screening process and those children who develop hearing impairment after passing their screening test. A recent review of school entry screening reported that of 3.47:1000 children with permanent hearing impairment at school screening age 1.89:1000 required identification after newborn screening[16]. The increased incidence is due to a combination of post- natal events (e.g. meningitis, chemotherapy), delayed diagnosis of pre-existing conditions, and later onset of effects of certain genetic mutations.[1,17].

The possibility of false negatives from AOAE screening raises the argument for the use of AABR as a routine, first step, universal screening tool, rather than reserving it for use in those children who are referred for further testing from AOAE. The argument against centres around the extra time needed for AABR and hence cost. However, this may be countered by the lower referral rate and may need revisiting as testing equipment evolves and the time required for AABR decreases. The optimal way of determining post-natal deafness is also under debate - although some children may have risk factors clearly warranting surveillance, many who go onto develop hearing loss would not have been identified using known risk factors[18]. Whether this group of

**Table 1.** *Assessment of child for aetiology of hearing loss identified by screening.*

| | |
|---|---|
| Family history | Congenital hearing loss<br>Consanguinity |
| Prenatal history | Viral illness (e.g. rubella)<br>Drug exposure<br>Endocrine disorders (e.g. hypothyrodism) |
| Perinatal history | Low birth-weight<br>Hyperbilirubinaemia<br>Sepsis<br>Ototoxic drugs |
| Post-natal history | Bacterial meningitis |
| | Cytomegalovirus |
| | Ototoxic drugs |
| | Global developmental delay |
| Clinical examination | Syndromic features |
| ECG | Long QT interval (Jervell and Lange-Nielsen syndrome) |
| Urine dipstick | Nephropathy |
| Genetic testing | GJB2 (Connexin-26) |
| Radiological imaging | CT and/or MRI |
| Opthalmology assessment | Visual acuity and fundoscopy |
| Infection screen | Cytomegalovirus<br>Rubella<br>Toxoplasmosa<br>Syphillis |

children is best identified through a second universal screening programme, or whether at-risk children will be identified through mechanisms such as genetic screening remains to be seen[19].

However, initial results from the screening programme as it stands are encouraging. A recent review of UK first-phase screening sites gave a median age of assessment of five weeks, with diagnosis at a median of 10 weeks and hearing aid fitting at 16 weeks. They reported 96% coverage, a referral rate of 3% including bilateral and unilateral impairment, and a subsequent yield of 1:1000 (95% confidence intervals: 0.78-1.22).12

Following identification of a child with hearing impairment, timely initiation of an appropriate strategy to assist the child is needed combined with investigations to attempt identification of aetiology of hearing loss. Investigation of aetiology may assist with prediction of outcome from intervention (e.g. Connexin-26 deafness), likelihood of progression (e.g. enlarged vestibular aqueduct syndrome), identification of other morbidities (e.g. vision, cardiac), as well as planning future care and providing improved advice and counselling to the family. Assessment to determine aetiology is performed as soon as possible and include a detailed clinical assessment and investigations (see Table 1).

Children who are identified prior to six months of age and are given appropriate support and early intervention can be seen to have substantial language benefits at age five[2,3]. However, the screening programme can only be as strong as the weakest link in the follow-up chain. Although the sensitivity of the screening programme may be 80-90%,1 if follow-up rates and intervention rates fall, the sensitivity will subsequently drop. This is undoubtedly an issue in many reports with rates of children who are lost to follow-up ranging from 10 to 84%[20,21,12].

This raises a number of issues with regard to being more proactive in following-up children with moderate hearing losses for further assessment and managing the ongoing care of patients who would benefit from aiding but are delayed due to parental choice. The importance of engaging the family in the decision-making process is crucial both because positive involvement of the family is a factor in language outcome at five years,[3] and because many of these children will need regular and prolonged follow-up with numerous visits to a hospital or clinic setting. This is often a factor in delayed diagnosis and subsequent attrition.

Two other groups of patients should be considered separately; those who go on to cochlear implantation and those that are diagnosed with possible auditory neuropathy. There is good evidence for improved outcome in terms of speech perception and language with earlier implantation in prelingually deaf children[22-24]. More recent work has looked at the effect of implantation at younger and younger ages with Govaerts et al.[25,] finding the best results in Categories of Auditory Performance (CAP) scores and mainstream school integration coming with implantation before two years of age with a significant decline in those implanted after four years of age. Schauwers et al[26]. found improvement in onset of age-appropriate CAP scores and babbling in children implanted as young as five months.

One of the considerations against very early implantation is the possibility of auditory neuropathy (AN). AN is a condition characterised by normal cochlear outer hair cell function, as judged by OAEs or the presence of a cochlear

microphonic, but abnormal VIII nerve function, as assessed by ABR[27]. Since this combination of findings covers a wide range of potential pathology, not all of which are neuropathy, it has been suggested that the more appropriate term auditory neuropathy / auditory dyssynchrony (AN/AD) be used. Since ABR is a test of neural synchrony in response to external stimuli, loss of synchronous discharge (auditory dyssynchrony) results in a failure to record an ABR or an abnormal ABR. The functional effect of this ranges from total deafness to normal hearing in a quiet environment but impaired hearing in background noise. However, the level of hearing loss does not correspond to ABR results and behavioural testing will normally need to be undertaken in infants to ascertain true hearing thresholds before definitive intervention can be undertaken[28]. The true incidence is unknown but identified risk factors include hyperbilirubinaemia, anoxia, hypoxia/prolonged assisted ventilation, prematurity under 28 weeks, presence of other congenital abnormalities, de-myelinating conditions, genetic factors, and syndromes associated with other peripheral neuropathies[29-31].

The natural history in AN is also variable: the abnormal ABR may regain normal morphology and become consistent with the behavioural threshold; perceptual ability may improve with persistence of abnormal ABR; OAEs / cochlear microphonic may disappear. One of the potential causes of this pattern on screening is delayed maturation of the auditory nerve secondary to prematurity with or without mild hyperbilirubinaemia. These children will tend to recover completely by 12-18 months and should undergo regular re-assessment. If recovery has not occurred by this time, another pathology should be suspected. With the push towards earlier intervention, including cochlear implantation, it is important to ensure that these children have had time to develop before significant interventions are undertaken. The failure to identify those children suffering AN adds weight to the inclusion of AABR as a universal screening tool in the NHSP.

## CONCLUSIONS

Newborn hearing screening programmes have been shown to be a cost-effective method of identifying children with permanent hearing loss, allowing early intervention and optimising long-term outcomes. Current issues surround the optimal screening methods to use, mechanisms for ensuring follow-up of children identified from the screening procedure, and identification of those that develop hearing impairment after screening or are missed in the screening programme. In addition guidelines are needed for the management of unilateral and mild hearing loss.

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# Management of the inflammatory airway in children

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## Abstract

The airway in children is relatively narrow with much less reserve than in adults. Hence inflammatory conditions in the respiratory tract in children can quickly progress to cause airway obstruction. Mucosal infection will cause oedema while extra-mucosal infections – such as neck space abscesss- may compress the airway. It is important that all clinicians involved in the management of these conditions in children understand the principles of emergency care of the obstructed airway. Once the airway is secure, definitive management of specific pathologies can take place.

This review outlines the main infective conditions that cause airway obstruction in children. It includes a resume of best current practice in initial assessment, diagnosis and management, and in definitive treatment of the commoner presentations.

## Key words

Airway obstruction, Croup, Epiglottitis, and Child

## Introduction

The paediatric airway extends from the nasal vestibule to the bronchioles. Inflammatory conditions can involve any segment of the airway either by direct involvement of the mucosa – e.g. acute laryngotracheobronchitis (ALTB) or croup- or by external compression of the air passages such as occurs in retropharyngeal and parapharyngeal abscess. Inflammatory disorders involving the bronchi and the bronchioles are largely the preserve of the respiratory paediatrician and are not covered here.

The aetiology, presentation and natural history of airway infections vary with the age of the child and with the segment of the airway affected.

## Presentation

As a general rule, airway infections cause acute and progressive airway obstruction. The history is short, typically hours or days. The child's breathing will become laboured and noisy. The respiratory rate increases, and the accessory muscles of respiration come into play as the child works harder and harder to maintain oxygen saturation in the face of increased airway resistance. The child – and the parents or carers- will become distressed and frightened. Breathing is noisy until the late stages when the onset of quiet breathing may suggest not a reduced airway resistance but a tired child who is close to respiratory arrest - apnoea. Reduced oxygen saturation is a worrying development that requires careful monitoring and early intervention. Cyanosis secondary to airway obstruction is a late and ominous sign and should be averted with appropriate management.

Airflow in the presence of an increased airway resistance loses its smooth laminar pattern and becomes turbulent. This is manifest as noisy breathing, the nature of which depends to some degree on the site of the pathology. Airway obstruction in the flaccid distensible portions of

the airway- i.e. the nasal cavities, the nasopharynx and the oropharynx- causes a low-pitched snore-like noise – 'stertor'. This is typically worse when the child sleeps as the pharyngeal tissues become lax and lose their tone. Laryngeal and upper tracheal obstruction causes a high-pitched whistling sound on inspiration– inspiratory 'stridor'. Mid and lower tracheal obstruction is often particularly marked in expiration as the tracheal airway collapses- expiratory 'stridor'. Bronchial and bronchiolar obstruction – e.g. asthma- causes 'wheezing'[1].

Some of the principle infective conditions that present to otolaryngologists are listed in tables 1 (a) and 1 (b).

## Emergency Management

The great majority of children with airway obstruction do not present 'in extremis'. The commonest condition is ALTB or Croup and it is important for those of us who work in hospital practice to remember that most cases are dealt with perfectly well in primary care, more commonly nowadays with the more widespread use of systemic glucocorticoids which has transformed the management of this once much more worrying condition. A less hurried approach can be adopted in early and less severe presentations; every clinician who may need to deal with airway disorders in children needs to understand the principles of Advanced Paediatric Life Support and have a structured approach to initial management of severe cases so as to avert disaster until the help of a more senior colleague is available[2]. Quickly assess child's general condition including the respiratory rate, look for recession of the chest and use of neck muscles and listen to the breathing pattern. Gasping is a sign of severe hypoxia and may need rapid intervention. Listen to the chest- a silent chest is extremely worrying. In the seriously ill child, you will need to move immediately to resuscitation. The first priority as always is to establish a patent airway first by lifting the chin and thrusting the jaw forward, then by use of an adjunctive airway e.g. a nasopharyngeal or oropharyngeal (Guedel) airway before going on to airway support via bag and mask ventilation. High flow oxygen (15 Litres per minute) may help reverse hypoxia. If the child does not quickly respond consider endotracheal intubation or very rarely if this is not possible an emergency cricothyroidotomy to bide time. Formal tracheotomy is one measure that will of course establish an alternative airway but it is almost never required. Modern management techniques for inflammatory airway diseases are so much improved from say twenty years ago that a tracheotomy is a very rarely performed procedure in a child with an acute infection causing airway obstruction – in a recent series of over 100 consecutive tracheotomies in children not one was needed where the primary indication was infection[3].

**Table 1 (a)**
**Stertor: Conditions of the nose and pharynx causing airway obstruction**

- Rhinitis ( May simulate choanal atresia in the newborn)
- Pharyngitis (Includes Tonsillitis, Infectious Mononucleosis and Diphtheria)
- Neck space infections (Includes retropharyngeal, parapharyngeal and submandibular space abscesses)

**Table 1 (b)**
**Stridor: Laryngotracheal conditions causing airway obstruction**

- Acute laryngotracheobronchitis (ALTB) or 'Croup'
- Acute bacterial tracheitis
- Acute epiglottitis

Assess the cardiovascular status by monitoring pulse and blood pressure. Once the airway is secure continue with ventilating the child and then go on to circulatory resuscitation, initially by securing intravenous or intraosseous access.

## Investigation and Diagnosis

### History and examination

The clinician needs to make a firm diagnosis in all cases of paediatric airway obstruction. This can be addressed in the more severe cases when the airway has been secured and earlier in less severe presentations where emergency measures are not needed. The history, the nature of the noisy breathing (Tables 1a and 1b) and the age of the child are important pointers.

***Acute laryngotracheobronchitis*** (ALTB) or Croup typically presents in children between the ages of six months and four years with progressive stridor, hoarseness and a cough. ***Acute epiglottitis*** is now extremely rare in communities where the Haemophilus Influenza virus (HiB) vaccine is routinely administered but clinicians still need to be alert to it. It presents typically in children under six years with progressive stridor – usually not as harsh as ALTB- of rapid onset (three to six hours) drooling, fever and a sore throat ***Bacterial tracheitis*** or '***preudo-membranous croup***' causes copious secretions and a very ill toxic child with high fever.

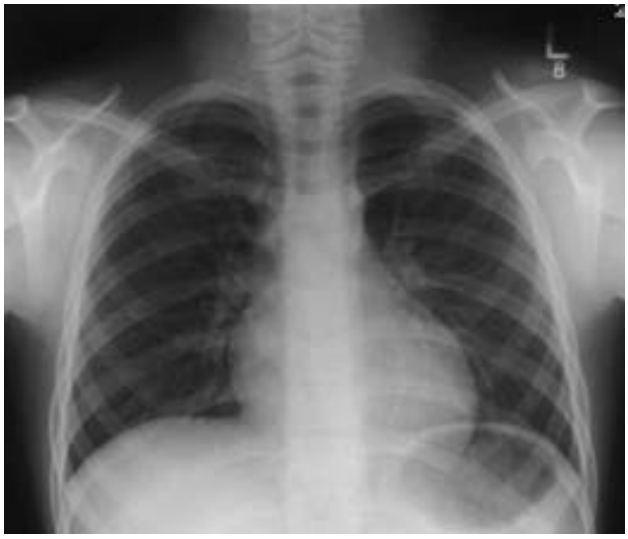

**Fig 1** *Plain X Ray of the neck showing narrowing of the subglottic airway in acute laryngotracheobronchitis (croup) - the 'steeple' or 'pencil tip' sign.*

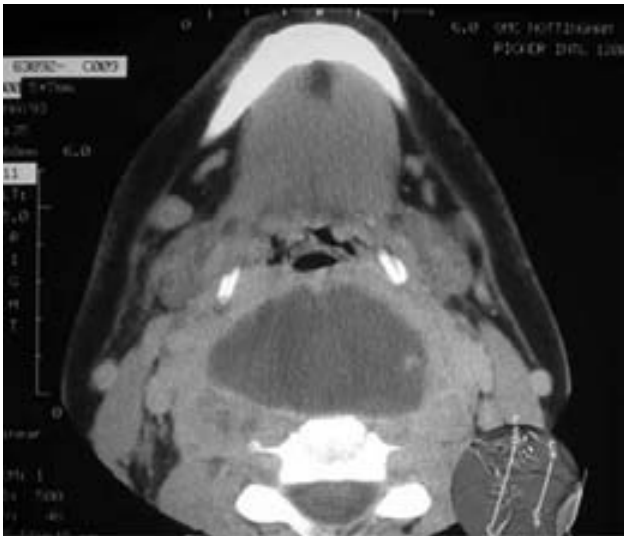

**Fig 3** *MRI Scan showing a retropharyngeal abscess partly obstructing the airway.*

Mild ALTB can be safely managed in primary care particularly now that systemic gluco-corticoids are widely used as first line management but acute epiglottitis and bacterial tracheitis in a child are indications for admission and the child is best managed on a paediatric intensive care unit (PICU) with endotracheal intubation. Hence the distinction is vital[4].

Conditions such as ***infectious mononucleosis, acute pharyngitis, acute tonsillitis and neck space infections*** will usually be apparent from the history and examination.

## Imaging

Provided the child is well enough to go to the X-Ray Department (or have an X-Ray taken on the ward or in the emergency room) imaging can be helpful[5]. A Chest X- Ray and a plain film of the neck may show the characteristic features of ALTB or Croup (Figure 1) or acute epiglottitis (Fig 2). CT and MR scanning may demonstrate retropharyngeal or parapharyngeal abscess but either examination will sometimes require general anaesthesia and may not be appropriate in a sick child (Fig 3). Decide on a case by case basis ideally in consultation with a paediatric radiologist.

**Fig 2** *showing the features of acute epiglottitis. Note the 'blurring' of the epiglottis - 'thumbprinting'.*

## Monitoring

Once the child's condition has stabilised and he has been admitted to a ward it is important to monitor his progress and response to treatment. Clinical assessment needs t focus on general condition including breathing, respiratory rate, cardiovascular measures and oxygen saturation. In the severely ill child where endotracheal intubation is considered the help of a paediatrician/ paediatric anaesthetist or paediatric intensivist will be needed. If the child needs endotracheal intubation he is ideally monitored on a paediatric intensive care unit (PICU) if available. Children with infective airway obstruction can deteriorate very quickly and if you have any concerns the child is not responding quickly it is better to be cautious and seek help.

## Endoscopy

In mild or croup or even severe croup where recovery is rapid and complete a clinical diagnosis is sufficient and the child may be discharged. In most other situations the definitive diagnosis of inflammatory laryngotracheal airway conditions is made by endoscopy. Pharyngeal pathologies may be apparent on examination of the throat in clinic but children with airway obstruction do not tolerate any intervention involving instrumental

inspection of the throat well.
If there is any suspicion of acute epiglottitis do not attempt any sort of instrumentation, seek senior help as soon as you can. Paediatric airway endoscopy is nowadays a highly skilled procedure ideally undertaken in a dedicated paediatric ENT unit by a skilled ENT surgeon with experience of the techniques and instrumentation needed and with the support of a dedicated paediatric anaesthetist[5].

## Management and Outcome for Specific Conditions

### Neonatal Rhinitis

Newborn babies sometimes present with severe nasal obstruction, mimicking choanal atresia. Examination confirms that the choanae are patent but the nasal mucosa is red and oedematous. The condition is usually self-limiting but can be severe enough to warrant treatment with a short course of intranasal steroids.

### Acute Tonsillitis

Acute bacterial tonsillitis can precipitate severe airway obstruction in a small number of children, particularly those with an antecedent history of sleep apnoea. Down syndrome children, children with craniofacial syndromes and children with neurodisability e.g. cerebral palsy are especially at risk. They may need endotracheal intubation and even urgent tonsillectomy, but a nasopharyngeal airway if tolerated will often bring about considerable improvement. In addition to management with antibiotics, systemic steroids (dexamethasone) can help resolution.

### Acute Pharyngitis

Severe acute pharyngitis – especially Infectious mononucleosis- can similarly precipitate airway obstruction. ***Diphtheria*** is now extremely rare but sporadic cases do occur and can cause rapid and sometimes fatal airway obstruction. Treatment is supportive management of the airway, antibiotics (penicillin) and antitoxin if it is available[4].

### Neck Space Infections

The fascial compartments of the neck give rise to a number of spaces where oedema and pus can collect, in some cases compromising the airway. Tonsillar infection can give rise to quinsy or ***parapharyngeal space abscess***. In young children –typically under the age of two years- with airway obstruction, fever and feeding difficulties, consider a ***retropharyngeal abscess.*** This is a collection of pus due to suppuration in a group of lymph nodes in the space behind the posterior wall of the oropharynx (fig 4). Treatment is support of the airway, antibiotics and surgical drainage as needed. An intra-oral approach with the help of a skilled paediatric anaesthetist is best. In ***submandibular space infection*** ('Ludwig's Angina') the oropharyngeal airway can obstruct. An oropharyngeal (Guedel) or nasopharyngeal airway will usually overcome this but some children will need endotracheal intubation. Definitive management is with antibiotics; surgical drainage is difficult as often the swelling is due to oedema rather than pus.

### Croup

Croup is usually due to the parainfluenza virus, the respiratory syncitial virus or an adenovirus. Management was traditionally expectant with therapy focussed on airway support but the widespread use of glucocorticoids has greatly reduced the distress and morbidity associated with this condition. If a presumptive diagnosis of croup is made give a single dose of dexamethasone (0.6 mgs per Kg). Oral steroids are at least as efficacious as inhaled steroids, easier to administer and better tolerated6-8. Intramuscular steroids are efficacious but now contra-indicated due to the risk of local muscle necrosis at the injection site[9]. Nebulised epinephrine (*1ml of 1 in 1000 epinephrine diluted in 3ml of 0.9% saline*) has a role in reducing mucosal oedema but benefit is short-lived, up to about one hour[4].

Humidification of inspired air has a long tradition in the management of croup but there is little evidence of efficacy[10]. Some of the pharmacological measures used to treat children with croup- applicable to airway obstruction in general- are shown in Table 2.

### Acute epiglottitis

This is now very rare in communities where the Haemophilus Influenza b (HiB) vaccine is routinely given to children. Occasional vaccine failures occur and a very small number of cases can be due to organisms other than haemophilus influenza, particularly in immune-compromised children[11]. Management is airway support with admission ideally to a PICU, endotracheal intubation and antibiotics – ideally a third generation cephalosporin as many strains of haemophilus influenza are now resistant to penicillin. Endoscopy confirms the diagnosis but should only be considered when the child has a secure endotracheal airway.

**Table 2**
**Pharmacological interventions in airway obstruction**

- Glucocorticoids – (Dexamethasone)
- Oxygen (may be humidified)
- Nebulised adrenaline
- Bronchodilators
- Antibiotics

## Bacterial Tracheitis

This is a more serious condition than viral croup. Older children (mean age four years) are typically affected and there is no response to steroids. Endotracheal intubation and sometimes therapeutic bronchoscopy with lavage are often needed. The child will require admission to a PICU.

Very sick newborn babies on a PICU- often with multiple pathologies- are at risk of a potentially fatal desloughing of the tracheal mucosa – necrotising tracheobronchitis[12].

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# Congenital Nasal Abnormalties

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**Abstract**
Congenital nasal abnormalities are uncommon but have the potential to cause life-threatening airway obstruction or meningitis. The management of choanal atresia, nasal dermoids, nasal encephaloceles and gliomata are discussed.

**Key words**
Congenital, nasal, choanal atresia

Congenital nasal abnormalities present an intriguing and challenging problem to the paediatric otolaryngologist. The implications of an obstructed nasal airway to the neonate often complicates investigation and treatment of these anomalies and the potential for many of them to have intracranial connections means the risk of meningitis is ever present if they are not managed correctly from the outset.

## Choanal Atresia.

Choanal atresia affects 1 in 8000 live births and may be unilateral or bilateral, unilateral being commoner1. The atretic segment, separating nasal cavity from nasopharynx, is classically described as either bony or membranous but is most commonly a mixture of the two. Entirely membranous atresias are rare. There is often an abnormality more complex than the presence of an atretic plate of bone, with excess bone laterally, narrowing the nasal cavity posteriorly. In children with bilateral choanal atresia the presence of the CHARGE association (colobomata of the eye, heart defects, atresia of the choanae, retardation of growth, genital abnormalities, ear abnormalities) should be excluded[2].

Bilateral choanal atresia presents classically as respiratory distress in the neonate, an obligate nasal breather. This may be life-threatening. Unilateral atresia may present may be detected in the neonatal period or may present in older children with unilateral nasal obstruction and discharge. In the neonate where the diagnosis is suspected the condition is suspected by the failure of a cold metal spatula to 'mist' when placed under the nose and confirmed by the inability to pass a nasogastric tube. False reassurance can be given if the tube rolls up in the nasal cavity. In cases of doubt decongesting the nose with topical vasoconstrictor can be helpful as can using a small endotracheal tube in place of the nasogastric tube.

Emergency management in the form of a correctly positioned oropharyngeal airway is life saving. This may be taped securely in position to secure a safe airway. An alternative to this is to use a specially adapted feeding nipple. With these interventions it is uncommon to need to resort to endotracheal intubation.

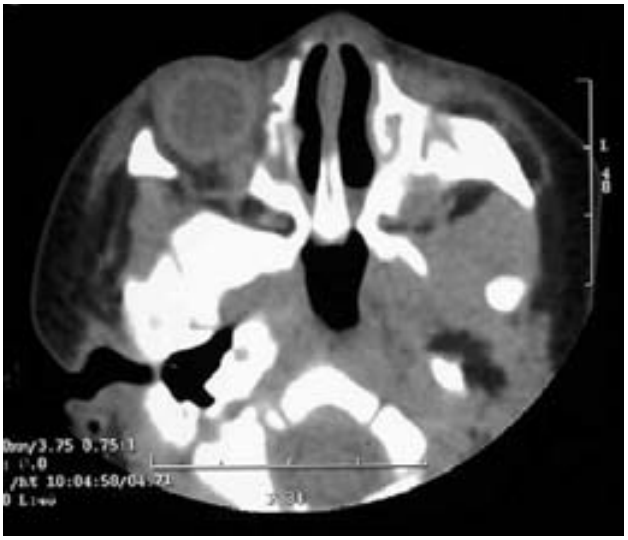

**Figure 1:** *Axial CT scan showing bilateral choanal atresia.*

Prior to considering surgery many surgeons obtain a computed tomography scan in order to determine the nature of the atresia and its relation to the skull base (fig 1). Acquisition of high quality images is facilitated by suctioning the nasal cavities immediately prior to the scan to remove excess nasal mucus. Some authors have also advocated the use of CT navigation to facilitate surgery[3].

Treatment is by surgical removal of the atretic bone and/or membrane. Surgery for bilateral and poorly tolerated unilateral lesions should be performed within the first few days of life. In the case of well tolerated unilateral lesions, surgery may be deferred until the child is one as the risks of anaesthesia are much reduced after this age compared to the neonate.

There are several approaches to this and the advent of the endoscope has allowed significant developments in this surgery[4,5,6]. The choanae may be visualised through the nasal cavity using a 0 degree endoscope or from the nasopharynx using a 120 degree endoscope (fig 2). Under direct visualisation the atretic plate can then be perforated using a urethral sound and the bony choanae enlarged using a cutting or diamond burr. Soft tissue can be removed using a microdebrider or a CO2 or KTP laser[7,8,9]. Removal of the posterior part of the vomer is felt by many to reduce the amount of restenosis. This is easily performed using a 'backbiting' punch. Application of mitmycin C postoperatively has been advocated to reduce restenosis[9,10].

The use of stents post-operatively is a subject for debate. Many surgeons leave a stent (either preformed or fabricated from a endotracheal tube) in place for 6 weeks. Not placing a stent often requires an early planned return to theatre for

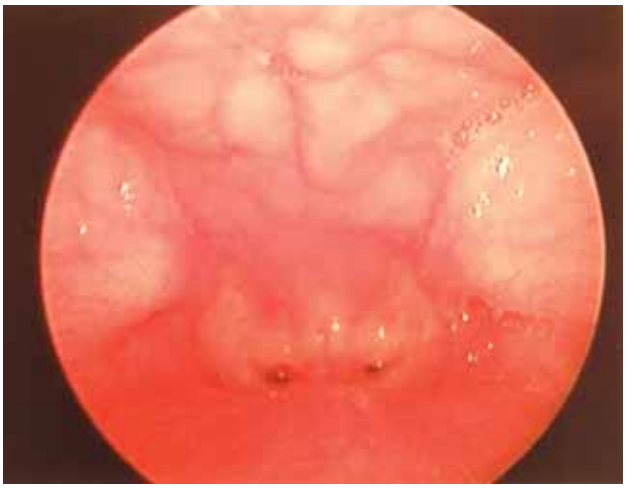

**Figure 2:** *Endoscopic view of posterior choanae using 120 degree endoscope. There is bilateral atresia.*

endoscopy to remove any excess tissue. Placing a stent does have the advantage of establishing and maintaining a safe airway for the child (if it is kept clear with regular suction and irrigation if necessary) and removes the need for early re-endoscopy where this is impractical. Some authors have suggested that stents may promote granulations and early restenosis. There is little evidence to support one view over the other.

The classically describe trans-palatine approach, whereby a posteriorly-based palatine flap is created and the bone drilled away from inferiorly, has gradually been superceded by the endoscopic techniques described above[1]. It does have some applications however, in the case of failure of endonasal techniques or when access for these techniques is limited. The transpalatal approach has been advocated as a primary technique for patients with CHARGE and bilateral atresia as this group has poor results generally after surgery[11]. It remains the case, however, that most surgeons would attempt and endoscopic repair primarily where this was feasible.

There is currently a significant rate of restenosis after surgery and/or stent removal. Many patients will require more than one procedure[12,13,14]. Post-surgical dilatations may be performed with metal dilators (such as Hagar's) or using a balloon dilatation technique. Restenosis is said to occur in most cases in the early post-operative period.

## Congental pyriform apeture stenosis

This is a rare congenital abnormality. There is stenosis of the pyriform apeture of the nose with bony thickening of the nasal processes of the maxilla. Depending on the severity of the stenosis the child may present in a similar manner to those with bilateral choanal atresia. There is an

association with dental abnormalities (a single upper incisor being classically described) and endocrine abnormalities. The diagnosis is suspected on the basis of clinical examination and confirmed on CT scanning. The excess bone can be drilling out via a sublabial approach to widen the nasal airway[15]. Stents may be placed in a similar manner to choanal atresia. Restenosis, in the xperience of the author, seems to be less of a problem than with choanal atreisa.

## Nasal dermoids

These represent a midline inclusion anomaly. They present with a midline lump on the nasal dorsum or glabella. There is often an associated punctum which may secrete sebum or fluid. A hair emerging from the punctum is said to be pathognomonic. The punctum may occur at any point on the midline of the nose and may be located as far caudally as the tip or columellar. The anomaly may consist of single or multiple cysts with or without the presence of a tract. They may be communication with the intracranial cavity and they may be a communication with the sudbural space[16].

When the diagnosis is suspected imaging is mandatory to determine the extent of the abnormality, to exclude intracranial connection and to plan surgery. CT scanning delineates the bony anatomy and may give indication of an intracranial connection. Many features are used to predict this such as an intracranial soft tissue mass, a bifid crista galli , inert orbital wideneing or a cribiform plate defect[17]. Some of these, however, may be present in the normal child and therefore MRI scaning is often required and is becoming the imaging modality of choice in these cases[18,19]. It is prudent in many cases (especially where the child requires GA or sedation for scanning) to either obtain both at a single sitting or to proceed directly to an MRI scan.

Treatment is surgical. There is little scope for conservative management unless there is a contraindictaion to surgery or anaesthesia. Recurrent infection can render surgery more difficult in the future or cause rupture of the cyst with fistulation onto the nasal dorsum. Removal of the lesion can be accomplished using a midline excision (which has the advantage of being technically easier and allowing excellent access to the skull base), an external rhinoplasty approach (which generally has a more pleasing cosmetic result but can limit access where an intracranial connection is suspected) or via an endosnasal rhinoplasty approach (which gives a better cosmetic result but is technically more challenging and further limits access to the skuul base). Many authors advocate the external rhinoplasty approachas offering sufficient access when there is no

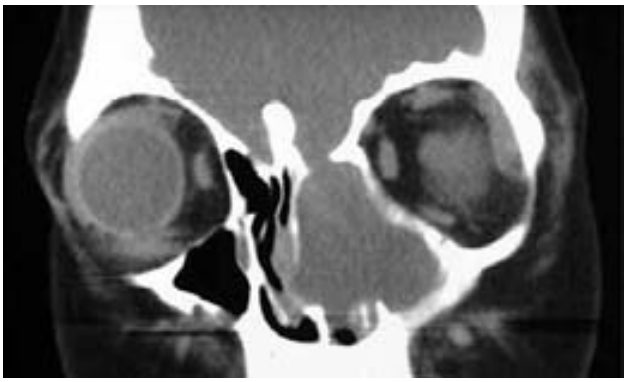

**Figure 3:** *Coronal CT scan of patient presenting with unilateral polyp showing appearance suspicious of encephalocele.*

intracranial extension and an acceptable cosmetic result[20]. Access to the skull base may be facilitated by medial osteotomies through the nasal bones which are displaced laterally. In the region of the skull base further bone can be removed for exposure and cyst removal using a burr. The aim of surgery is complete removal of the lesion. Where there is doubt, for instance in the case of a lesion attached to the dura by a fibrous cord, serial MRI scanning can be greatly reassuring.

## Nasal encephaloceles

Nasal encephaloceles are herniations of intracranial contents through a defect in the skull base. Acquired causes include skull base fracture and intranasal surgery. They are classified into basal or frontoethmoidal lesions. Basal encephaloceles herniate into the nasal cavity through a central defect in the anterior skull base and my be subclassified as transethmoidal, transsphenoidal, sphenoethmoidal or transfrontal. They typically present with a mass in the nose which can be mistaken for a unilateral inflammatory nasal polyp. Frontoethmoidal lesions present with a mass on the lateral side of the nose which should transilluminate. In both cases Furstenberger's sign (increase in the size of the mass when the ipsilateral inetranl jugular vein is occluded) should be positive. The absence of this sign however does not preclude further investigation.

Any unilateral rhinorrhoea associated with a unilateral nasal mass should be sent for beta2-transferrin anaylsis if a CSF fistula is suspected. Imaging of unilateral nasal lesions is mandatory. CT scanning may show a bony defect (fig 3) and MRI imaging will show the herniation of the intracranial contents (fig 4).

The traditional management of these lesions has been with a craniotomy, removal of the lesion and repair of the dural

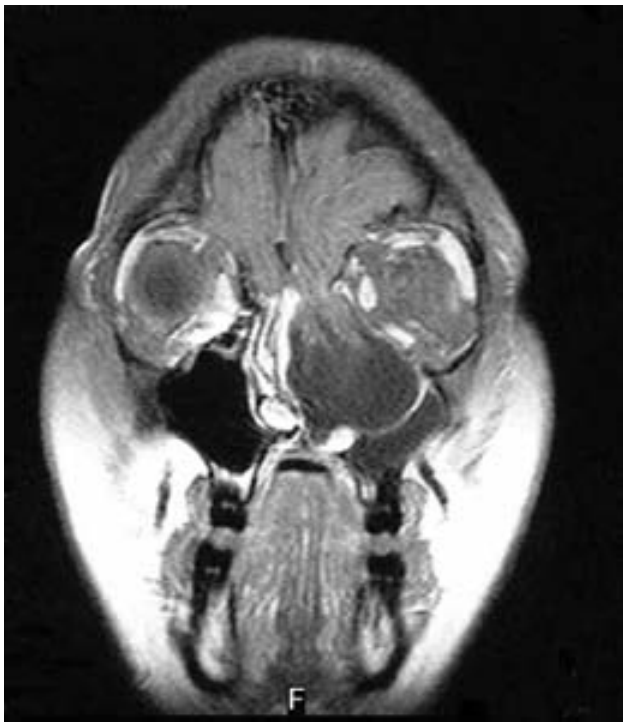


**Figure 4:** *MRI scan of patient in figure 3 showing a left sided basal encephalocele.*

defect. More recently advances in endoscopic sinus surgery has allowed many patients to undergo endoscopic removal and simultaneous repair of the skull base defect with autologous material such as fascia lata, avoiding a craniotomy[21].

## Nasal Gliomata

Nasal gliomata consist of ectopic neural tissue occurring in the within the nose (30%), extranasally (60%) or communicating between nose and lateral wall of nose through the nasal bones (10%). Histologically they consist of neuroglial tissue on a connective tissue matrix covered with respiratory or cutaneous epithelium. The may occasionally have a connection with the intracranial cavity[22,23]. Imaging of these lesion is mandatory as is exclusion of csf fistula in those patients with associated rhinorrhoea.

If there is no associated intracranial connection the treatment of choice for intranasal lesions is endoscopic excision. Those having a component extranasally, or occurring completely extranasally are best treated surgically using an appropriate skin incision, complete excision of the lesion and meticulous skin closure.

## Nasopharygeal teratoma

Teratomata occur in I in 4000 live births. Those occurring in the head and neck region account for 5% of these[24]. Of these the nasopharynxis a relatively uncommon site. They present as a sessile or pedunculated mass which may be identified on antenatal ultrasound scanning. The presence of the mass may interefere with development of surrounding structures and the may consequently be associated abnormalities such as a cleft palate. In the neonate the nasal obstruction caused by such a lesion may cause serious airway obstruction.

In those patients where the lesion is identified antenatally, intra-uterine MRI may be helpful in delineating the lesion further. Maternal serum alpha-fetoprotein may be elevated as may…

Before investigating the nature of the lesion in the neonate the airway must first be secured. Imaging in the form of CT and/or MRI scanning will help distinguich between a nasopharyngeal teratoma and an encephalocele. The appearance of a part solid, part cystic mass helps to differentiate them from lymphatic malformations which are entirely cystic in nature. Then treatment consists of surgical excision and repair of any associated abnormalities. The majority of congenital teratomata in the head and neck are benign[25]. They require careful follow up with monitoring of tumour markers (alfafetoprotein and beta human chorionic gonadotrophin)

## Arhynia and polyrhynia

The absence of the nose is very rare as is the presence of multiple noses. There are a handful of these cases presented in the world literature. Unsurprisingly there is a high incidence of other associated craniofacial abnormalities.

## Cleft nose

The presence of a nasal midline cleft is rare and when occurring often associated with a cleft lip and palate.

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# Paediatric Laryngeal Papillomatosis

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## Introduction

Laryngeal papilloma is the most common benign laryngeal neoplasm in children and the second most common cause of hoarseness among paediatric patients[1]. The condition was first recognized as "warts in the throat" by Marsellus Donalus in the seventeenth century[2]. Morel MacKenzie has differentiated the lesion from other laryngeal masses and coined the name papilloma in 1871[3]. The larynx is the most common site of involvement in the upper aerodigestive tract. The propensity to recurrence and the involvement of extralaryngeal sites including the trachea, esophagus, lungs, parenchyma, oropharynx, oral cavity and nasal cavity, justify the use of the term recurrent respiratory papillomatosis (RRP).

## Epidemiology

RRP has a bimodal age distribution[4]. Juvenile onset RRP presents in children usually younger than 5 years of age, with approximately 25% of juvenile cases presenting in infancy. Adult RRP typically presents during the third decade of life[5]. Juvenile RRP is more aggressive, has a more significant impact on quality of life, and accounts for greater health care costs. The incidence of recurrent respiratory papillomatosis (RRP) in the United States has been estimated at 2 per 100,000 in adults and 4 per 100,000 in children[6]. European studies report a 10 fold lower incidence of laryngeal papillomatosis of between three to seven cases per million[7-9]. Both genders are equally affected in juvenile onset disease but in the adult onset disease males are more commonly affected in the ratio of 2-4 to 16,[10-11]. Approximately 75% of affected children are the first-born, vaginally delivered infants of teenage mothers, a clinical triad of recognized risk factors[12].

## Aetiology

The condition is caused by the human papilloma virus (HPV), a small, non-enveloped, 20-sided, capsid virus with double-stranded circular DNA that is responsible for skin warts, genital condyloma, and cervical cancer in humans. Of the 90-plus identified subtypes of HPV two sub-types cause RRP namely HPV-6 and HPV-11[13-14]. Type 11 is believed to be more virulent, associated with earlier presentation, longer disease activity, higher mortality rate, and more frequent malignant transformation[15].

Materno-neonatal transmission via an infected birth canal is the most commonly accepted theory for juvenile-onset RRP transmission[16]. In adults re-activation of latent virus present from birth, or infection through oral or sexual contact is considered to be the mechanism[12]. Evidence of alternative transmission routes are provided by the work of Armbruster-Moraes et al who demonstrated that HPV DNA can be isolated in amniotic fluid aspirates of women prior to delivery who had clinical and slot-blot hybridisation evidence of cervical papilloma, providing evidence of in-utero transmission[17]. This can explain the failure of Caesarean section to abolish the development of juvenile onset laryngeal papilloma disease[18-19].

Borkowski et al in 1999 first suggested a correlation between RRP and gastro-oesophageal reflux (GORD) by showing that controlling reflux resulted in reduced growth of laryngeal papillomas[20]. Holland et al suggest antireflux treatment in patients who undergo surgery for RRP to avoid soft tissue complications such as scarring[21]. McKenna and Brodsky linked the presence of GORD and RRP. The inflammation induced by chronic acid exposure may result in the expression of HPV in susceptible

tissues. Prompt diagnosis and effective treatment of GORD should be considered in all patients with difficult to control RRP or with features of GORD[22].

## Clinical Presentation

Patients usually present with hoarseness, or airway obstruction. Less commonly, children may present with chronic cough, recurrent pneumonia, failure to thrive or dysphagia[23]. Children with a history of chronic hoarseness should undergo microlaryngoscopy to rule out RRP or other laryngeal pathology. Extralaryngeal spread has been reported in approximately 30% of children. The most common sites of extralaryngeal spread are, in decreasing order of frequency, the oral cavity, trachea, bronchi and oesophagus[24-25]. Tracheostomy predisposes to papilloma extension to the lower airways[26-28].

## Staging

There is no uniformly accepted RRP staging system. Derkay et al's system[29-30] based on an anatomical breakdown of the aerodigestive tract into 25 subsites demonstrates a high level of inter-observer reliability. The different anatomical areas are evaluated according to the presence and the severity of the disease. The lesions are scored 0, none; 1, surface lesion; 2, raised lesion; 3, bulky lesion. Symptoms are likewise evaluated and the summation of these scores gives an overall evaluation of the extent of the disease.

## Treatment

### Conventional

The primary treatment of RRP is surgical excision under microlaryngoscopic control. Surgical excision aims to secure an adequate airway and improve and maintain an acceptable quality of voice. Most patients undergo multiple procedures as persistence or recurrence is the rule. Several methods of endoscopic excision are used to remove papilloma, including CO2 laser ablation, cold steel excision using microlaryngoscopic instrumentation, microdebrider and more recently pulsed dye laser treatment. Tracheostomy should be avoided, if possible, because this procedure is associated with a substantially increased risk of distal tracheal spread[26-28,31].

The CO2 laser is the preferred method of treatment in a recent survey of paediatric otolaryngologists in the United Kingdom[32]. The CO2 laser has an emission wavelength of 10,600 nm and converts light to thermal energy that is absorbed by intracellular water; the result is controlled destruction of tissues by cell vaporization and cautery of tissue surfaces. The newest application of the CO2 laser allows it to be used through a flexible bronchoscope, providing access for its use in the distal airway. Dedo and Yu described a series of 244 patients with RRP treated with the CO2 laser every 2 months, "remission" was achieved in 37%, "clearance" in 6%, and "cure" in 17% of cases[33].

The drawbacks of the CO2 laser include the need for special precautions to reduce the risks of airway fire and the exposure of the staff to the virus. The laser smoke plume has been found to contain active viral DNA, and is a potential source of infection, so smoke evacuators and laser masks are advised[34-36].

Microdebrider laryngeal blades allow precise removal of papillomatous tissue from the laryngotracheal airway, with no risk of thermal injury to surrounding tissues. In addition, laryngeal and tracheal disease can be accessed with the microdebrider blade. It has been proven to be relatively safe and effective and is currently the preferred technique amongst members of the American Society of Paediatric Otolaryngology[25]. Pasquale et al's randomized prospective study comparing CO2 laser excision with the microdebrider in children reported less operating room time and a cost benefit for the microdebrider[37].

### Novel Treatments

The Pulse dye laser (PDL) has recently been recommended for use in patients with pediatric RRP[38-40]. The pulse dye laser at 585 nm demonstrates effectiveness in vascular tissue. Papillomatous lesions are benign angiomatous neoplasms with a microvascular core. This microvasculature is targeted by the PDL to involute the disease while minimizing trauma to the surrounding tissue. Bower et al confirmed the feasibility and safety of the flash pump dye laser in children and reported good early results[39]. Franco et al's study on 41 adult cases of RRP concluded that the pulse dye laser at 585 nm was most effective for smaller, sessile lesions[38].

## Adjuvant Therapy

The frequent recurrence of papillomas has resulted in the use of different adjuvant treatments alongside surgical removal of macroscopically obvious disease in the attempt to reduce recurrence and obtain greater local control.

## Cidofovir

Cidofovir (Vistide®, Pharmacia GmbH, Germany) is a nucleoside analog acting as a potent inhibitor of viral DNA polymerases after intracellular activation[41]. Cidofovir is capable of inducing cell apoptosis dependent upon time and concentration[42]. The effectiveness of intralesional injections of Cidofovir, with or without primary excision of laryngeal papillomas or their reduction, has been investigated in various studies since 1995 These studies demonstrated an

improvement in disease severity scores, reduction in recurrence and consequently less need for surgery[43-49]. Although few side effects of cidofovir have been reported there has been concern about the potential carcinogenicity of cidofovir[50]. Broekema and Dikkers systematic review on the side effects of Cidofovir in the treatment of recurrent respiratory papillomatosis concluded that intralesional cidofovir does not increase the risk of laryngeal dysplasia[51]. 3 mg/kg is the maximum recommended intralesionally injected dose of cidofovir in adults and 1mg/kg for children, which could be repeated every 2 – 4 weeks[52-54]. Intravenous administration of cidofovir up to 5mg/Kg is justifiable if there is evidence RRP Pulmonary involvement[55-57].

## Photodynamic therapy

A photosensitizing dye is given to the patient, and when the dye is exposed to light of a certain wavelength (red light laser), a singlet oxygen reaction occurs resulting in the killing of cells. The dye has a predilection for tumors, including papillomas. It localizes to vascularized structures and is therefore retained longer in papillomas and other tumors because they typically are more vascularized than normal tissue. Each agent has a different 'wash-out' time where the dye leaves the normal cells allowing a safe window for treatment[58]. Older studies used the photosensitizing drug haematoporphyrin derivative (HPD)[59]. Unfortunately, this dye left the patient light sensitive for up to 2 months. Trials using a different photosensitizing dye –meso-tetra hydroxyphenyl chlorine (mTHPC)– are likewise encouraging. A randomized clinical trial using m-tetra (hydroxyphenyl)chlorine as a photosensitizer in 23 patients ages 4 to 60 with severe RRP resulted in improvement in laryngeal disease; however, papillomas recurred in 3 to 5 years, and the therapy was poorly tolerated by a quarter of the patients[60].

## Interferon

The exact mechanism of interferon action is unknown. It has a variety of antiviral, antiproliferative, and immunomodulating activities. Antiviral effects are mediated by inhibition of viral penetration, or uncoding, synthesis or methylation of mRNA, viral protein translation, or viral assembly and release[61-62]. Szeps et al reported better response to interferon _ in HPV 6 cases compared to HPV 11 or HPV negative cases. They also stated that there was no significant difference in viral load and hyperproliferative state of the HPV affected epithelium post-treatment in patients who responded well to interferon _[63]. Gerein et al analysed the results of use of interferon a in patients with RRP over a 20 years follow up period. The rate of event free survival was 42.8% and the overall survival was 82.6%[64]. Side effects include flu-like syndrome, leucopenia, coagulopathy, alopecia, and neurological complications. Interferon is administrated intramuscularly, intravenously, or subcutaneously. The dose is increased gradually to a target of 3 MU/m2 body surface daily for a month, and then the dose is reduced to 3 times/week for at least 6 months. Afterward, the dose may be slowly tapered or reintroduced in those children with recurrence. The role of intralesion injection of interferon is under investigation[65].

## Acyclovir

Acyclovir is a purine analogue that is phosphorylated into its active form by thymidine kinases coded by herpes viruses[66]. Human thymidine kinases do not activate acycolvir, which is why this compound specifically kills cells with an active herpes virus infection. The analogue incorporates into DNA causing strand breaks in the viral DNA. The papillomaviruses, much smaller viruses than herpes viruses, do not code for any thymidine kinase. Therefore, the rationale for using acyclovir to treat RRP is uncertain. However, some clinical response was observed in a number of trials. The hypothesis is that the clinical response may be correlated to co-infection with herpes simplex virus[67-68].

## Ribavirin

Ribavirin is an antiviral commonly used for certain RNA viruses such as hepatitis C and respiratory syncytial virus[69-70]. Ribavirin is a guanosine analogue and inhibits synthesis of GTP by an effect on inosine monophosphate dehydrogenase, thus limiting RNA synthesis. McGlennen et al showed that ribavirin resulted in an increased interval between surgery[71].

## Indole-3-Carbinol (I-3-C)

I-3-C found in high concentrations in cruciferous vegetables. The rationale is that RRP lesions exhibit increased binding of estrogen, and a study in immunocompromised mice showed that inhibition of estrogen metabolism using indole-3-carbinol reduced the formation of HPV-induced papilloma tumors by nearly 75%[72-73]. Rosen and Bryson found that after 8 months or more of treatment, one third of patients had cessation of papilloma growth and did not require further surgery, one third had reduced papilloma growth rate, and one third had no evident response[74].

## Retinoids

Retinoids (metabolites and analogues of vitamin A) has been used as an adjunct therapy for RRP. They induce cell differentiation and inhibit proliferation and angiogenesis. They should be used with caution due to teratogenic and psychiatric side effects[75-79].

## Experimental Treatments

### Gene therapy

Gene therapy may be important in the treatment of juvenile RRP. It targets genes that are expressed exclusively in pathologic tissues and not by normal cells. Epidermal growth factor receptor (EGFR) is expressed in laryngeal papillomas. Bostrom, et al reported the use of EGFR tyrosine kinase inhibitor in a patient with end-stage disease in whom other therapies had failed. They noted marked reduction in the papillomas growth[80]. Sethi and Palefsky designed an HPV specific therapy using the herpes simplex virus type 1 thymidine kinase gene. They transferred this gene into HPV 16 infected cells expressing E2 protein. Treatment of these cells with either ganciclovir or acyclovir resulted in cell death. They suggested that this may be a clinically feasible therapeutic strategy[81].

## HPV Vaccines

The currently available HPV vaccines Gardasil and Cervarix have been developed to stimulate immunity to the most common HPV subtypes that cause cervical cancer but Gardasil also targets HPV6 and 11 responsible for recurrent respiratory papillomatosis. The vaccines are virus-like particles that simulate the surface of HPV combined with an aluminum adjuvant to boost immunogenicity[82]. Gardasil is highly effective in preventing the development of cervical neoplasia and wide scale immunization if implemented should reduce or eradicate laryngeal papillomatosis[83].

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# Treatment of Otosclerosis: Current trends

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## ABSTRACT

Otosclerosis is a condition of the bone derived from the otic capsule resulting in progressive hearing loss. It is inherited in an autosomal dominant pattern with incomplete penetrance. The measles virus may be a trigger in those who are susceptible.

The main treatment alternatives include hearing aids, bone achored hearing aids or stapes surgery. The laser and the use of newer prostheses have improved outcome. Cochlear implants can be used in advanced bilateral otosclerosis. Revision surgery is complex and the surgeon needs to be prepared to deal with several unexpected findings.

The current ideas on aetiopathogenesis and management of otosclerosis are reviewed here.

## Key Words

Otosclerosis, etiology, management

## INTRODUCTION AND HISTORY

Otosclerosis is a process of progressive demineralisation of the otic capsule with fixation of the stapes footplate and is usually diagnosed on clinical and audiological grounds. It is associated clinically with both sensorineural and conductive hearing loss. Initial attempts at stapedectomy were undertaken by Kessel in Gras in 1878 followed by Blake in the US; both faced mounting criticism from the leading otologists of the day. Holmgren in Stockholm accidentally discovered fenestration of the lateral semicircular canal in the early 1920s. Rosen then developed stapes mobilisation in the 1950s. Introduction of operating microscopes and microsurgical instruments in otology allowed for the revival of stapedectomy by Shea. The main principles of the surgery, "prosthetic restoration of ossicular continuity from the incus to the tissue covering of oval window" remains essentially unchanged today with minor modifications in technique.

## AETIOPATHOGENESIS

There are a number of theories behind the aetiopathogenesis of otosclerosis. The general consensus appears to be one of it being of multifactorial origin; human leucocyte antigen alleles, measles virus and genetic markers all have been implicated[1]. It has been alleged that antiretroviral therapy may cause otosclerosis too[2].

### Genetic influences

Otosclerosis has an autosomal dominant inheritance with low penetrance to a degree of approximately 40%. There are thought to be 6 main loci for these genes, on the long arms of 3, 6,7,15 and 16, as well as the short arm of 6[3,4,5]; A further locus has been seen more recently on chromosome 9[6]. Abnormal collagen formation in the otic capsule has also been suspected as an underlying factor and a gene (COL1A1) has been implicated[1,7].

A cytokine variant called Transforming Growth Factor-beta 1 (TGF-beta1) appears to correspond significantly with the likelihood of suffering from otosclerosis[8].

### Measles virus

This theory evolved in 1986, when McKenna *et al* noticed the presence of filamentous structures similar to the virus nucleocapsids of subacute sclerosing panencephalitis concentrated in the rough endoplasminc reticulum of osteoblastic cells in actively diseased otic capsules[9]. Subsequently, the same researchers identified measles virus nucleocapsids in active osteoblasts by electron microscopy and immunofluorescence[10].

Consequently, a 2007 study has shown that measles RNA was present in 62 out of 102 subject otic capsules whilst being absent in bony samples from other locations in the same body [11]. Additionally, it has been hypothesised that the particular measles virus receptor on the cells of the otic capsule, known as CD46, becomes upregulated with active infection[12].

Epidemiological support for the measles virus hypothesis comes from a large case control study of over 64,000 patients in Germany which showed a significant decrease in otosclerosis incidence in those who received compulsory measles vaccination[13] with similar observation being made in the American literature as well[14].

## MANAGEMENT

### Preoperative counselling

It is essential to explain in detail all the surgical and non surgical treatment options available to the patient including conventional hearing aids or bone anchored hearing aids in order to have an informed consent from the patient. The risks of surgery (including hearing deterioration, dead ear, vertigo, tinnitus, taste alteration, early or late failure and facial palsy) should be mentioned and recorded in the notes. The reported incidence of sensorineural hearing loss varies from 0.5% to 4% in experienced hands[15].

### Outcomes

If the patient is to appreciate significant improvement in hearing then the postoperative air conduction average over the speech frequencies has to be around 30dB or there should be a less than 15 dB interaural difference[16]. The more recent American Academy criteria define a successful hearing outcome as the postoperative air conduction being within 10dB of the postoperative bone conduction on PTA[17].

### Non-surgical management

Different patterns of hearing loss are associated with otosclerotic foci in differing parts of the otic capsule[18]. It has been suggested that lowered serum levels of measles virus IgG levels in the presence of a conductive hearing loss could be a sensitive indicator of otosclerosis, as opposed to non-otosclerotic ossicular chain fixation[19].

Medical management of otosclerosis involved the use of sodium fluoride in the past. It is thought to inhibit the activity of the diastrophic dysplasia sulphate transporter[20], increased activity of which is associated with increased bone turnover[21]. Even fluoridated drinking water was found to have a favourable effect on the course of established otosclerosis[22]. The use of sodium fluoride has been associated with less widespread lesions when otosclerosic temporal bones have been examined by computed tomography[23].

Hearing aids have often been advocated as the first line of treatment for patients with otosclerosis. Bone anchored hearing aids (BAHAs) have become increasingly popular for treating this disease and do appear to significantly improve quality of life when used in otosclerosis as well as a number of other ear diseases[24]. A recent article suggested placing a second, spare BAHA fixture to minimise disability in the event of failure of a fixture[25].

The future non-surgical treatment of otosclerosis may well involve the emerging science of osteoimmunology[26] involving the interaction between bone and the immune system[27].

### Surgical management

Surgical management remains the mainstay of otosclerosis management. Stapes surgery is performed either with local anaesthesia and sedation (popular in the US and many European centres) or under general anaesthesia. The proponents of the former technique claim that it is easier to assess the change in hearing and development of vestibular symptoms in the perioperative period with this technique.

### Surgical steps

- Infiltration with local anaesthetic and vasoconstrictor
- Harvesting of vein graft
- Incision : endomeatal or small endaural
- Elevation of tympanomeatal flap
- Confirmation of diagnosis by palpation
- Division of incudo-stapedial joint
- Division of stapedeus tendon
- Laser crurotomy
- Laser stapedotomy
- Fenestration of footplate
- Measurement of prosthesis length
- Placement of soft seal on oval window
- Placement of prosthesis
- Closure

## Variations in technique

- The prosthesis

The prostheses vary in the material and the size and shape. Teflon, stainless steel, platinum and titanium have all been used either alone or in combination. The choice of material is largely guided by the preference of the surgeon.

Recently there has been a lot of interest in the "Smart" nitinol (nickel / titanium alloy) (Gyrus)[28] piston which allows heat crimping and in the "Clip Piston MVP" (Kurz) which allows crimp free attachment to the malleus handle[29]. The ease of use of the nitinol prosthesis was noted by many users[30,31].

A multicentre study of ninety patients treated with the nitinol prosthesis compared to patients treated with the titanium prosthesis show significant improved outcomes in hearing in the former group[32].

- The laser and fenestration

A small fenestra stapedotomy is advocated. This has been traditionally fashioned with a microdrill or a pick, which practically offer very little difference from each other[33].

Recently a piezoelectric handpiece, working at low ultrasonic frequencies has been used to divide mineralised tissue effectively with a bloodless field and minimal soft tissue involvement[34].

The laser was introduced into ear surgery by Rodney Perkins in 1980 with further improvement in outcome. The laser ensures a bloodless field, reduces risk of footplate subluxation, reduces trauma during fenestration and atraumatically frees any scar tissue from the oval window.

Use of the Erbium: yttrium-aluminum-garnet (Er:YAG) laser[35], the carbon dioxide (CO2) laser[36,37], the argon laser[38,39] and KTP laser[40] have all been advocated, although there is no clear evidence that any particular device is superior.

However, it has been seen that there is sporadically a transient loss of inner ear function as seen on audiological testing after stapedotomy, independent of the surgical method.

It has been hypothesised that this may be due to an inflammatory reaction[41]. One study did find that the best results were obtained from using a combination of conventional and laser techniques[42].

## Perioperative difficulties

1. Facial nerve anomalies
2. Floating footplate
3. Tympanic membrane tear
4. Obliterative otosclerosis
5. Perilymph gusher
6. Damage to chorda tympani
7. Facial nerve injury

## Post operative problems

1. Severe sensorineural hearing loss
   - Immediate
   - Delayed onset
2. Progressive conductive loss
3. Perilymph fistula
4. Incus necrosis
5. Displaced prosthesis

## Challenging surgical situations

- **Far Advanced Otosclerosis –** This is a situation where the otosclerotic process has deteriorated to the point that the patient has suffered a profound hearing loss. A high resolution CT of the temporal bones determines the extent of ossification of the cochlea. A grading system by Rotteveel has been proposed, which categorises ossification by its location near the oval window and loss of cochlear architecture[43]. The realistic treatment alternatives are limited to stapes surgery and cochlear implant (CI). A retrospective 2007 paper showed that stapedotomy combined with a hearing aid was a viable first choice option for managing this problem with CI in reserve if this fails[44].

- **Floating Footplate –** Use of the laser to prevent a floating footplate was recommended; however, this remains a problem during stapes surgery. The suggested ways of managing this problem include removing the stapes arch only after perforating the footplate[45].

- **Anatomical variations of the facial nerve** can complicate surgery. It was noted in a prospective observational study that 23/357 facial nerves were seen to be dehiscent[46]. The use of 0° and 30°oto-endoscopes has been advocated to avoid facial nerve injury intra-operatively[47].

- **Revision stapedectomy** may become necessary in less than 20% patients over a 20 year period to correct further conductive loss[48]. The most frequent indications for revision surgery are prosthesis displacement or necrosis of the long crus of the incus[49,50]. Complications such as intravestibular protrusion, oval window fibrosis, incudomalleolar dislocation, labyrithitis and perilymph

fistula often require revision surgery[51,52]. There is a view that revision stapedectomy should not be carried out after the patient had been subject to two previous revision procedures[53].

- A **perilymph fistula** presents with disequilibrium, roaring tinnitus, fluctuating hearing loss and distortion of sound. Closure can be achieved by the use of a vein graft or adipose tissue[54].

## Otosclerosis and cochlear implantation

Middle ear implants are a relatively new addition to the otologist's armamentarium and there is limited mention in the literature showing their effectiveness in otosclerosis[55,56].

The cochlear implant is a viable alternative in bilateral profound deafness due to otosclerosis[57]. However with disease progression the implant sometimes needs adjustment, with the signal input having to be increased over time[58]. One of the most notable problems with CI in otosclerosis is the unwanted stimulation of the facial nerve due to current passing through the diffuse foci of sclerosis in the otic capsule. A large retrospective review of patients in 4 major CI centres showed 38% patients encountered this but that it could be overcome by deactivating electrodes in the proximity of the geniculate ganglion[59]. The small number of cases resistant to this strategy have benefited from reimplantation[60]. Other problems include difficulty in electrode insertion and electrode migration.

## Conclusion

Otosclerosis is thus a relatively common condition, the aetiology of which is slowly being revealed. The measles virus has been strongly implicated and treatment may be tailored to this in the future. Present management is centred on the use of hearing aids and, if necessary, subsequent surgical intervention; use of lasers and nickel alloy prostheses is becoming increasingly popular. Cochlear implantation is an expensive but effective last resort.

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# Management Options For Skull Base/ Petrous Apex Lesions

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## Abstract
Surgeons approach lesions of the skull base with understandable reluctance. The problems being surgical inaccessibility, the obstacles of vital neural and vascular anatomy and the overwhelming surgical mortality rate as a result of haemorrhage and sepsis. There has been a technical revolution in microsurgery, anaesthesia and neurodiagnosis. Armed with technology, surgery has become the mainstay in management of these dreaded lesions.

This article focuses on glomus tumour and its associated lesions. Their diagnosis and new treatment concepts are discussed. The various choices available for these lesions are discussed.

## Key words
Skull base surgery, management, interventional neuroradiology, skull base tumour, diagnosis, conservative treatment (or therapy), petrous apex

The management of skull base and petrous apex lesions is uniquely challenging as they arise in an area which is anatomically complex and involves critical neurovascular structures. The lesions are usually histologically benign but they behave as if locally malignant with extensive invasion of bone, soft tissue and nerves[1]. The skull base can be classified into three distinct areas. The lateral skull base - temporal bone and cerebellopontine angle (CPA); anterior skull base - cribriform plate and the anterior cranial fossa; and central skull base - greater and lesser wings of sphenoid, sella turcica and the clivus[2]. The petrous apex is a pyramid shaped structure that is the most medial aspect of the temporal bone. When viewed from above, this region can be divided into anterior and posterior segments by drawing a parallel line through the internal auditory canal[3]. Disease processes most frequently involve the much larger anterior portion, which lies anteromedial to the cochlea and internal auditory canal. The smaller and clinically less significant posterior portion lies between the semicircular canals and the IAC.

## Presentation
Petrous apex lesions present with hearing loss as the most common symptom followed by vestibular dysfunction, headache, tinnitus, facial spasm, diplopia, facial paralysis, and otorrhea. These symptoms often present months or years before diagnosis, and incidental discovery is not uncommon[4].

**Investigations:** Audiology - Air and bone conduction pure tone audiometry is the minimum requirement for patients with lateral skull base tumours. Speech audiometry is essential when contemplating hearing preservation surgery.

**Vestibular function tests** – Caloric testing is by far the most common vestibular function test described in relation to skull base lesions[2].

**Tests of facial function** – Electroneurography (ENoG) is used as a predictive test both pre- and post-operatively in patients with skull base lesions.

**Radiology –** Principal reasons for imaging include: (1) screening; (2) investigation of suspicious symptoms or signs; (3) surgical planning and navigation and (4) for monitoring size, extent or recurrence of lesions. In several instances both CT and MRI are complementary and essential[5, 6] (Table 1).

Some patients may also require carotid and vertebral artery angiography. Magnetic resonance angiography and venography is a low risk technique of assessing the skull base vasculature. Although the resolution of these studies is good, the primary disadvantage is the inability to perform interventional measures[7]. CT angiography and venography allow for another detailed means of assessing petrous apex lesions and vessels. This technique uses ultra-thin slices with timed administration of contrast and provides incredible detailed information. An additional advantage of temporal bone CT angiography compared with its counterparts is the ability to define the vascular structures and their relationship with the lesion and other structures in or adjacent to the petrous apex[3, 8].

Positron emission tomography (PET) and single photon emission computerized tomography (SPECT) can be extremely helpful in certain circumstances. PET is useful in differentiating granulation or scars from recurrent or residual disease[2]. SPECT is superior to CT in detecting skull base erosion[9] and in vascular tumours the radiotracer shows specific uptake followed by rapid 'wash-out'[10]. However PET and SPECT have limited resolution and can fail to detect small lesions[11].

The detection of multiple paragangliomas or metastatic disease has been facilitated by radio nucleotide scintigraphy with metaiodobenzylguanidine (MIBG) or indium-11-octreotide.[12]

**General investigations –** Endocrine activity has been reported in a small subset (1%-3%) of head and neck

**Table 1 Differential Diagnosis**[3, 36]

| Lesion | MRI | | | | CT | Other | Treatment |
|---|---|---|---|---|---|---|---|
| | T1 pre | T1 post | T1 fat saturated gadolinium | T2 | | | |
| Paraganglioma | Isointense | Enhancement | Enhancement | Hyperintense<br>cells | Opacified and destroyed air salt and pepper | Flow voids, blush on angio Radiotherapy, | Surgery, Stereotactic radio,<br>Somatostatin |
| Meningioma | Isointense/ hyperintense | Enhancement | Enhancement | Isointense/ hyperintense hyperdense, calcification | Hypeostosis isointense or | Dural tails, sessile eccentric | Surgery, Stereotactic radio, thalidomide |
| Schwannoma | Isointense | Enhancement | Enhancement | Hyperintense or hypointense | Dilation of internal auditory canal | Centered in internal auditory canal | Surgery, Stereotactic radio, Wait and see |
| Epidermoid | Hypointense | No enhancement | | Hyperintense | FLAIR – hyperintense, diffusion-weighted imaging,hyperintense | | Surgery |
| Cholesterol Granuloma | Hyperintense | No enhancement | | Hyperintense | Smooth erosion contralateral apex highly pneumatised | | Surgery |
| Cholesteatoma | Hypointense | No enhancement | | | Hyperintense contralateral apex often not pneumatized | Smooth erosion | Surgery |
| Petrous apicitis | Hypointense | Rim enhancement | Rim enhancement | Hyperintense | Destroyed septae irregular bone erosion | | Surgery |
| Effusion | Hypointense | Mucosal enhancement | | | Hyperintense | Usually pneumatized contralateral apex | |
| CSF cyst/ cephalocele | Hypointense | No enhancement | No enhancement | Hyperintense | Smooth erosion, FLAIR-hypointense, diffusion-weighted, hypointense | | Surgery, if symptomatic |
| Mucocele | Isointense | No enhancement | No enhancement | Hyperintense | Destroyed septae | | Surgery |
| Carotid aneurysm | New thrombus, Hypointense; older thrombus, hyperintense | | | Hyperintense | Smooth expansion of carotid canal, heterogenous contrast enhancement | MRI, central flow void, onion skin appearance | Embolisation Surgery |
| Chordoma | Hypointense/ isointense | Enhancement less intense than chondrosarcoma | Enhancement | Hyperintense | Lobulated, bone destruction with residual bone fragments | Centrally located in clivus with lateral spread to petrous apex | Surgery |
| Chondrosarcoma | Hypointense/ isointense, homogenous | Enhance | Enhancement | Hyperintense, heterogenous | Infiltrative, remnants of eroded bone | Centered in petrous apex in region of foramen lacerum, calcified areas may show as signal voids | Surgery |
| Metastasis | Depends on primary | Enhancement | Enhancement | Depends on primary | Bone erosion | Depends on primary tumour | |

chemodectomas[13]. Twenty-four hour urinary vanillyl-mandelic acid (VMA) detects a secreting tumour that could cause problems during surgery.

Biopsy is the only diagnostic technique that allows tissue diagnosis of skull base tumors. In many cases, the clinical presentation and diagnostic imaging provide sufficient information upon which to base a treatment decision. Because surgical excision is the treatment of choice for the vast majority of benign skull base tumors, a histological tissue diagnosis is unnecessary prior to definitive resection. However, an attempt at biopsy is indicated for cases in which diagnostic imaging has not sufficiently narrowed the diagnostic possibilities, in very slow-growing lesions for which observation is contemplated, or when the patient is not a good surgical candidate. Depending on the tumor location, both open biopsy and needle biopsy have indications. Open biopsy of tumors manifesting with palpable masses close to the surface can be approached through a simple skin incision. Biopsy of sinonasal masses can be performed with endoscopic guidance. Needle aspiration biopsy using either CT or MRI guidance can be used to safely biopsy deeper skull base tumors[14].

## Diagnostic and Therapeutic Angiography

Many skull base/ petrous apex tumours are either intrinsically hypervascular or secondarily involve arteries and veins of the brain that enter and exit the cranium through the skull base. Angiography, embolization and major artery occlusion have a pivotal role in investigation and treatment of these conditions. The potential benefits that these procedures offer must outweigh the risks of their possible complications.

Diagnostic angiography is considered especially when evaluating the suitability of tumour to embolisation. It also provides the surgeon with information regarding the anatomy of the circle of Willis and the likely tolerance to potential carotid sacrifice[15].

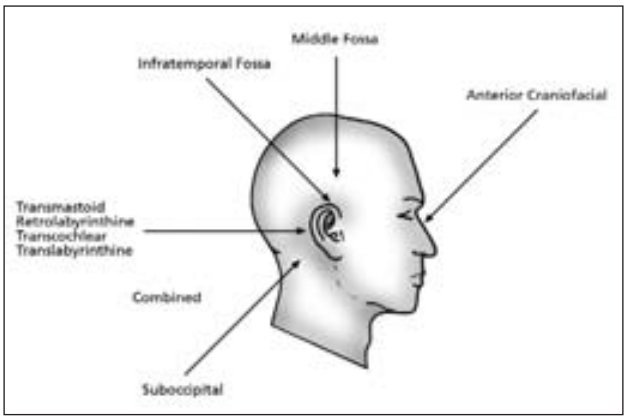


**Fig. 1:** *Surgical Approaches to the skull base*

Embolisation is carried out to reduce intraoperative blood loss and improve visualization of the operative field during surgery. It is rarely curative but reduces the rate of radical tumour removal, surgical complication rate and incidence of recurrence. The tumours that benefit include glomus tumours, meningiomas, chordomas, sarcomas, oestrogenic tumours, metastases, olfactory neuro-blastomas and juvenile angiofibromas[15].

Internal carotid artery (ICA) test and permanent occlusion is carried out in tumours intimately related to the ICA or tumours that receive significant arterial supply from extradural ICA branches. The assessment of cerebral circulation to tolerate permanent sacrifice of a major vessel is warranted in these cases. Permanent balloon occlusion can follow successful test occlusion of the ICA if the patient does not experience any neurological dysfunction during the test and if there is adequate venous phase opacification when injecting contralateral carotid artery. An external-internal carotid bypass should be considered for those patients who fail the test procedure yet need carotid occlusion[16].

## Treatment

As a result of specific challenges presented to the surgeon by the lesions of the skull base, it is understandable that several therapeutic options for their treatment exist. However they are all not equally successful in accomplishing a curative end. Total surgical excision is the only treatment modality that offers cure for patients with tumours of skull base[17].

## Surgical approaches to the Skull Base (Figure 1)

### Infratemporal fossa approach (ITF)

This approach provides access to the cavernous sinus, clivus, nasopharynx, and petrous apex. Fisch described several lateral ITF approaches centered around the subtemporal exposure and rerouting of the facial nerve **(Figure 2)**.

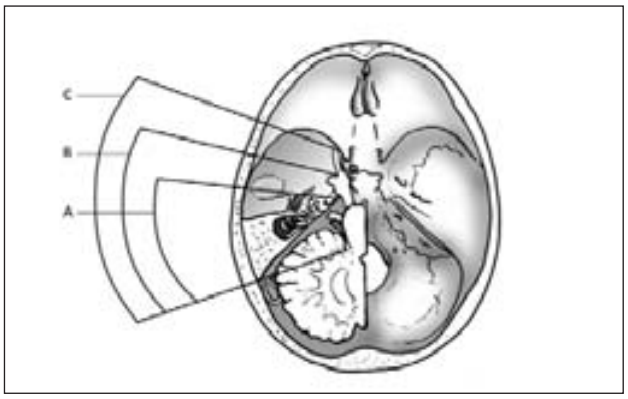


**Fig. 2:** *Fisch lateral infratemporal fossa approaches. Type A, B and C*

The Fisch A approach is indicated for lesions within the temporal bone, such as glomus tumors. This approach involves the exenteration of the middle ear, a subtotal petrosectomy, and a permanent anterior transposition of the facial nerve.

The Fisch B and C approaches are designed to approach more anterior pathology involving the petrous apex and clivus. The critical maneuvers in the type B ITF approach are the reflection of the zygomatic arch and temporalis muscle inferiorly and removal of the bone of the skull base floor to provide access to the ITF. A key to this extradural exposure is the subtotal petrosectomy. This step includes a canal-wall down mastoidectomy including complete skeletonizing of the labyrinth, facial nerve, sigmoid sinus, middle and posterior fossa dura, and the jugular bulb, as well as exenteration of all hypotympanic air cells and skeletonizing of the ICA.

The type C approach is an extension of the type B and is used for lesions of the anterior ITF, sella, and nasopharynx. The feature distinguishing the type C from the type B approach is resection of the pterygoid plates. This permits exposure of the lateral wall of the nasopharynx, eustachian tube orifice, posterior maxillary sinus, and posterior nasopharyngeal wall past the midline. The type D approach is a preauricular ITF approach that uses orbitozygomatic osteotomies and resection of the floor of the middle fossa to expose the medial middle cranial fossa without a lateral temporal craniotomy. Subtype D1 addresses tumors of the anterior ITF, while the subtype D2 is designed for lateral orbital wall lesions and high pterygopalatine fossa tumors[18].

### Retrolabyrinthine

The retrolabyrinthine approach is a true skull base approach that preserves hearing by following a direct route through the temporal bone to expose the cerebellopontine angle without manipulation of neural structures. The most common indications for this approach are resection of cerebellopontine angle and posterior petrous ridge tumors, vestibular neuronectomy, partial section of the sensory root of the fifth cranial nerve, fenestration of symptomatic arachnoid cysts, and biopsy of brain stem lesions.[19]

### Transcochlear

This approach is accomplished by forward extension of the translabyrinthine opening into the cerebellopontine angle. The facial nerve is mobilized in the temporal bone from the stylomastoid foramen to its entrance into the internal auditory canal. Having removed the barrier of the facial nerve, additional bone removal can be carried forward to the internal carotid artery, which now becomes the forward limit for temporal bone resection. The access attained through this exposure allows removal of tumors arising from the petrous tip, as well as tumors arising directly from the clivus[20].

### Translabyrinthine approach

This was reintroduced by Hitselberger and House21. This approach primarily used in cerebellopontine angle lesions provides wide access to the posterior fossa with little or no need for brain retraction. It is also used in the surgical management of petrous apex lesions when hearing is poor or the tumour is large[22]. The bony exposure is performed in three stages: complete mastoidectomy, labyrinthectomy, and IAC dissection. The primary disadvantages of this approach are the loss of any residual hearing, worsening balance function, and vertigo that occurs immediately after the surgery.

### Combined

The combined approaches provide exposure for lesions that extend in the middle and posterior fossa. These approaches use a transtemporal approach (retrola-byrinthine, translabyrinthine, and transcochlear) in addition to a middle fossa craniotomy. The primary advantages of these combined approaches are decreased brain retraction, improved exposure and the possibility for hearing preservation (retrolabyrinthine). The primary disadvantage is sacrifice of hearing if either translabyrinthine or transcochlear approach are used3, [22].

### Suboccipital

The areas exposed in this approach are the jugular foramen, occipital condyle, lower clivus to the midline, petrous apex, tympanic cavity, the vertical portion of the intrapetrous carotid artery below the level of the eustachian tube, cerebellopontine angle, the jugulocarotid space in the upper neck. The approach is indicated for extra-, intra-, and transdural lesions of the jugular foramen area. The main advantages are no cerebrospinal fluid leak, preservation of the facial nerve, middle and inner ear functions. Lower cranial nerve deficit formed the major morbidity in the present series and is still an unsolved problem in such cases[23].

### Anterior craniofacial

A Weber-Fergusson incision is employed and the approach is transmaxillary[24] .

### Middle fossa

This is most commonly used in Vestibular Schwannoma surgery when attempting to preserve hearing. The primary disadvantages being limited accessible tumour size, temporal lobe retraction, limited posterior fossa exposure and increased risk of tumour recurrence[25].

## Surgical Approaches to the petrous apex

### Infracochlear

This approach is utilized in cystic lesions of the petrous apex in patients with serviceable hearing. The main advantages being a dependant drainage in a well aerated middle space adjacent to the eustachian tube, adequate access to the petrous apex despite a high jugular bulb, simple revision if required and preservation of the normal middle ear mechanisms[3, 26].

### Subtemporal

This approach provides variying degrees of exposure to the petrous apex, clivus, ventral brainstem and anterior cerebellopontine angle[27].

### Infralabyrinthine

This is the most common approach to cystic lesions of the petrous apex in patients with serviceable hearing. A high-riding jugular bulb necessitates the use of infracochlear approach. The advantages of the infralabyrinthine approach include an anatomy familiar to most otologists, direct route to most cysts of the petrous apex, and avoidance of entering the middle ear[3].

### Subarcuate and sinodural angle approaches

These are mainly used in suppurative processes of the petrous apex[3].

### Supracochlear approach

This approach allows for drainage or biopsy of lesions in the anterior superior aspect of the petrous apex. The advantage being the preservation of the external auditory canal and the labyrinth. Unfavourable aspects include a significant risk to the labyrinthine facial nerve and the potential need for removal of the malleus head and incus.[3]

### Retrosigmoid approach

This approach gives excellent access for tumours that arise in the cerebellopontine angle and involve the posterior cranial fossa. The suprameatal extension of the retrosigmoid approach allows improved access to the petrous bone anterior to the internal auditory canal[3].

### Transnasal endoscopic approach

An endoscopic approach requires a wide corridor created with the removal of the middle turbinate ipsilateral to the lesion, a posterior septectomy, and bilateral wide sphenoidotomies. This allows a two-surgeon, four-hands technique, which involves the introduction of the scope, suction, and dissection instruments through both nares[28].

## Non-Surgical Management:

Advanced age, poor physical condition and extremely slow progress of the disorder are some of the indications for a non-surgical management to be considered.

Wait-and-see policy – A good alternative in glomus tumour, schwannoma or meningiomas which are small in size and are slow growing on meticulous follow-up examinations[29].

**Medical therapy –** There are few indications for medical treatment in skull base lesions. In meningiomas that may be unresectable or refractory, complete tumour resection may not be possible, or surgery may be contraindicated adjuvant therapy is helpful. Trials have been undertaken but with disappointing results with tamoxifen, thalidomide glucocorticoids, hydroxyurea and several chemotherapeutics[29].

Petrous apicitis is an inflammatory process often secondary to suppurative otitis media. Medical therapy is aimed at eliminating bacterial infection and promoting drainage with aggressive antibiotic therapy. Streptococcus pneumoniae, Haemophilus influenzae, and Staphylococcus aureus are the primary pathogens responsible for petrositis. Steroids may help decrease inflammation, pain, and swelling. Early surgical intervention is critical because of the severe complications secondary to chronic otitis media and petrous apicitis.

Skull base osteomyelitis is primarily a medical disease requiring long-term antimicrobial therapy directed against Pseudomonas aeruginosa. Severe otitis externa with granulation tissue in an immunosuppressed patient is the most common clinical setting. Often, the pain is described as deep and boring, with this symptom seeming out of proportion to physical findings. Aminoglycosides, coupled with an antipseudomonal penicillin derivative, are the antibiotics of choice. Quinolone antibiotics offer enteral therapy with encouraging results. Gallium-67 scanning is used to monitor the course of the disease. Technitium-99 scanning is more specific in the diagnosis, but findings remain positive after the course of the disease so they cannot be used to monitor therapy[30].

**Somatostatin therapy for glomus tumours –** Histologically these tumours present a high concentration of somatostatin hormone-binding sites on their cell surface[31]. Somatostatin 20 milligram deep intramuscular injections given once every three months can be considered as a further treatment option in recurrent or inoperable tumours[32].

**Radiotherapy –** Radiotherapy alone has a significant role in the management of these tumours. Radiotherapy

however carries the disadvantage of damaging the surrounding structures such as the cochlea, the facial nerve and adjacent brain tissue. Consequently radiotherapy is only applied to patients whose tumour is impossible to remove surgically or those who refuse surgery, are elderly or have a poor physical condition[29].

**Stereotactic Radiosurgery -** Gamma knife radiosurgery has been proposed as an alternative to conventional external beam radiotherapy as it has the capability of delivering high-dose single fraction radiation while sparing adjacent neurovascular structures.

This modality is used as an alternative to surgical treatment in vestibular schwannoma (tumours < 3.0 cm size)[33], paragangliomas[34]. Its role in meningioma is much more as an adjuvant to surgery, especially valuable in parts of the disease that is surgically inaccessible[35].

## SUMMARY

A technical revolution in microsurgery, anaesthesia and neurodiagnosis has made the management of skull base and petrous apex lesions less intimidating for the modern surgeons. There is need for more knowledge on the biological behaviour of the most common pathologies in the skull base. The role of radiotherapy and stereotactic radiosurgery still has to be defined. Prospective randomised studies are difficult due to the rarity of the lesions.

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# Sudden Sensorineural Hearing Loss – Aetiology and Management

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## ABSTRACT

Sudden sensorineural hearing loss (SSNHL) is a medical emergency for which a definitive aetiology and treatment remain controversial. It is defined as a hearing loss of 30 dB or more, over at least three contiguous audiometric frequencies, that develops over 72 hours or less. There are a long list of possible causes, but the vast majority of cases are idiopathic. Factors including auto-immunity, endolymphatic hydrops, vascular insult and infection have been postulated in the pathogenesis.

The ideal treatment of SSNHL remains controversial. Steroid treatment either systemically or via transtympanic injection are advocated, but other treatment regimes have been explored. It is noteworthy that many cases do improve spontaneously.

This is an area of active research at both the basic science and clinical level and should lead to further advances in our understanding of the condition and its treatment.

Sudden sensorineural hearing loss (SSNHL) is a medical emergency for which definitive aetiology and treatment is still controversial. It was described in the literature by De Kleyn as early as 1944[1]. SSNHL is commonly defined as a hearing loss of 30 dB or more, over at least three contiguous audiometric frequencies, that develops over 72 hours or less.[2,3].

The estimated annual incidence of SSNHL is 5-20 per 100,000 persons[2,4] and 99% of cases are unilateral[5]. The aetiology is identified in less than 5%-10% of cases and 50% of patients spontaneously recover[3].

Possible identifiable causes include infectious, traumatic, neoplastic, auto-immune, toxic, circulatory, neurologic and metabolic.

| | |
|---|---|
| **Infectious** | Meningococcal meningitis |
| | Encephalitis |
| | Herpes virus (simplex, zoster, varicella, cytomegalovirus) |
| | Mumps |
| | Measles |
| | Human immunodeficiency virus |
| | Lyme disease |
| | Rubella |
| | Syphilis |
| | Toxoplasmosis |

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| **Traumatic** | Barotrauma |
| | Perilymph fistula |
| | Intense noise exposure |
| | Inner ear decompression sickness |
| | Temporal bone fracture |
| | Ear surgery (stapedectomy) |

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| **Neoplastic** | Cerebellopontine angle tumours e.g. acoustic neuroma, meningioma |
| | Leukemia |
| | Myeloma |
| **Autoimmune** | Wegener's granulomatosis |
| | Rheumatoid arthritis |
| | Sjogren's |
| | Polyarteritis Nodosa |
| | Relapsing polychondritis |
| | Lupus erythematosus |
| | Polyarteritis nodosa |
| | Ulcerative colitis |
| | Cogan's syndrome |
| | Antiphospholipid Syndrome |
| | Sarcoid |
| | Autoimmune inner ear disease (AIED) |
| **Toxic** | Aminoglycoside antibiotics |
| | Loop diuretics |
| | NSAIDS |
| | Salicylates |
| | Platinum based chemotherapeutic agents |
| | General anaesthesia |
| **Circulatory** | Vascular disease/alteration of microcirculation |
| | Vascular disease associated with mitochondriopathy |
| | Vertebrobasilar insufficiency |
| | Red blood cell deformability |
| | Sickle cell disease |
| | Cardiopulmonary bypass |
| **Neurologic** | Multiple sclerosis |
| | Focal pontine ischemia |
| | Migraine |
| **Metabolic** | Hyperlipidaemia |
| | Thyrotoxicosis |
| | Diabetes |

Despite this long list of possible causes the vast majority of cases are idiopathic. Several factors have been postulated as central to the aetiology of idiopathic sudden sensorineural hearing loss. Possible causes include labyrinthine viral infection, vascular insult, intracochlear membrane rupture, autoimmune inner ear disease.

## Viral

Viruses particularly the Herpes family, can cause sensorineural hearing loss in acute infection and it is possible that reactivation of the latent virus could cause SSNHL[6,7,8,9].

Patients with SSHL have been shown to have a statistically significant increase in viral titres for seroconversion for CMV, influenza B, mumps, rubeola and varicella zoster[10]. Temporal bones examined at post-mortem exhibit histopathologic evidence consistent with viral infection in patients with SSNHL.[11]

Animal experiments have demonstrated viral penetration of the inner ear [12] and the isolation of virus and viral antigens in perilymph of affected patients provides further evidence for the viral aeitiology.

## Vascular

SSNHL can be explained by a blood viscosity change, leading to ischaemia, however there is a lack of evidence from experimental and clinical studies. Patients with ISSNHL are no more likely than the general population to have a hyperviscosity disorder.

However patients with sickle cell anaemia and Waldenstroms macro-globulinaemia have a higher risk of SSNHL which is usually reversible with treatment[13, 14].

Strokes involving the anterior inferior cerebellar artery are associated with auditory and vestibular symptoms, but also cerebellar symptoms. In addition SSNHL following cardio-pulmonary bypass has been reported[15].

## Intracochlear membrane rupture

Rupture of the intracochlear membrane was proposed as a cause of sudden hearing loss but the evidence is only coincidental and studies looking at temporal bones of patients with SSNHL found no evidence of Reissner's or basilar membrane rupture[11].

## Autoimmune

Historically the inner ear has been regarded as an immuno-privileged site, separated by the blood labyrinthine barrier. However we now know that immunoglobulins predominantly IgG are found in the perilymph at a fraction of their serum concentrations[16]. The endolymphatic sac is thought to be the likely site for immune processing due to the presence of lymphocytes in the perisaccular tissues[17].

SNHL has been reported in many systemic autoimmune disorders such as Wegeners granulomatosis[18], rheumatoid arthritis[19], polyarteritis nodosum[20], Sjogrens syndrome[21], Cogans syndrome[22], systemic lupus erythematosus[23], ulcerative colitis[24] and relapsing polychondritis[25] providing evidence that autoimmunity can damage the inner ear although it does not address organ specific disease.

In 1979 McCabe described autoimmune inner ear disease (AIED) a rapidly progressive bilateral SNHL that responded to steroid therapy. The cause is thought to be due to either antibodies or immune cells that damage the inner ear there are several theories as to how these may arise[26].

Yoo et al reported that rodents injected with type II collagen developed new onset SNHL and pathologic cochlear changes that appear to be immune mediated[27,28]. However in a more recent study Lopez –Gonzalez et al found the incidence of anti type II collagen antibodies to be very low and disputed it as a cause of AIED[29].

Harris and Sharp used bovine inner ear extract as antigen in Western blot assays and detected antibody to a 68kDa antigen in 35% of patients with progressive SNHL[30]. There is evidence linking the 68kDa antigen with highly inducible heat shock protein (hsp)70[31].

Damage to the inner ear results in the release of cytokines, which trigger immune reactions. TNF-alpha, IL-1A, NFkB and IkBa have all been found in the cochlea[32].

Activation of cochlear nuclear factor kappa B (NF_B) has been proposed as a mechanism of SSNHL as it would account for clinical and histological observations but there is no direct evidence.[33]

The inner ear may share common antigens with a potentially harmful substances and T-cells and antibodies may damage the inner ear when trying to fight these antigens. COCH5B2 has been proposed as a target antigen[34].

Further research is required fully understand the aetiology of AIED and to develop diagnostic tests.

## Menieres

The first presentation of Menieres Disease may be as SSNHL and therefore it is important to consider in the differential diagnosis. The classic triad of Meniere's is episodic vertigo, tinnitus and deafness. The aetiology is unknown and theories include autoimmune activation and labyrinthine ischaemia., patients develop endolymphatic hydrops which results in the classical symptoms. The audiogram classically shows a low frequency hearing loss.

## History

The aim in evaluating any patient with SSNHL is to identify any treatable causes. Points to cover in the history are:

- The onset of the hearing loss, patients with SSNHL often first notice their hearing loss on awakening in the morning and a better prognosis is associated with a short history.
- A poorer prognosis is associated with increasingly profound hearing loss.
- The pre morbid hearing level, SSNHL can either be a new loss or an incremental deterioration in an ear with a pre-existing loss. Conditions such as Meniere's disease can cause sudden fluctuations in hearing.
- Is the loss unilateral or bilateral? Unilateral loss is commoner but autoimmune disease and ototoxicity are more likely to be bilateral.
- Associated symptoms such as tinnitus, vertigo, dizziness and aural fullness should be asked about and may point to a diagnosis of endolympatic hydrops. Vertigo is a poor prognostic indicator in SSNHL.
- Any history of trauma, straining, diving, flying and intense noise exposure should be noted. Patients should be questioned about previous or concurrent viral infections.
- A past medical history of other diseases associated with sudden hearing loss should be explored as SSNHL can rarely be the first presentation of a systemic disease.
- Any history of previous ear surgery should be noted.
- A full drug history should be elicited to rule out ototoxicity.

## Examination

A complete examination of the head and neck should be carried out on all patients with SSNHL. Otoscopy should be performed to exclude middle ear effusions, infections, cholesteatoma and wax impaction. A fistula test may help identify a perilymph fistula. A thorough neurological examination of cranial nerves and cerebellar signs is essential.

## Investigations

Audiometry must be performed and may give an indication of prognosis as a downward sloping audiogram is associated with a poorer outcome.

Bloods including FBC, ESR, urea and electrolytes, lipid profile, glucose, thyroid function tests, clotting screen, VDRL and autoantibodies should be requested.

An MRI scan with gadolinium enhancement should be performed to exclude an acoustic neuroma but is also useful in evaluating multiple sclerosis and cerebrovascular accidents.

## Treatment

The high spontaneous recovery rate for ISSNHL approximately 50% and its low incidence make validation of empirical treatment difficult. Many treatment regimens have been proposed;

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|---|---|
| **Anti-inflammatory/ immunosuppression** | Steroids[3,35]<br>Prostacyclin[36] |
| **Antiviral agents** | Acyclovir[37,38]<br>Valcyclovir[39] |
| **Vasodilators 5% carbon dioxide with 95% oxygen** | (Carbogen)[35,40]<br>Papaverine[40]<br>Pentoxifylline41,42,43 |
| **Volume expanders/hemodilutors** | Hydroxyethyl starch[42,44]<br>Dextran[40,42, 45] |
| **Calcium antagonists** | Nifedipine[46] |
| **Other agents and procedures** | Iron[47]<br>Vitamins [46,48]<br>Procaine[45]<br>Hyperbaric oxygen[49]<br>Gingko biloba[41] |

Steroid therapy is widely used as the standard treatment for SSNHL, however a systematic review and meta-analysis revealed no evidence of benefit of steroids over placebo[50,51]. The evidence for steroids comes from Wilson et al who found that steroids had a significant effect on the recovery of hearing in patients with hearing loss between 40 and 90 db[3]. Moskowitz et al confirmed Wilson's findings in 1984[52]. However the methodology of these studies has been criticised. Cinamon et al compared treatment with prednisolone, placebo, carbogen and room air inhalations and found no significant differences between the four groups[35].

Super high dose steroid therapy has shown greater hearing recovery than standard dose treatment but further research is required[53]. Caution should be taken when prescribing high dose steroids to reduce the risk of serious complications.

Intratympanic steroid therapy is gaining popularity as a treatment for SSNHL, particularly in refractory cases or those in which systemic steroids may be hazardous, but again evidence is lacking[54-57].

Ahn at al looked at 120 patients with SSNHL and found that the addition of intratympanic dexamethasone (0.3ml on days 1,3 and 5) to 48mg methyl prednisolone did not result in significant improvements in treatment of idiopathic SSNHL[58].

However Battaglia et al conducted a multicenter, double blinded, placebo controlled randomized study comparing hearing results in ISSNHL patients who have received 1. high dose steroid only, 2. intratympanic dexamethasone only and 3. a combination of high dose steroid and intratympanic dexamethasone. The results showed that high dose prednisolone plus intra tympanic dexamethasone significantly improved hearing but the numbers in this study were smaller[59].

Michel et al compared intravenous prostacylin therapy with saline and found no significant difference between the groups[36].

Acyclovir has been used for the treatment of SSNHL both alone and in conjunction with steroids but neither shows any significant improvement in hearing. Valcyclovir has also been used in conjunction with steroids but again offers no improvement above controls[37,38,39].

Agents thought to increase cochlear blood flow, papaverine, pentoxifylline, hydroxyethyl starch, dextran, nifedipine and ginkgo biloba show no difference between active treatment and controls[41-46].

Kronenberg et al compared intravenous procaine, dextran and placebo and found no significant differences in outcomes[45].

Hyperbaric oxygen treatment shows limited evidence of hearing improvement only in patients that present early. This improvement was not functionally important therefore the treatment is not widely recommended[49].

## Prognosis

Four factors have been shown to affect recovery from ISSNHL:

1) Time since onset – the earlier the presentation the better the prognosis.
2) Age – there is a worse prognosis in the over 60's.
3) Vertigo - a poor prognostic indicator.
4) Audiogram - Patients with profound hearing loss and a downward sloping audiogram have a poorer prognosis.

It is important to reassure patients that 50% of cases have spontaneous recovery with no treatment. Due to the lack of evidence for any single treatment it is important to discuss the risks and benefits of each treatment to enable the patient to reach a decision about their care. Patients should be followed up to monitor for delayed symptoms and repeat audiograms. Evidence shows that improvement rate in the first 2 weeks may predict long term outcome[60,61].

## Conclusion

The aetiology and treatment of SSNHL remains controversial. Current research supports several possible aeitiologies and although a variety of treatment options have been investigated there is no clearly optimum management. There is a need for high quality evidence and further research is required.

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# The management of lesions of the cerebellopontine angle

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No competing interests

## Introduction

Lesions of the posterior cranial fossa, whilst uncommon have historically held a particular fascination for the neuro-otologist/skullbase surgeon and remain a surgical challenge. Over the last decade however the philosophy behind the management of the majority of such lesions has changed. This article summarises the contemporary approach to the more common abnormalities encountered in modern posterolateral skullbase practice.

Over a ten year period as a subspecialist skullbase surgeon, the author has encountered the following posterolateral skull base conditions:

| | | |
|---|---|---|
| Vestibular schwannoma | 389 | 74% |
| Petrous/CPA meningioma | 28 | 5.5% |
| Cholesteatoma (epidermoid) | 18 | 3% |
| Paraganglioma | 21 | 4% |
| Facial schwannoma | 5 | 1% |
| Squamous carcinoma | 21 | 4% |
| Cholesterol granuloma | 13 | 2% |
| Arachnoid cyst | 8 | 1.5% |
| Miscellaneous | 26 | 5% |
| **TOTAL** | **529** | |

The spectrum of pathology seen and relative frequencies is entirely consistent with the experience of other skullbase teams as reported in the literature (Springborg et al, 2008, Moffat et al, 1993, Brackmann and Bartels, 1980). This article considers the current management of those CPA pathologies in which there has been a shift in management strategies in recent years, namely vestibular schwannoma, meningioma, cholesteatoma and facial schwannoma.

## Vestibular schwannoma

Vestibular schwannoma (VS) constitutes between 70% and 80% of tumours of the CPA and the management philosophy has changed greatly over the last decade. Prior to the advent of CT scanning and particularly MR imaging, patients with a VS presented late with large tumours and surgical removal was the only viable proposition to prevent the patient's demise. In such instances the morbidity and indeed mortality following surgery was significant (Ramsden and Saeed). In recent years, with universal availability of MR imaging and its increased utilisation in patients presenting with unilateral audiovestibular symptoms, the majority of such tumours are diagnosed at an earlier stage. Early diagnosis of small tumours in patients with no neurological deficits aside from those relating to hearing coupled with the observation that the majority of small tumours, particularly in the more elderly population do not grow has led to the widespread emergence of the "wait-rescan" management option. In addition, refinements in the utilisation of stereotactic radiotherapy aimed at stopping tumours from growing means that a large number of patients with a VS have three management options available to them: microsurgical removal, stereotactic radiotherapy and observation by way of serial MR imaging. In order to explain to patients which of these options apply to them, the author finds it useful to stratify cases by tumour size, referring to the largest intracranial diameter on MR imaging or intracanalicular if there is no extension of the tumour into the cerebellopontine angle.

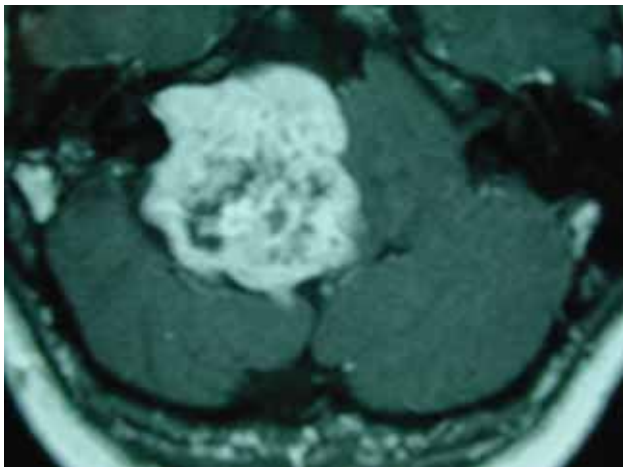

**Figure 1:** *Axial T1 weighted MR image with contrast showing a giant vestibular schwannoma with gross distortion of the brainstem and cerebellum.*

## Tumours 3cm or greater

A posterior fossa lesion of this size will be indenting the adjacent cerebellum and brainstem with distortion of the 4th ventricle (figure 1). There may be clinical and / or radiological signs of hydrocephalus and many such patients will have trigeminal nerve symptoms and signs. The management of tumours of this size is microsurgical removal (Saeed and Ramsden, 2008), particularly since most centres that advocate stereotactic radiotherapy advise that between 2.5 and 3cm intracranial diameter is the maximum tumour size suitable for such treatment. This is because of the risk of neurological deterioration during the first few months after treatment due to oedema at the periphery of the lesion. There remains some debate as to the optimal surgical approach to large tumours. Patients presenting with large tumours usually have significant hearing loss in the affected ear and even in the occasional medially placed large tumour with good hearing, the chances of preserving the hearing at the same level are slim. The transtemporal (middle fossa) approach is inappropriate for such a large CPA lesion. The proponents of the translabyrinthine approach argue that as long as the petrosectomy is undertaken adequately, there is no limit in terms of tumour size and there are advantages in identifying the facial nerve at the fundus of the internal meatus as the chances of preserving it are enhanced (figures 2 and 3). Those that prefer the retrosigmoid (posterior fossa) approach argue that the surgeon will have a panoramic view of the CPA, particularly around the lower cranial nerves. In fact both parties are correct. The important issue is that the surgery is undertaken by a team dedicated to the management of such patients and that they can draw on their experience and expertise in accessing the posterior fossa and removing the tumour. One issue that has changed and evolved over the last decade concerns the extent of tumour removal with large lesions. Unless the patient is particularly elderly or medically unfit, the aim of surgery should be total tumour removal. Partial removal does the patient a dis-service in that whilst the posterior fossa may well be decompressed the biology of large tumours is one of growth and a sizeable remnant will undoubtedly require intervention at a later date when revision surgery may be more difficult. What has become apparent in recent years however is that it is entirely appropriate to leave tiny pieces of tumour capsule which are proving difficult to remove from the facial nerve or brainstem in order to preserve neurological function (or the patient's life). The post-operative imaging 1 year later often shows that such "nubbins" of tumour have either disappeared due to loss of their blood supply or remain inert on subsequent serial imaging and rarely require re-operation (Lye et al, 1992). It is therefore the policy of the

**Figure 2:** *Translabyrinthine removal of right vestibular schwannoma showing the eggshell of bone being removed from the tumour in the skeletonised internal auditory meatus.*

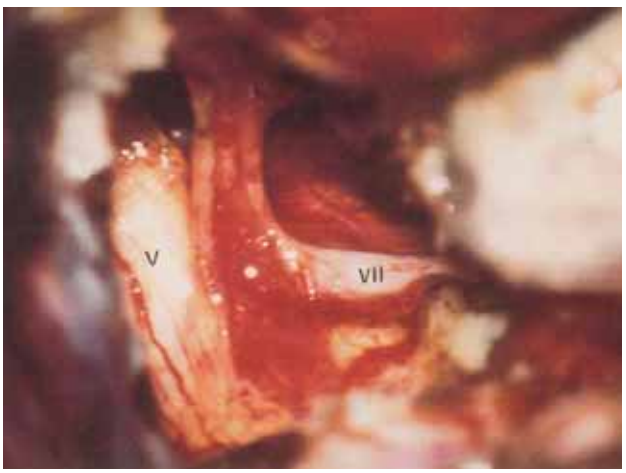


**Figure 3:** *Translabyrinthine vestibular schwannoma surgery following tumour removal, showing the CPA, trigeminal and facial nerves.*

author to always attempt total tumour removal but to be prepared to leave a tiny fragment, (usually where the facial nerve is most vulnerable just medial to the porus acousticus) in order to maintain good post-operative facial function.

### Tumours between 2cm and 3cm

Patients with tumours of this size require treatment as there has clearly been a period of sustained growth of the lesion and therefore serial imaging to establish this fact only serves to delay intervention. In addition, one of the key determinants of facial nerve outcome in the case of microsurgery is the size of the tumour and allowing the tumour to grow whilst waiting for imaging may tip the patient across the threshold at which facial nerve preservation rates begin to fall further. The great debate is whether the patient should undergo microsurgical removal of the tumour or stereotactic radiotherapy to stop the tumour growing any larger. The team dealing with such cases therefore needs to be able to present (both verbally and in writing in the case of the author) the patient with the facts about the two treatment modalities and the attendant risks. Whilst it is beyond the scope of this article to discuss such issues in detail, an overview is appropriate. Microsurgical tumour removal has evolved over the last 30 years to become an established viable option. The two major determinants of outcome after surgery are the size of the tumour being removed and the experience and skills of the team removing it.

There is no place for the occasional vestibular schwannoma surgeon and therefore during the counselling process the surgeon should draw on his or her own audited data when discussing outcomes and complications (Saeed et al, 2006, Gooden et al, 2006). The chances of a catastrophic event such as loss of life or stroke is significantly less than 1% in centres with a large VS caseload. The risk of serious complications such as meningitis, lower cranial nerve palsies and pulmonary embolus is around 2%. Perhaps the best barometer of the success of surgery is facial function outcome coupled with residual tumour rates as additional neurological injury (brainstem, lower nerves) with preservation of facial function is unusual. The residual tumour growth rate in planned total removal or in cases where a tumour fragment is left deliberately is 1% whilst facial outcome is related to the size of the tumour at surgery. Generally speaking, for *all* tumour sizes the chances of anatomical preservation of the facial nerve is 94% with normal or good facial function at one year post-operatively in 86% (House Brackmann grades I or II) (Saeed and Ramsden, 2008) (figure 4). Clearly surgical removal of a VS is a major procedure and whilst the majority of our patients come through surgery relatively unscathed, the attendant risks need to be understood especially since the patient has an alternative option.

The utilisation of stereotactic radiotherapy to prevent further growth of a VS has snowballed over the last 15 years. There is no doubt that the radiation doses used in earlier series caused unacceptable rates of complications such as facial palsy (worse than the microsurgical rates), trigeminal injury and hydrocephalus. In addition, much of the initial literature referred to series that failed to establish that the tumours were growing pre-treatment and therefore were inherently flawed when presenting "tumour control" rates. In recent years however the marginal doses of radiation have been reduced, imaging is more sophisticated and the outcome data is more robust. Encouragingly, reliable centres are reporting tumour control rates of between 75% and 97%, depending on tumour size, over several years of radiological follow up (Rowe et al, 2003, Lunsford et al, 2005). In addition, the facial palsy rates are very low, the incidence of trigeminal injury has fallen significantly and a proportion of patients treated this way have preserved hearing (see below). Before one relegates microsurgical removal of all tumours below 3cm to the history books however a number of issues need to be considered. Firstly, the patient still has a tumour and as time passes it will become apparent as to whether stereotactic treatment renders such tumours biologically inert permanently or whether there is a significant late (20 years? 30 years?) re-growth rate This may not be an issue for patients who are 65 or 75 years old but is certainly an issue for say a 40 year old. Secondly, will the patient require radiological surveillance for the rest of his or her life, and if so, at what intervals should the scans be done? Thirdly, some patients cannot accept the idea of having a tumour in their head and prefer to have it removed

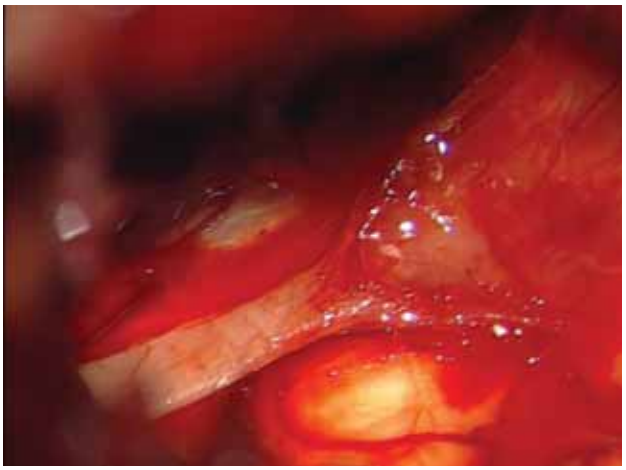

**Figure 4:** *Retrosigmoid removal of a vestibular schwannoma showing how the tumour had splayed the facial nerve. Note the small nubbin of tumour still to be removed.*

(conversely, some patients will flatly decline surgical removal). Fourthly, there is some evidence that salvage microsurgery after failed radiotherapy may prove more difficult particularly with regards to facial nerve preservation (Limb et al, 2005). Finally, over the last few years sporadic reports have emerged in the literature of patients who have developed a fatal intracranial malignancy many years after stereotactic treatment for their VS (Thomsen et al, 2000). If there is a causal link between the two then it possibly relates to the older radiation dose schedules but the low incidence of such a complication raises the issue as to whether the risk is any greater than that of chance. Nevertheless the reports are in the public domain and need to be discussed appropriately with the patient.

From the above discussion it is evident that the manner in which the patient is counselled will have a bearing on the decision making process and it is therefore is imperative that the two options are presented in as balanced a way as possible. Indeed, if the centre managing such patients can not offer both treatment modalities then the patient should always be given the option to discuss the alternative treatment with a centre that does offer it before reaching a final decision.

## Tumours between 1cm and 2cm

Patients with small to medium sized tumours often have little in the way of additional symptoms aside from their hearing impairment and tinnitus. Any initial balance symptoms usually disappear and most individuals function perfectly well on a day-to-day basis. For this reason, these patients have all three management options available to them. It is in this group that serial imaging to establish growth is a viable proposition. However if the tumour is already beginning to indent the brainstem or impinge on the trigeminal nerve most surgeons will advocate intervention rather than delaying treatment by waiting for the outcome of the next MR scan. This of course gives rise to the difficulty that stereotactic radiotherapy is utilised in such situations without establishing tumour growth and if the subsequent imaging shows the tumour to be radiologically static, one can not be sure that this was due to the treatment or the natural history of the treated lesion.

Nevertheless, in this group of patients, many surgeons will advocate a repeat scan either 6 months or 1 year after the diagnostic scan. If there is evidence of growth (defined as an increase in intracranial diameter of 2mm or more) then the patient can be counselled along the lines described above and treatment instigated. If however there is no change then the "wait-rescan" policy can continue with annual scans and then subsequent scans every 2 years if the tumour remains unchanged.

The only other issue in this group is that of hearing preservation and this is discussed in more detail below.

## Tumours less than 1cm or intracanalicular tumours

It is in these patients that perhaps there has been the greatest change in management philosophy in recent years. Once again it is likely that aside from the audiological symptoms the patient is otherwise well. The majority of these individuals will be advised to undergo serial scanning, reserving intervention for those in whom growth of the tumour is demonstrated. A question however arises in those patients in this group who have good or normal hearing: what is the optimal way to preserve this hearing for as long as possible? The literature in this respect is confusing and in many instances flawed. Reports in the past have failed to formally classify the hearing resorting instead to terms such as useful hearing, serviceable hearing and so on. In addition, it has been well recognised by ENT surgeons that overall hearing disability relates primarily to the hearing in the *better* hearing ear which is often normal in patients with a vestibular schwannoma. It also well recognised through the evaluation of outcomes in middle ear surgery that if the better hearing ear is normal then the operated ear has to have average thresholds that are within 30db of the better ear in order for the patient to perceive benefit. This raises the question as to why certain centres attempt to preserve hearing that is substantially poorer than the normal opposite ear. In order to standardise hearing classification the American Academy of Otolaryngology has described four classes (A to D) based on mean pure tone threshold and speech discrimination scores in the affected ear. There are now two main schools of thought with respect to hearing preservation in patients with small tumours. The first of these is to advocate serial imaging based on the fact that as many as 80% of such tumours do not grow, particularly in older patients and that the best way to preserve the patients hearing is to leave the tumour alone. Of those that do grow, there are those that advocate surgical removal (transtemporal or retrosigmoid approach) in an attempt to preserve the pre-operative hearing. In reality, even the most experienced centres are only able to preserve the hearing at the pre-operative level in around 60% of their patients (Friedmann et al, 2003). The alternative is to treat with stereotactic radiotherapy to halt the tumour growth and to attempt to preserve the hearing. The emergent literature in this respect does not necessarily substantiate this stance in that the hearing preservation rates after such treatment are not that different from the

natural rate of hearing deterioration in untreated tumours. The second school advocates microsurgical removal of the majority of small and intracanalicular tumours in order to preserve hearing, minimise the risk to the facial nerve and to render the patient tumour free. This would be fine were it not for the fact that a small proportion will suffer a facial palsy and the hearing will be lost or significantly impaired in as many as 40 to 50 %. In addition the transtemporal approach has inherent risks such as epilepsy, which will have an impact on activities such as driving (Aggarwal et al, 2005).

On this basis, the author currently advocates serial imaging in patients with intracanalicular / small tumours with intervention if there is evidence of growth. Only in those patients with class A hearing (for reasons outlined above), intracranial tumour size up to 1cm and no extension of the tumour to the fundus of the IAM are the merits and risks of immediate surgical removal or stereotactic radiotherapy discussed and the patient given a choice. In reality, few patients in our centre meet all these criteria and of those that do, most elect to undergo serial imaging in the first instance. These patients need to be aware however of the fact that they may lose their audiometric candidacy for hearing preservation intervention if their hearing deteriorates during the observation period.

## Meningioma

Meningiomas account for around 10% of neoplasms found in the CPA and therefore constitute the second commonest tumour pathology after vestibular schwannoma found in this anatomical area (Lalwani, 1992). In addition, such tumours exhibit clinical and radiological features that distinguish them from vestibular schwannomas. Because of the variable relationship to the eighth cranial nerve, hearing impairment and tinnitus is less prominent at presentation. Conversely, symptoms attributable to other posterior fossa cranial nerves, particularly the trigeminal nerve are more prominent than in patients with a vestibular schwannoma. Radiologically, these tumours tend to have a variable relationship to the internal auditory meatus (figure 5), are more sessile with respect to the face of the petrous bone and typically exhibit dural enhancement ("dural tail") on MR imaging with contrast (figure 6). This extension of tumour along the dura may be associated with local bone infiltration giving rise to localised hyperostosis or lysis.

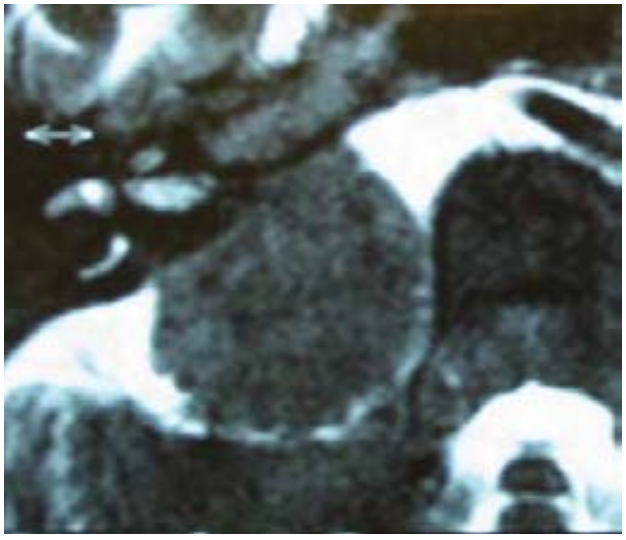

**Figure 5:** *T2 weighted MR image of a large right CPA meningioma with a broad base and little extension into the internal auditory meatus.*

Meningiomas may be classified according to radiological anatomical location, extent of surgical resection (Simpson grade) or histopathological features (World Health Organisation) in an attempt to correlate such parameters with outcome (Sekhar et al, 2001). The traditional management philosophy for such tumours was total surgical excision including the contiguous dura and abnormal bone in all but the medically unfit patient or the elderly with small tumours (Springborg and Thomsen, 2008). As with the management of vestibular schwannoma, this approach has changed in recent years for several reasons. Firstly, the propensity of CPA meningiomas to involve neurovascular structures is such that attempted complete excision of large tumours has always carried the risk of serious morbidity (lower cranial nerves, cavernous sinus) or mortality (brainstem). This merits of this approach have rightly been questioned. Secondly, even with smaller lesions, the nature of this pathology is such that even total macroscopic removal may be associated with small tumour rests being left in the adjacent dura or bone. Thirdly, the role of alternative treatments such as stereotactic or radical radiotherapy or brachytherapy is increasingly being considered though the

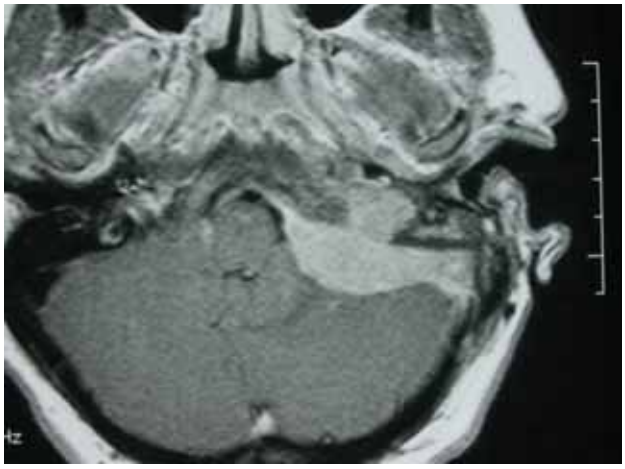

**Figure 6:** *T1 weighted MR image with contrast showing a left CPA meningioma with marked dural involvement.*

literature is limited currently with respect to long-term follow up Kumar et al, 1993). Nevertheless, microsurgical excision remains the intervention of choice in most instances. The approaches to the CPA are similar to those for removal of a VS with the exception of those meningiomas that extend into the clivus or Meckel's cave. In these instances the trans-otic approach (translabyrinthine with transcochlear) afford the additional anterior and medial exposure required. This approach may be combined with a transtentorial approach for tumours that involve or extend around the free edge of the tentorium.

## Cholesteatoma

Cholesteatoma or epidermoids account for around 1% of all intracranial mass lesions of which one third are in the CPA (Safavi-Abbasi et al, 2008). In the CPA they are thought to arise from epithelial cell rests that become sequestrated during otic capsule migration. As with normal skin and the typical tympano-petro-mastoid cholesteatoma, these lesions enlarge by accumulation of desquamated epithelium and keratin. This slow process often renders them asymptomatic for long periods. In addition the matrix of the lesion tends to encase and adhere to CPA nerves and vessels giving rise to a very variable clinical presentation when compared to vestibular schwannoma. In particular facial palsy is more common as a presenting symptom as are symptoms of trigeminal irritation (Mallucci et al, 1999).

The radiological diagnosis merits further consideration and is based on specific characteristic features that help distinguish cholesteatoma from other CPA lesions, in particular cholesterol granuloma. On CT scanning, cholesteatoma appears hypo intense and tends not enhance with contrast. In addition there may be characteristic irregular erosion of the contiguous petrous bone though sometimes there is smooth scalloping of the bone. MR imaging shows a heterogeneous low signal, poorly enhancing lesion on T1 images with a hyperintense lesion on T2 weighted images (figure 7). This distinguishes cholesteatoma from cholesterol granuloma which is hyperintense on T1 and T2 images. More recently, diffusion sequence MR imaging has further refined the radiological characteristics and allowed small lesions to be distinguished from surrounding structures (Dutt et al, 2002). This has important implications for radiological surveillance of post-operative residual disease.

The management of CPA cholesteatoma is essentially that of an expanding, potentially life-threatening posterior fossa lesion – surgical extirpation. Such lesions are readily approached via the retrosigmoid route if the lesion is

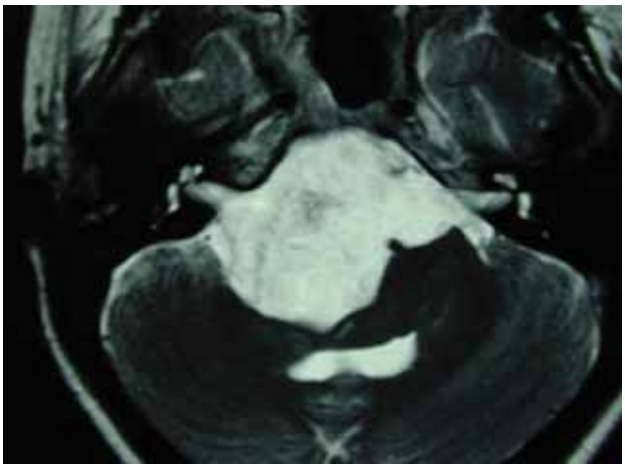

**Figure 7:** *T2 weighted MR image showing gross left CPA cholesteatoma extending across the midline.*

predominantly intracranial or by the transpetrous approaches (translabyrinthine, transotic) if there is significant temporal bone involvement. In the latter situation the large petrosal cavity will require fat packing and blind-end closure of the external auditory meatus. The aim of surgery is to eliminate the mass effect in the posterior fossa and excise as much of the squamous matrix as possible. Whilst the former is straightforward as the "cyst material is typically soft and can be aspirated, the latter can be difficult due to the adherence of the matrix to nerves, vessels, brain and dura. In addition, unlike benign tumours of the CPA which displace and stretch neurovascular structures, cholesteatoma engulfs these structures. The historical philosophy of attempted total removal of every last bit of matrix has been brought into question for three reasons in particular. Firstly, such an approach was associated with a significant risk of causing additional neurological harm, particularly with reference to the facial nerve. Secondly, despite perceived total macroscopic removal, it was unlikely that every last squamous cell was removed and so residual/recurrence rates were significant and thirdly, modern MR imaging allows accurate post-operative surveillance and judicious revision surgery. Currently, most surgeons advocate removal of as much of the lesion as possible with preservation of the neurovasculature of the CPA. The use of the endoscope may facilitate intraoperative inspection of awkward areas such as medial to the internal carotid and further enhance near-total resection (Schroeder et al, 2004). Despite this, the residual/recurrence rates are as high as 35% and the author invariably advises the patient that they may require more than one operation to deal with this problem, against a background of regular interval MR imaging.

## Facial Schwannoma

Facial schwannomas are uncommon, accounting for up to 3% of all CPA schwannomas (Axon et al, 2008). The

commonest sites of predilection for tumour development are the geniculate ganglion and the intralabyrinthine segment of the facial nerve (Kertesz et al, 2001). In addition two-third of these tumours may be multicentric, particularly in neurofibromatiosis type 2. The site of origin of these lesions dictates the pattern of proliferation and as such, facial schwannomas may grow into the middle ear, internal meatus or middle cranial fossa. A proportion however extend into the CPA. The management of these tumours evokes some debate though in recent years a consensus seems to be emerging. Patients may have normal or near normal facial function and present with other manifestations of the anatomical location of the tumour such as hearing loss or a mass in the middle ear. Conversely, the presenting symptom may be a slowly progressive facial palsy, recurrent facial palsy (often with incomplete recovery on each occasion) or indeed a sudden palsy that fails to recover, initially mimicking Bell's palsy. This serves to underpin the importance of MR imaging in any patient who presents with a facial palsy that does not recover or behave in the typical Bell's palsy manner.

The management of these tumours needs to take into account a number of factors. Firstly, there are advocates of tumour removal with preservation of the facial nerve in patients with normal or near normal pre-operative facial function. This is only likely to be successful with small lesions and nevertheless there is risk of causing a significant facial palsy, hearing loss and tumour recurrence. Secondly, resection of a facial schwannoma and repair (usually cable grafting of the nerve) is likely to give a House-Brackmann grade 3 outcome at best. Thirdly many patients presenting with a small tumour and good facial function maintain this situation for many years, particularly in the more elderly group. On this basis, the author advocates surgical resection of the tumour and repair of the facial nerve in specific instances dictated by the size of the tumour and the facial function at that point. If the patient has a significant CPA or middle fossa extension that puts the patient at risk of additional morbidity, the tumour is removed irrespective of the presenting facial function. If the patient has a small tumour but already has persistent grade 4 or worse facial function, then again tumour removal is offered with facial nerve grafting. In the remaining instances, that is good facial function and a small, otherwise asymptomatic tumour, robust serial MR imaging is recommended with surgical intervention if the tumour continues to grow or if the facial function deteriorates to grade 4 or worse during the observation period. The actual surgical approach to the tumour is dictated by the anatomical location of the tumour and the patient's hearing. On this basis, transmastoid/

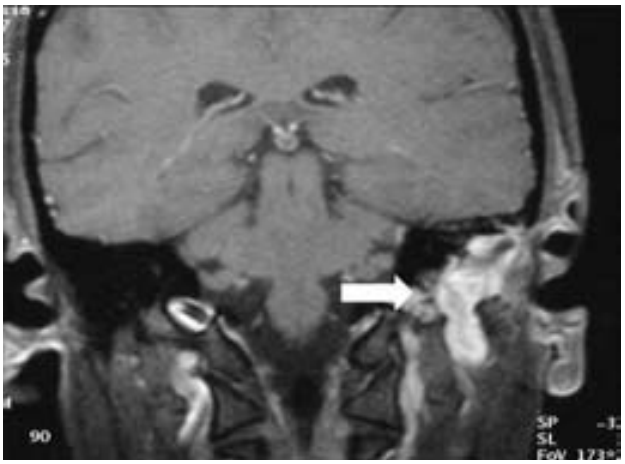


**Figure 8:** *T1 weighted coronal MR image with contrast showing a dumbbell facial schwannoma (arrow).*

transtympanic, transtemporal and translabyrinthine approaches have been utilised.

Finally, there is emergent literature on the utility of stereotactic radiotherapy for this pathology with encouraging results but for an uncommon pathology, as expected the numbers treated and reported are small (Magana et al, 1999).

## Summary

Tumours of the cerebellopontine angle continue to represent a significant surgical challenge for the lateral skullbase surgeon. Advances in imaging in recent years coupled with an increased availability and propensity to utilise such techniques has resulted in the diagnosis of these lesions at an earlier stage. This in turn has led to the historic management philosophy being questioned with the result that many tumours are being managed conservatively with serial imaging and an increasing number are being treated with stereotactic radiotherapy. In addition, the need for absolute total tumour removal with increased risk of neurological complications is also being scrutinised.

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# Local flaps for facial soft tissue defects

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Soft tissue defects of the face occur from skin tumour excision or following other trauma such as a road traffic accident. Face being the most noticeable part of the body these defects must be reconstructed with least possible sequlae. Following reconstruction it is inevitable to have scar along the junction of the reconstruction. By replacing the defect with tissues similar to the surrounding tissues in texture, colour and thickness as well as placing the scar along the relaxed skin tension lines (RSTL) (fig1) or margins of the facial units we can hide the scar to a great extent.

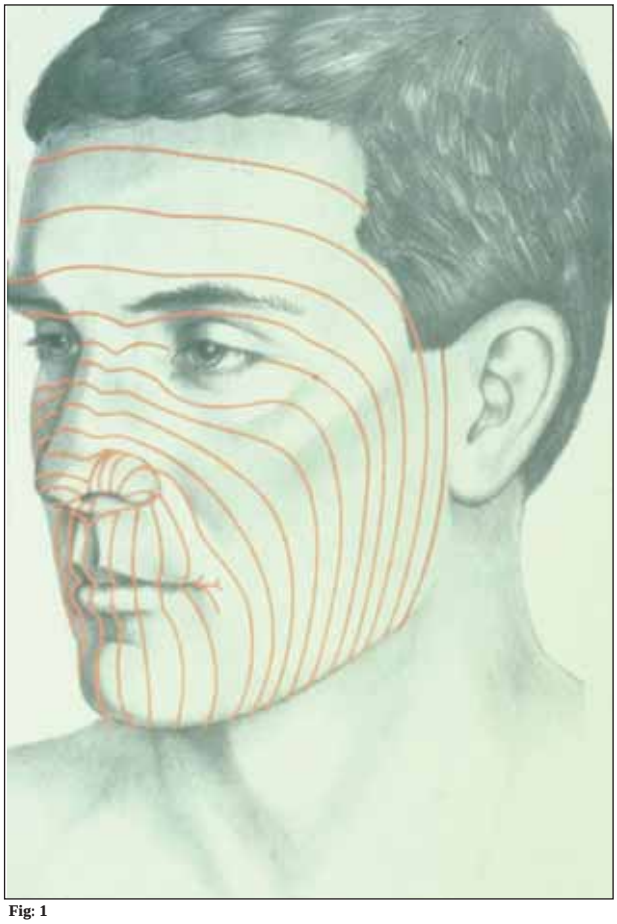


**Fig: 1**

The face is divided into aesthetic units by Gonzalez – Ulloa[1] viz: forehead, temple, cheek, nose, eye and chin. Each unit is further subdivided into subunits (fig:2) (Table 1).

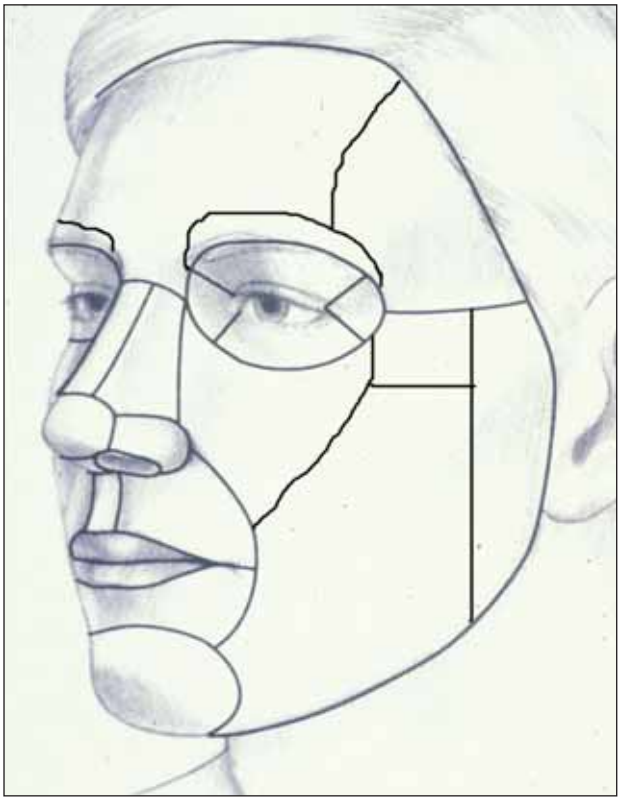


**Fig: 2**

**Table 1**

| Aesthetic units | Aesthetic Subunits |
|---|---|
| Forehead | Central, temporal and eyebrow |
| Eye | Upper lid, lower lid, medial canthal and lateral canthal |
| Nose | Doral, lateral, tip, ala. Soft tissue triangle and columella |
| Cheek | Medial zygomatic, buccal and lateral |
| Lips and chin | Upper and lower mucosal lips, philtrum, lateral subunits of upper lip, lower lip and chin |

Aesthetic subunits are segments of contour broken by a change in undulation, skin quality or shadow. Different facial regions have their own colours, textures, mobility and contour. Every region is distinguished from other regions by its pattern of hair growth, quality and skin texture[2]. It is considered ideal to replace the whole subunit if more than 50% of the subunit is involved in the defect[3]. This may not be possible in all subunits as it may result in developing large flaps eg: medial subunit of cheek. When more than one subunit is involved in the defect it is advisable to reconstruct each subunit using different flaps. Reconstruction of facial defects must result in proper function and an aesthetically pleasing appearance. In areas like eyes and nose a full thickness defect must be repaired with soft tissue lining on both sides with scaffolding in between. Full thickness defects of the lips may damage the nerve supply to the sphincter muscle and it may not be possible to rectify this completely using local flaps. Sometimes it may be necessary to alter the anatomy to achieve the right result. Alar margin do not have a cartilage support and consists only of skin and fibrofatty tissue. However when the alar margin is involved in the defect it must be reinforced with a cartilaginous graft to avoid notching. Huge defects of the face involving adjacent facial units may require free flaps or pedicled flaps brought in from other areas.

Facial defects can be closed by a variety of techniques.

## Primary closure

This is one way to close a defect provided it is small (less than 0.5cm) and is in an area where mobilisation of the edges can be done without distorting the neighbouring structures. The edges are undermined for at least 4 times the width of the defect. This allows mobilisation of skin with minimal distortion. If the defect follows a tumour excision then the axis of the defect can be arranged to fall in the RSTL so that the skin can be released along the line of maximum extensibility (fig 3) and when approximated the scar will be along the RSTL.

## Secondary intention

This technique is simple, does not require further surgery or hospitalisation and it avoids donor site scarring and pain4. Wounds allowed to heal by secondary intention do not necessarily give a bad scar[5] particularly in favourable sites such as the concave surfaces of nose, ear, eye and temple (NEET areas)[6]. Variables like position, depth and size of the defect and skin colouration and patient age should be considered before deciding for secondary intention healing[7]. The disadvantages are inconvenience due to a prolonged healing time, pain, infection, hypertrophic granulation tissue and scarring, hypopigmentation and distortion of adjacent structures through cicatrisation.

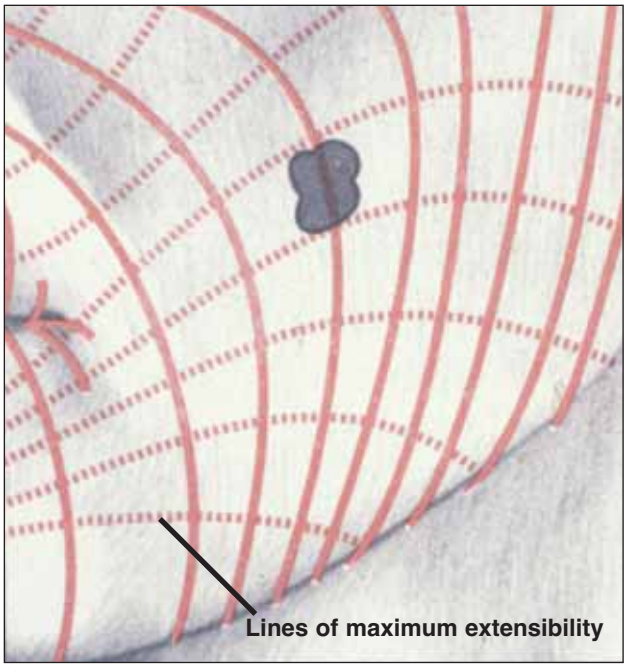
## Skin grafts

Skin grafting is a simple procedure, and provided the techniques are right and postoperative period uneventful, they almost always heal. However they can cause contracture, poor colour match, a tendency to contract around the edges and donor site morbidity resulting in unacceptable cosmetic result[8]. This is worse with split thickness skin graft and hence do not have a role in most facial reconstruction.

Full thickness skin graft (Wolfe graft) contains most of the structures of the skin. They give better cosmetic results than split thickness grafts but still inferior to local flaps. The full thickness skin graft is limited by its donor site availability and has an unpredictable 'take' over 2.5cm. They work better for defects involving the upper third of nose where as for the lower third of the nose the smooth thin graft will stand out among the thick sebaceous skin. For a full thickness graft to heal the underlying periosteum and perichondrium should be healthy and vascular and the graft must remain immobile for vascularity to develop. The preauricular, postauricular and supraclavicular areas are good donor site for Wolfe's graft.

## Local flaps

Local skin flaps have their own blood supply, and when designed well the healing rate is high with minimal postoperative contraction. The local skin flaps are of two



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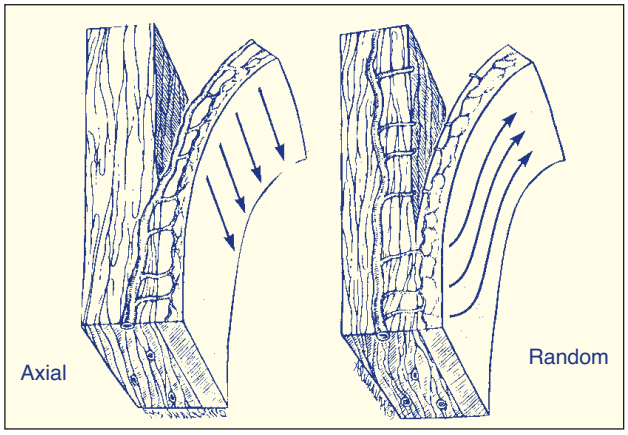


Fig: 4

types axial and random. The axial flaps have a named blood vessel supplying it (fig 4) eg: paramedian flap supplied by supra trochlear artery. Random flaps do not have a named vessel and is dependent on minor arteries, arterioles and subdermal plexus for its vascularity eg: rhomboid flap. Because of this there are limits to the length and size of random local flaps[9]. Wide undermining is needed to reduce tension and increase the mobility of the skin and subcutaneous tissue.

Local flaps are subdivided into advancement flaps, rotation flaps and transposition flaps.

## Advancement flaps:

These are the simplest of local flaps. The tissue is undermined and advanced in a straight line towards the defect. Unilateral advancement flap has limited use in the head and neck because of reduced flexibility[10]. Bilateral advancement flaps can be created on either side to cover the defect. Length of each flap can be varied to bring their junction to a favourable position eg: philtrum of upper lip. The length to width ration of each flap is 4:1. Examples of advancement flaps are the rectangular flap for forehead and upper lip defects (may need Burrows triangles excising to avoid "dog ears") (fig 5), the cheek advancement flap and the V-Y advancement flap[11].

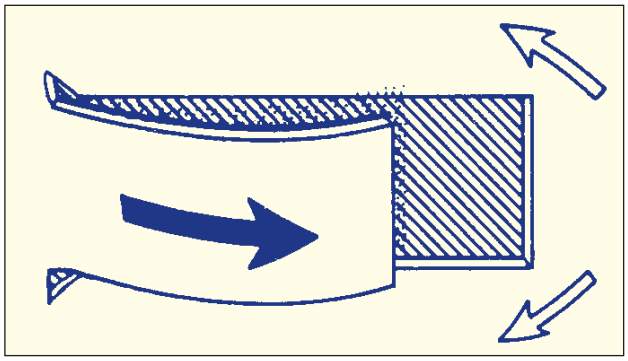

Fig: 5

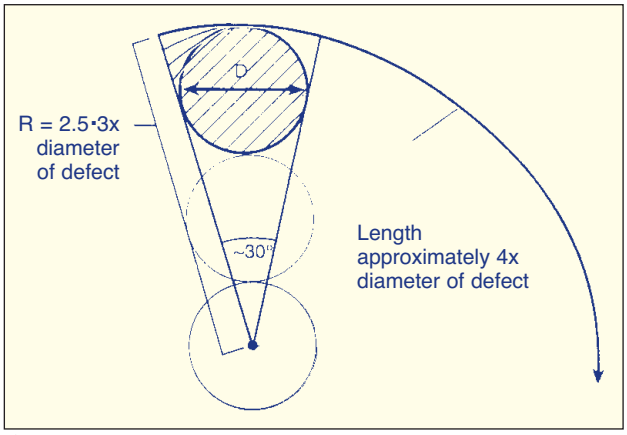


Fig: 6

## Rotation flap:

Here the flap rotates around an arc to close the defect. The entire flap and the surrounding skin need to be undermined in all directions. The length of the flap must be 4-6 times the diameter of the defect[12]. Failure to do this results in excessive tension during closure, buckling and possibly compromise vascularity[11] eg: cheek rotation flap, scalp rotation flap. (Fig 6)

## A-T flaps:

In this technique two rotation flaps used together and is

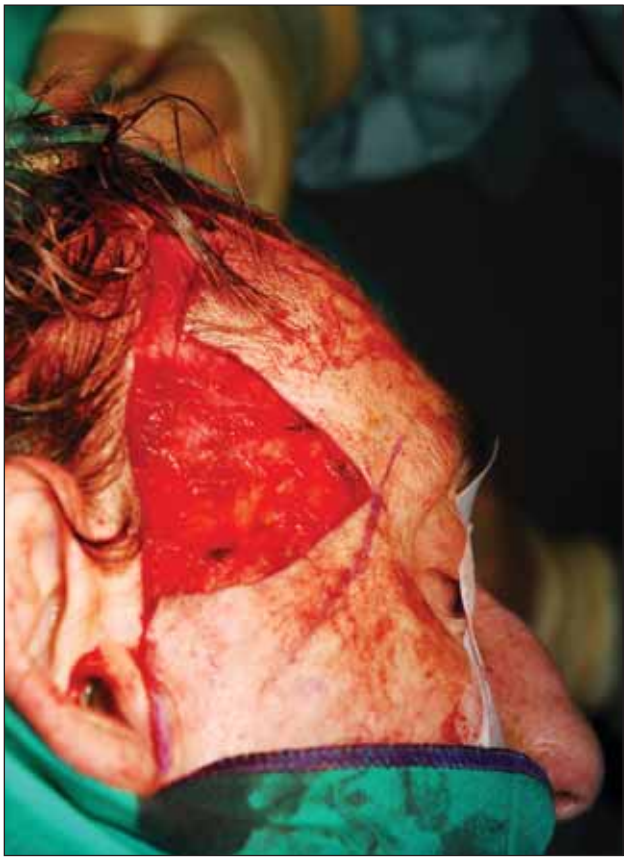

Fig: 7a

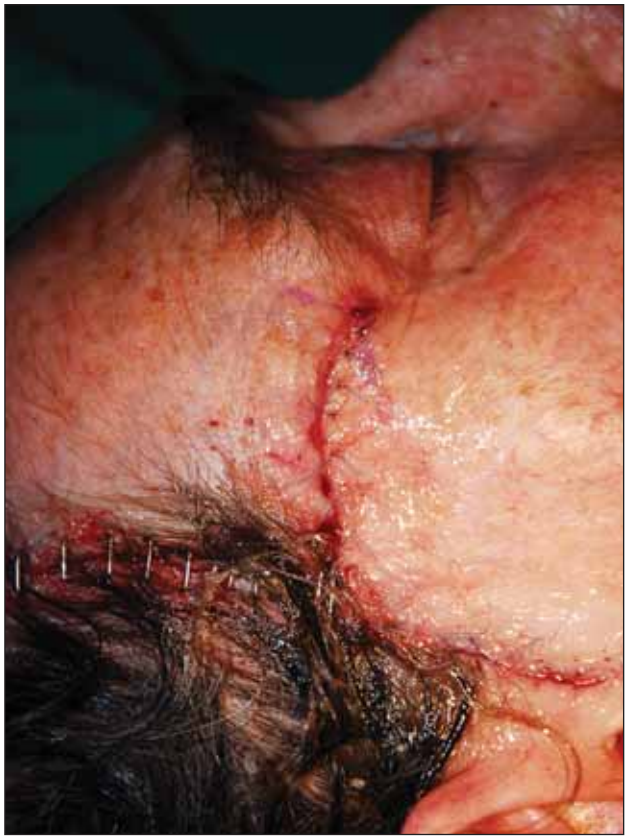

Fig: 7b

ideal for lesions in temple and forehead region close to hair line. A 'V' shaped excision of the lesion is done with the mouth of 'V' open towards the hair line. Then two flaps are raised on either side and rotated to close the defect. (fig 7)

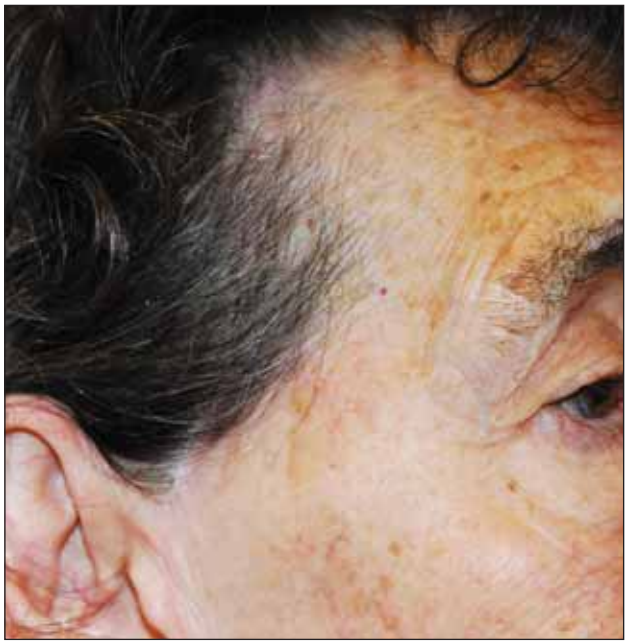

Fig: 7c

## Dorsal nasal flap

This is useful to cover a defect of the lower third of the nose with similar tissue but is not the ideal choice. The flap is elevated off the periosteum and perichondrium over the dorsum and sidewall of the nose up to the glabella. Then it is slid down to cover the defect. The advantages are that the skin is brought from an area of excess, the glabella, to the lower third of nose and the defect is covered by tissue similar to the lost one. However there are disadvantages. The thick and pitted skin of the glabella covers the medial canthal region causing an epicanthal fold. The flap does not coincide with the subunit excision lines. It is difficult to correct the large dog-ear made by this flap[13]. (Fig 8)

## Transposition flaps:

Transposition flaps are also called interposition flaps. These flaps are raised and rotated from the donor site over adjacent tissue to cover the defect. These flaps allow movement in more than one plane and examples of this are the bilobed transposition flap, the nasolabial flap and the rhomboid transposition flap[14].

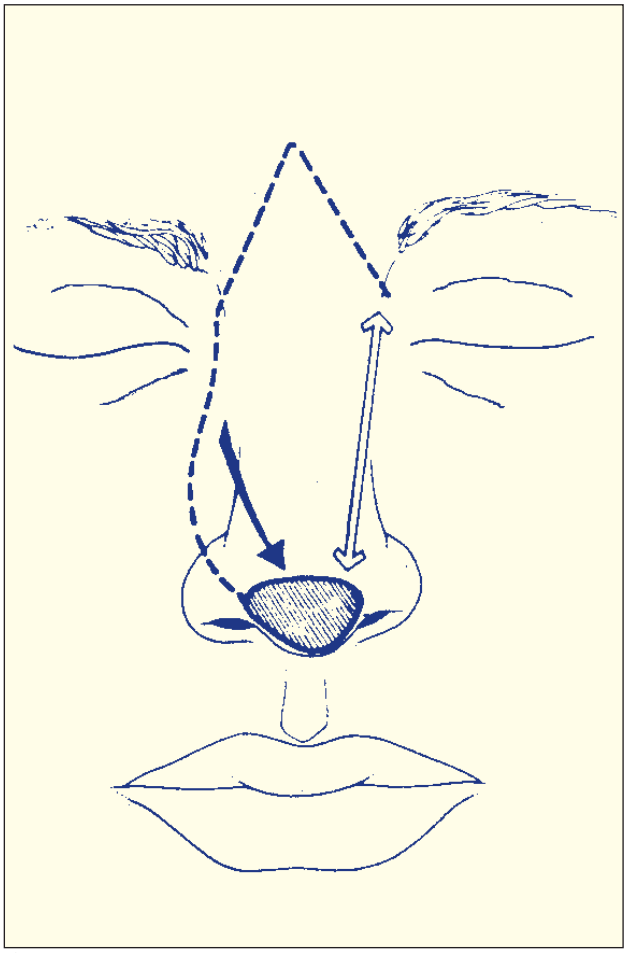

Fig: 8

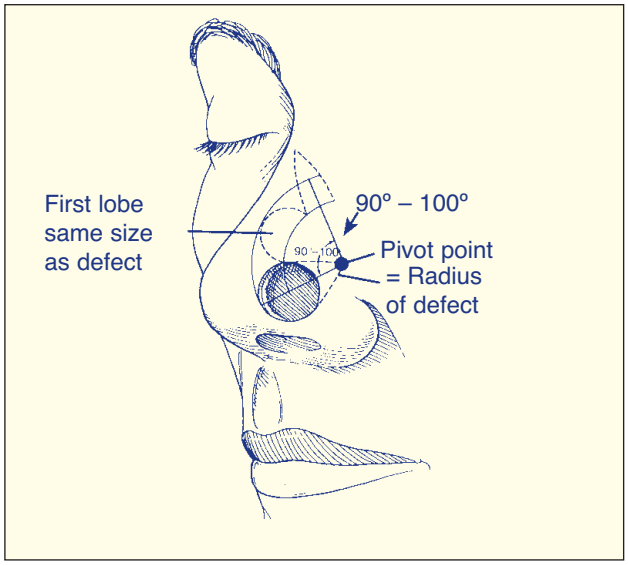


Fig: 9

## Bi-lobed flap

This is a random double transposition flap ideal for defects 0.5 cm to 1.5 cm in diameter in the lower third of nose. It is useful for defects of the lateral side of nose, where local skin of the same thickness and colour can be used to fill the defect. To avoid anomalies in the contour each lobe should not rotate more than 50 degrees. The angle between the axis of the defect and the second flap should be less than 110° to avoid dog-ear[13]. When the flap is designed care should be taken to avoid placing the first flap over the dorsal subunit as this may leave a depressed are on the dorsum even after reconstructing this defect with the second flap. A piece of skin is excised between the defect and pivotal point of the flap before rotation. The pivotal point is located away from the margin of the defect at a distance equal to the radius of the defect. It is never placed close to the medial canthus or alar margin. The diameter of the first lobe is equal or slightly less than the defect and the width of the second lobe is half of the first[13]. (Fig 9)

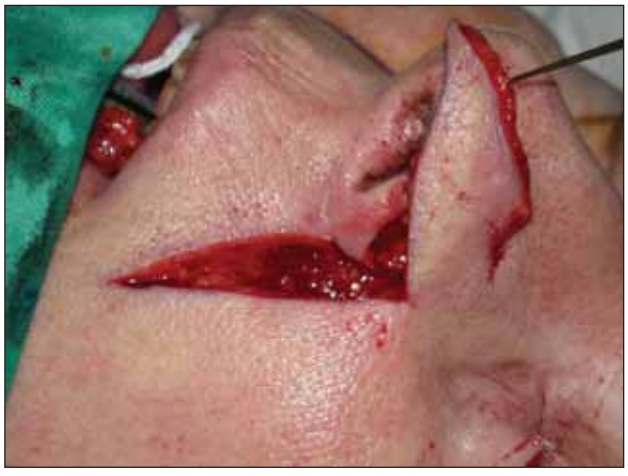

Fig: 10

## Nasolabial flap

This flap is suitable to correct the skin loss of the alar subunit, vestibule of nose and upper lip. The flap can be based inferiorly or superiorly, and the pedicle divided at a second procedure. Alternatively an island flap can be rotated into position[15,16]. The perforating branches of facial and angular arteries supply this flap and an island flap can be rotated 1800 to allow primary closure. In order to obtain a groove around the alar margin the nasolabial and cheek skin can be advanced a few millimetres more than might seem necessary and the rim left unsutured so that when healing takes place the reconstructed ala contracts a little and rolls up to form a more natural edge[17]. (Fig 10)

## Rhomboid flap

For defects of cheek and temporal fossa this is an ideal flap. The defect is modified into a rhomboid shape. Eight flaps can be designed for each defect. The one that causes least distortion to neighbouring structures and with the scar mostly in RSTL is selected. The rhomboid flap will give a '?' shaped scar and so is not possible to get the entire scar in RSTL. (Fig 11)

## Septal flaps:

Septal flaps are useful to recreate the inner lining of nose when reconstructing a full thickness defect. An anterior septal mucosal flap based on the septal branch of the superior labial artery or alternatively a posterior flap based on the septal branch of the sphenopalatine artery can provide an internal lining[18]. A septal flap produces a well vascularised lining and whilst it tends to crust for several weeks it will eventually provide a normal lining. If the defect is large and requires septal flap from both sides it will result in a septal perforation. It is important to raise these flaps under the mucoperichondrium to give them strength.

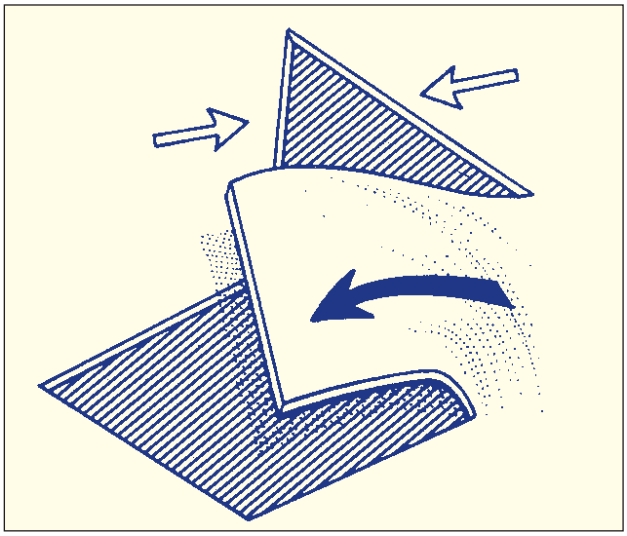

Fig: 11

**Fig: 12**

## The Paramedian Forehead Flap: (Fig 12)

This is an improved modification of the midline forehead flap and is the best alternative in dealing with major nasal defects[19,20]. If available a Doppler is used to identify this vessel and this helps to develop a narrow pedicle. The paramedian forehead flap is not only robust but the donor site often heals well even when it is not possible to close its upper part and this is left to heal by secondary intention. One of the main problems of this flap is its thickness, particularly if it is used to reconstruct the alar margin. It is possible to thin this skin down up to 1.5cms from its distal rim unless there are factors affecting its vascular bed. About 4 weeks later the pedicle is divided.

Vast majority of the defects of the face can be reconstructed with local flaps. The choice of the flaps depend on the site and size of the defect, neighbouring structures, general condition of the patients etc. Placing the scars in the RSTL or in the margin of the subunits make them less noticeable. As far as possible replace each subunit separately. For full thickness defects of nose and eyelids reconstruction must be in three layers, outer and inner soft tissue layer with middle scaffolding. If the defect involves the margin of the ala of nose, cartilage graft must be used to support the alar margin to avoid notching of the alar margin.

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# Rhinitis

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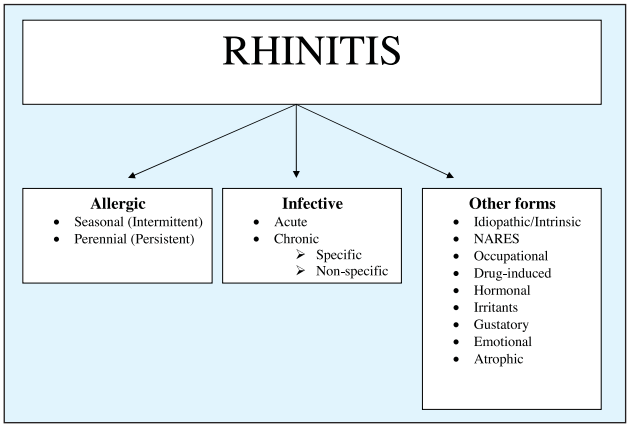
## Abstract
Rhinitis, which is recognised by the anterior nasal symptoms of itch, nasal discharge, sneezing and nasal stuffiness, is a very prevalent problem with a range of aetiologies. Allergic and infective causes are most common and have a substantial socio-economic impact. Allergic rhinitis significantly impairs quality of life and affects both school and work performance. The recognition of the disease, which is under diagnosed, and often considered "normal" by the patient, who does not perceive their symptoms as out of the ordinary for them, is important as the correct diagnosis allows the implementation of an appropriate treatment plan. The recognition of rhinitis is also of importance on account of its impact on the severity of co-morbid conditions, such as asthma, which may be improved with appropriate management of the rhinitis.

## Key words
Rhinitis, Classification, Epidemiology, Diagnosis, Quality of life

## Classification of rhinitis and clinical characteristics
A general classification for rhinitis is shown in table 1. Allergic rhinitis describes an inflammatory condition of the nasal mucosa, characterised by the anterior nasal symptoms of pruritus, sneeze, discharge and stuffiness, which is induced by an IgE-mediated response.[1] In addition, there may be an associated loss of sense of smell and inability to taste. This is most common in chronic rhinitis. The symptoms are periodic with seasonal disease, occurring in temporal relationship to the presence of seasonal allergens in individuals who are appropriately sensitised. The predominant allergens causing seasonal rhinitis are aeroallergens, commonly outdoor allergens, such as tree, grass or weed pollens. The time of pollination and hence the "season" for different allergens will vary from country to country depending upon the climate. In

**Table 1** – *General classification of rhinitis (NARES – Non Allergic Rhinitis with Eosinophilia Syndrome)*



temperate climates the typical pattern would be for tree pollination to occur in early and late spring, grass pollination in late spring and throughout the early summer months and for weed pollens, such as ragweed, to be present in the air in late summer and autumn. Perennial disease, which may be present all year round, relates to sensitisation to perennial allergens. These are typically indoor aeroallergens, such as those related to house dust mites, cockroaches, pets (cats, dogs) or, in certain climates, moulds. Individuals with perennial rhinitis may of course also be sensitised to outdoor allergens and experience worsening of their disease during the appropriate seasonal exposure.

Recent guidelines for the management of rhinitis have classified the disease as intermittent or persistent (Table 2), rather than seasonal and perennial[2,3]. There are several reasons for this. Firstly polysensitisation is common, with individuals sensitised to pollen allergens, such as those from trees, grass and weeds, having long lasting disease that potentially extends from early spring to late autumn in the temperate climates of the world. Their disease is thus more persistent than that in an individual with typical seasonal allergic rhinitis due to a single sensitisation. In the more tropical climates pollen sensitisation may lead to disease all year round, as there may be several periods of pollination and as such typical seasonal allergens may give rise to perennial disease. Conversely sensitisation to the typical perennial allergens does not always give rise to perennial disease. Depending upon the level of exposure and the degree of sensitisation the rhinitis may be intermittent or focused at one particular time of year. In those sensitised to animal allergens who do not own pets, the exposure and symptoms may only be intermittent and transient so the subdivision into intermittent and persistent disease is now preferred. Intermittent rhinitis is defined on the basis of symptoms that are present for less than four days per week and for less than four weeks in duration. If symptoms are present for more than four days per week or have lasted more than four weeks, regardless of the number of days per week, then the disease is classified as persistent. Much of the information on the pathophysiology of the disease has, however, been gained from those with allergic rhinitis who have been categorised as having either seasonal or perennial disease. It is probable that much of the information previously gained from naturally occurring disease reflects persistent disease, whereas detailed studies on allergen challenge, whilst not necessarily physiological, provide information relating to acute intermittent allergic disease.

**Table 2** – *Classification of allergic rhinitis according to the ARIA guidelines*

1- " Intermittent" means that the symptoms are present:
- Less than 4 days a week,
- Or for less than 4 weeks

2- " Persistent" means that the symptoms are present:
- More than 4 days a week,
- And for more than 4 weeks.

3- " Mild" means that none of the following items are present:
- Sleep disturbance
- Impairment of daily activities, leisure and/or sport,
- Impairment of school or work,
- Troublesome symptoms.

4- " Moderate-severe" means that one or more of the following items are present:
- Sleep disturbance
- Impairment of daily activities, leisure and/or sport,
- Impairment of school or work,
- Troublesome symptoms

Allergy is only one cause of rhinitis, albeit a common basis for persistent disease expression, with a range of other aetiologies giving rise to a similar spectrum of symptoms as allergic rhinitis. Whilst aetiologies such as upper respiratory tract viral infection are usually self-evident, on account of the constitutional upset and associated features, it is not always apparent which individuals with persistent disease have an allergic basis for their disease expression. The clinical diagnosis of perennial/ persistent allergic rhinitis is thus more difficult than the typical seasonal allergic rhinitis and is more dependent upon the ascertainment of the atopic status, by skin-prick testing or immunological testing of a peripheral blood sample for the presence of elevated immunoglobulin E (IgE) directed against specific allergens, along with a carefully taken history. The history will be important in separating the different conditions contributing to the non-allergic aetiologies. Gustatory rhinitis, for example, typically describes nasal symptoms after eating. Although this could be related to an IgE-mediated reaction against a food protein, this is much more commonly associated with the ingestion of hot and spicy foods or alcohol, particularly wines, and is likely to represent an irritant response or chemical sensitivity to naturally occurring chemicals, spices, preservatives and additives within the food. Changes in hormonal status, such as puberty and pregnancy, may be associated with nasal blockage and watery rhinorrhoea in elderly men (old man's drip) has been attributed to testosterone deficiency[4]. Some endocrine diseases such as hypothyroidism and acromegaly may be associated with the presence of nasal symptoms and certain systemic drugs, mostly those used for cardiovascular disease, may induce nasal obstruction due to alteration in nasal vascular tone. The topical use of decongestant sprays for nasal stuffiness is classically associated with rebound hyperaemia, producing progressively worse nasal obstruction, and rhinitis

medicamentosa with continued use. A careful and searching drug history is important, as the patient may not perceive as relevant the use of a topical decongestant brought over the counter from a pharmacy. In late onset rhinitis a good occupational history, assessing the relationship of symptoms to work and any relevant work related exposure is essential. It has also to be remembered that the presence of an elevated specific IgE does not necessarily mean that that atopic sensitisation is the underlying basis for the clinical disease manifestation. Those with rhinitis, who have no relevant sensitisation and in whom other causes of rhinitis and other disease that may manifest with nasal symptoms (Table 3) have been considered and excluded, are categorised as having idiopathic rhinitis. This is typically not an inflammatory nasal disorder and in such individuals with persistent non-allergic rhinitis, the symptom expression can be explained on the basis of an underlying neurovascular or neuroglandular disturbance[5,6].

Allergic and non-allergic forms of rhinitis may also be associated with nasal hyperreactivity. Nasal hyperreactivity describes an increased sensitivity of the nasal mucosa to irritants and non-specific stimuli, such as changes in temperature and strong odours[7]. The induction of nasal hyperresponsiveness may lead to persistent symptoms of nasal blockage and secretion for some time after the removal of the aetiological agent, e.g. upper respiratory tract viral infection[8]. Nasal challenge with a variety of stimuli, including methacholine, histamine and kinins, has been used to explore nasal reactivity[7]. These studies identify increased reactivity in rhinitics as compared to non-rhinitic controls,[9-12] and a tendency for greater reactivity in allergic as compared to non-allergic rhinitic subjects[7]. Although there is considerable overlap in measures, making clinical measurement of nasal reactivity in rhinitis less valuable diagnostically than bronchial responsiveness recordings in lower airways disease, such as asthma, end-point titration of the reflex-mediated response to histamine (sneezing and secretion) but not the nasal obstructive response has been shown to differentiate disease from non-disease,[11] and to correlate with clinical symptom scores.[12] The presence of nasal hyperreactivity means that individuals with rhinitis experience an enhancement of their nasal symptoms when exposed to ambient factors within the air, such as tobacco smoke, strong odours, perfumes, car exhaust pollutants and photochemical pollutants for example. The exaggerated response to these common environmental exposures may limit the life style of subjects with rhinitis and thus have an additional impact on their quality of life.

**Table 3** – *Differential diagnosis of rhinitis*

**Polyps**

**Mechanical Factors**
- Deviated nasal septum
- Hypertrophy of the turbinates
- Adenoidal hypertrophy
- Anatomical variants in the ostiomeatal complex
- Foreign bodies
- Choanal atresia

**Tumours**
- Benign
- Malignant

**Granulomas**
- Wegener's Granulomatosis
- Sarcoid
- Infectious
- Malignant - midline destructive granu-loma

**Ciliary defects**

**Cerebrospinal fluid rhinorrhoea**

## Quality of life and the socio-economic impact of rhinitis.

The impact of rhinitis on the individual is often underestimated. As rhinitis is not life threatening and may be seen purely as a nasal disorder, the disease is often trivialised. Quality of life evaluation reveals, however, that allergic rhinitis has a significant impact on well being beyond the presence of nasal symptoms[13,14]. Quality of life can be defined as "the functional effects of an illness and its consequent therapy upon a patient, as perceived by the patient".[15] There are several instruments for measuring quality of life in rhinitis. Specific instruments for different age groups of patients with rhinitis have been developed. The Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ),[13] and the Rhinitis Quality of Life Questionnaire,[16] have been tested in adult patients with seasonal allergic rhinitis and perennial allergic rhinitis respectively. These explore domains such as sleep, emotion, practical difficulties and life style limitations as well as nasal and eye symptomatology. They identify that patients with rhinitis may be bothered by sleep disorders, emotional problems, impairment in activities and social functioning. Also in general terms, patients with allergic rhinitis are impaired in physical and mental functioning, with low vitality and poor perception of general health. A further adolescent RQLQ questionnaire has been developed, covering patients in the age range of 12-17 years, which takes into account that adolescents may experience different limitations to adults[17]. This questionnaire is a slightly modified version of the adult version as problems in doing schoolwork and in general not feeling well have been found to be more relevant to adolescents than adults. A Paediatric RQLQ Questionnaire has been developed for children aged 6-12 years[18]. This questionnaire differs from others ones, as children are less bothered by emotional problems and rhinitis

interferes less with day-to-day life. These specific questionnaires have allowed the exploration of the impact of the disease and have also allowed exploration of the extent of benefit with a range of interventions. As they are disease specific, however, they do not permit comparisons of the impact of rhinitis on quality of life with other diseases. For this purpose, non-disease specific questionnaires, such as the Medical Outcomes Survey Short Form 36 (SF-36), have been used.[19] Although this is a relatively blunt instrument, not being sensitive to the depth of specific disease, it does nevertheless identify significant impairment in patients with moderate to severe perennial allergic rhinitis, in comparison to healthy non-rhinitic subjects,[20] to a level that is comparable to the limitations perceived by asthmatic patients with a moderate to severe disease.[21] There appears less impairment in patients suffering from seasonal allergic rhinitis,[22] possibly related to the shorter duration of their disease.

Allergic rhinitis has been found to impair work and school performance,[23-28] as well as learning ability and is a major cause of lost school attendance and work absenteeism.[29] It has been calculated that in one year in the USA, there is a staggering 811,000 missed workdays, 4,230,000 reduced productivity days and 824,000 school absences due to rhinitis.[29] There are thus, not only personal health costs, but also direct and indirect costs of the disease in health economic terms. While it is possible to cost the economic impact of days absent from work, it is more difficult to evaluate the financial impact of work impairment. One such study, which evaluated data on self-reported work performance and related it to variation in mould and pollen exposure, calculated months salary-equivalent work impairment costs for each allergy sufferer of between $109 and $156.28 Within the USA, it was calculated that this amounted to an annualised national projection of between $5.4 billion and $7.7 billion. The extent to which these costs could be recovered if all allergy sufferers were successfully managed is undefined. Allergic rhinitis is one of the 10 top conditions that commonly lead to consultation in managed case populations in the USA,[30] and for 1996, it was calculated that the direct financial cost of rhinitis in the USA exceeded $3 billion, while there were additional costs of $4 billion for its impact on concomitant conditions such as asthma and otitis.[31]

The association between allergic rhinitis and other conditions including asthma, sinusitis, otitis media, nasal polyposis, lower respiratory tract infection and even dental malocclusion have also to be considered when evaluating the socio-economic impact of the disease.[32] The relevance of rhinitis to the health care costs of these co-morbid conditions has been illustrated by a study of direct medical costs of illness in US children with and without asthma.[33] There were 3.1 times as many prescriptions, 2.2 times as many emergency department visits and 1.9 times as many ambulatory care visits in children with asthma as compared to children without asthma. Further analysis of the data, however, revealed that only 26% of these additional costs were related to asthma-specific medical care and that a substantial part of these additional costs were related to upper airways illness as such as rhinitis. Rhinitis commonly co-exists with asthma,[34] and may be overlooked if the individual is not assessed as a whole, and it is probable that a substantial amount of these additional costs may be saved with appropriate management of rhinitis. In populations in whom the treatment of rhinitis has been the focus of attention, this has been found to lead to reduced antibiotic prescribing, reduced consultations and to improved asthma control.[30,35,36]

It is thus apparent that rhinitis has an impact on the patient beyond the classical nasal symptoms and is a major cause of impaired work and school performance. The socio-economic impact of allergic rhinitis is particularly evident due to the change in the prevalence of the disease in the last century.

## Epidemiology of rhinitis.

Allergic rhinitis represents a global health care problem, affecting an estimated 10-25% of specific populations,[3] with higher figures from some countries in which approximately 40% of children have symptoms compatible with allergic rhinitis.[37,38] There is considerable variation in the prevalence of rhinitis between countries in different parts of the world, as identified by the use of a standardised methodology in the ISAAC (International Study of Asthma and Allergy in Children) study.[37] The prevalence ranged from 0.8% to 14.9% in 6-7 yr olds (data from 91 centres in 38 countries) and from 1.4% to 39.7% in 13-14 yr old children (data from 155 centres from 56 countries). One of the problems raised with this study was that only a questionnaire was applied and that this may not provide true information as to the real prevalence of the disease. In the SCARPOL (Symptoms with respect to air pollution, climate and pollen) study in Switzerland, the validity of the ISAAC core questions on rhinitis was tested in a population of 2,954 Swiss school children aged between 6 and 15 yrs old by comparing them to skin prick test results.39 The specificity of the ISAAC questions was high, ranging from 77.5% to 97.6%, but the sensitivity was low (2.6% to 42.7%). The positive predictive value for atopy among children with symptoms was 63% for sneezing accompanied by itchy-watery eyes, 67% for symptoms occurring only during the pollen season and 70% for reported seasonal allergic rhinitis. The authors

concluded that the ISAAC core questions on rhinitis are highly specific and therefore useful for epidemiological screening and also were found to have a high positive predictive value in detecting atopy among children with symptoms. In the SCARPOL study, sensitisation to any allergen was strongly associated with reported seasonal allergic rhinitis, nose problems accompanied by itchy-watery eyes, symptoms occurring only during pollen season (March through September), and a combination of these latter two in this age group.

Other epidemiological studies have also identified a significant relationship within communities between the prevalence of specific IgE sensitisation and the prevalence of rhinitic symptoms,[40-43] indicative of the relevance of atopic sensitisation to the development of rhinitis. The SCARPOL study found that the under-diagnosis of allergic rhinitis was common within the community and analysis of the ISAAC questionnaire responses has suggested that the timing of administration of questionnaires was important, in that there was a recall bias relating to recent symptoms.[44] On both these accounts it is probable that face-to-face interviews provide more reliable data than that from self completed questionnaires. This has been suggested from an interview survey of 12,355 23-year old UK residents born in March 1958, which reported considerably higher prevalence figures[45] than a population survey published at a similar time.[46] The interview reported a prevalence of seasonal allergic rhinitis of 16.5% as compared to 11% from the postal questionnaire involving 2969 adults. This interview-derived prevalence is comparable to a reported prevalence in Europe at that time of 16% in 15-24 year olds,[47] and to prevalence reports in student populations for hay fever of 18% and 21.1%.[48,49] It is possible that the lower figures from the postal questionnaire survey, which identified pure seasonal rhinitis in 3%, mixed seasonal and perennial disease in 8% and perennial rhinitis in 13%, reflects the more elderly population range in this study, 16-65 year olds, than the surveys focusing on the younger age groups. It is recognised that the peak prevalence for hay fever is in the younger age group, with peak prevalences being reported in 15-25 year olds in England and Wales,[50] 10-19 year olds in Denmark,[51] 24 year olds within the USA,[52] and 25-35 year olds in Australia.[53]

After these ages the percentage of the population consulting for hay fever therapy declines. There are a number of reasons for this but it is recognised that with increasing age there is a natural tolerance to the pollen allergens, in that in more elderly populations skin prick test responses remain but symptom reporting abates. There is also likely to be a cohort effect accounting for the differences between younger and older populations, in that the evidence suggests that hay fever is increasing in prevalence in children and teenagers,[2,47,54-58] and it will thus take several generations before this is reflected in the general population.

The figures for the prevalence of seasonal allergic rhinitis are more reliable than those for perennial allergic rhinitis, in that the disease is more characteristic in its periodicity and defined time of appearance. The figures for perennial rhinitis will encompass allergic and non-allergic forms of the disease and unless there is an evaluation of the atopic status and the findings evaluated in relationship to the history, it would not be possible to clearly differentiate these forms of rhinitis. The UK postal survey already alluded to, found a prevalence of perennial disease of 21%,[46] and a student survey has reported a prevalence of 37%.[48] Studies to apportion the basis for perennial rhinitis into allergic and non-allergic forms have been relatively small and may have a tendency to bias in that they are often from specialist clinics and thus reflect the referral pattern. Studies from allergy clinics[59-61] have variably reported that as a percentage of those patients seen with perennial rhinitis, that non-allergic rhinitis accounted for 17% (362 patients), 30% (152 patients) and 52% (142 patients) respectively.

An analysis of 1,142 subjects participating in the European Community Respiratory Health Survey, selected on the basis that they had a history suggestive of allergic rhinitis, concluded that 25% had non-allergic disease.[62] One of the difficulties is that a significant proportion of such patients tend to have mixed disease, in that they may have both allergic and non-allergic components to the clinical disease expression, and the categorisation of such patients, when dividing into either allergic or non-allergic forms, will depend on the perception of the categoriser. A retrospective analysis of 975 patients attending 15 allergy practices in the USA found that 23% could be classified as having pure non-allergic rhinitis, 43% as pure allergic rhinitis and 34% as having mixed rhinitis.[63]

On the basis of this study non-allergic disease could account for 23-57% of rhinitis and allergic disease for 43-77%, depending on the criteria used. The presence of mixed disease could thus account for some of the reported differences in prevalence. On the basis of such figures it has been estimated that up to 40 million individuals within the USA suffer annually from allergic rhinitis and that an additional 17 million are considered to suffer from the non-allergic form of this disease[20]. The appropriate treatment of such patients depends upon the accurate diagnosis, an understanding of the relevant aetiologies, and

knowledge of how the underlying disease pathophysiology can lead to symptom expression.

For a more detailed overview of the pathophysiological basis of allergic rhinitis, summary of the management protocols and pharmacological treatment modalities currently available, including interactions between asthma and rhinitis, the following reviews may be of interest[2,3,64-66].

## Concluding Comments

Allergic rhinitis is an increasingly prevalent airway disorder that significantly impairs the quality of the life of the sufferer. It is a common manifestation of a more systemic disorder affecting other mucosal surfaces, such as those of the conjunctiva, soft palate and lower airways. There is also a systemic perception of ill health. Others do not always appreciate the impact of the disease. Allergic rhinitis has been shown to adversely affect both school and work performance and to be a cause of absenteeism from school and work. The disease can only be appropriately managed once the disorder has been recognised, correctly evaluated and diagnosed.

The understanding of the pathophysiological basis for the disease expression allows the rational choice of therapy. The basis for other disorders manifesting with rhinitis such as, for example, occupational sensitisation, salicylate intolerance and infective and non-infective non-allergic rhinitis needs to be understood and considered when evaluating the patient. The evidence suggests that the appropriate use of treatment based on guidelines for management leads to a better outcome than non-guidelined management. The advantage of this in socio-economic terms is yet to be evaluated but in view of the substantial health care costs that arise due to the impact of rhinitis on the individual and on the severity of co-morbid conditions, rhinitis deserves to be given serious consideration.

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# Endoscopic management of Cerebrospinal Fluid Rhinorrhoea

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## ABSTRACT

Cerebrospinal fluid (CSF) rhinorrhoea is the result of fistula formation between the subarachnoid space and the nasal cavity. Most cases reported in the literature are post-traumatic with endoscopic sinus surgery being the commonest cause. Cases of spontaneous leak have increasingly been reported and pose a particular challenge due their higher tendency for recurrence after repair. Other aetiologies include hydrocephalus and tumours. The current review discusses the senior author's approach to and current controversies in managing this condition.

## INTRODUCTION

Cerebrospinal Fluid (CSF) rhinorrhoea was first described by Galen in the 2nd century AD as a 'normal' periodic release of CSF into the nose via the sella and ethmoid regions[1]. It results from a breakdown in the integrity of structures which separate the subarachnoid space and the nasal cavity, namely the subarachnoid membrane and dura mater, the bony skull base and periostia, and the upper aerodigestive tract mucosa[2]. This interferes with normal cerebrospinal fluid circulation which can result in symptomatic orthostatic CSF hypotension and puts the patient at risk of ascending intracranial infections[3]. Causes of CSF rhinorrhoea can be classified as traumatic or non-traumatic. Traumatic CSF rhinorrhoea can be further classified as iatrogenic or accidental with endoscopic sinus surgery being its commonest cause[4]. Non-traumatic CSF rhinorrhoea is further divided into congenital or idiopathic. This condition can also be classified based on whether the underlying CSF pressure is normal or elevated[5].

The aim of surgery is complete and durable separation of the subarachnoid space from the nasal cavity to reduce the risk of ascending intracranial infections, which, untreated, approaches 20%[3]. This furthermore restores normal CSF circulation which is critical for maintaining brain buoyancy and for preventing orthostatic CSF hypotension. CSF leak repair was first reported in 1911 by Dandy and the operation involved an intracranial approach[6]. The first endonasal endoscopic CSF leak repair was described by Wigand in 1981[7] and since then endoscopic endonasal repair has become the standard of care for repairing CSF fistulae. The current review discusses recent advances in diagnostic, surgical and postoperative management of CSF

rhinorrhoea, provides an overview of the senior author's approach to this problem and discusses some of the controversies surrounding this topic.

## PREOPERATIVE ASSESSMENT

**History.** The commonest symptom of CSF fistula is clear, often unilateral rhinorrhoea which is classically made worse by stooping or performing a Valsalva manoeuvre and can be associated with headaches, particularly on standing, which is due to CSF hypotension. The index of clinical suspicion should be raised if a patient with clear rhinorrhoea has a history of trauma or paranasal/cranial-base surgery, or in obese middle-aged females who are at increased risk of spontaneous CSF leaks[8]. Less commonly, a patient may primarily present with neurological deficits caused by a complication of an undiagnosed CSF fistula such as ascending bacterial meningitis, pneumocephalus or brain abscess[4]. Clinical history should ascertain the exact nature and chronology of symptoms, specifically enquire about history of trauma or surgery, and include a neurological history directed towards symptoms suggestive of past episodes of, or current meningism and intracranial sepsis.

**Clinical Examination.** The rhinological examination is important in excluding primary nasal pathology causing rhinorrhoea but is often normal in patients with CSF leak. Occasionally a clear CSF or an encephalocoele may be identified during endoscopic nasal examination (Figure 1). A neurological examination should be undertaken and be specifically directed towards excluding active meningism. In our practice all patients with non-traumatic CSF leak are reviewed by a neurologist prior to surgery to exclude benign intracranial hypertension.

**Intranasal Biochemistry.** Nasal glucose testing has been shown to have a false-positive rate of 45-75% and is not in routine use[9]. All patients undergo ß2-transferrin testing, which is a protein produced by neuraminidase activity in the brain, and only found in the CSF and perilymph. This test requires only 0.4ml of clear liquid and

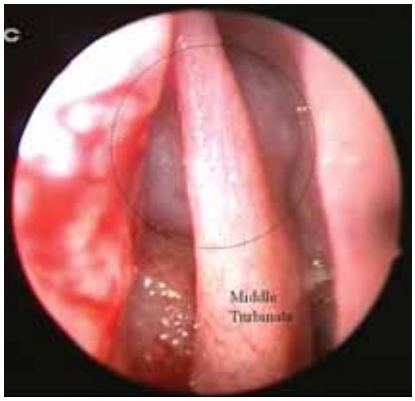


**Figure 1:** *Endoscopic view of the left nasal cavity showing an encephalocoele (interrupted circle) secondary to a defect of the cribriform plate*

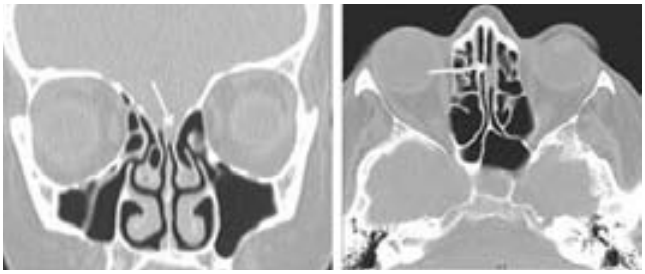

**Figure 2:** *Coronal (A) and axial (B) high resolution CT scans of a patient with a defect in the left olfactory niche (arrows) without history of trauma*

if the patient is unable to produce rhinorrhoea during consultation, a small sterile container is provided to the patient for later collection[10]. Beta-trace protein (prostaglandin D synthase) is an alternative, more recently described assay with comparable sensitivity and specificity to ß2-transferrin[11].

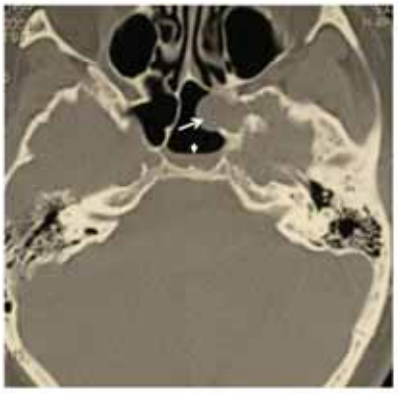

**Figure 3:** *An axial CT scan showing a left sphenoid encephalocoele (short arrow) with pooling of CSF (arrowhead).*

**Imaging.** All patients undergo 1mm-thickness high-resolution coronal computed tomography of the anterior skull base and the paranasal sinuses[12]. Defects or encephalocoeles can often be identified on the scan but occasionally only signs indicative of CES rhinorrhoea such as pooling in the sphenoid can be seen. Defects of less than 1mm in diameter are often missed on CT and MRI. There is no added value in CT Cisternography and it is not ordered in the authors' practice. CT images are

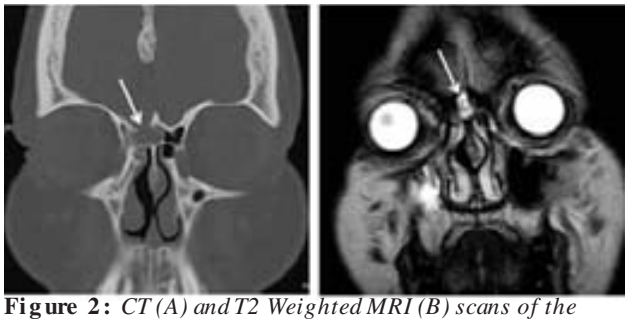

**Figure 2:** *CT (A) and T2 Weighted MRI (B) scans of the same patient showing a right sided encephalocoele secondary to a defect in the ethmoid plate (arrows). Note the bright signal of the CSF in the MRI scan*

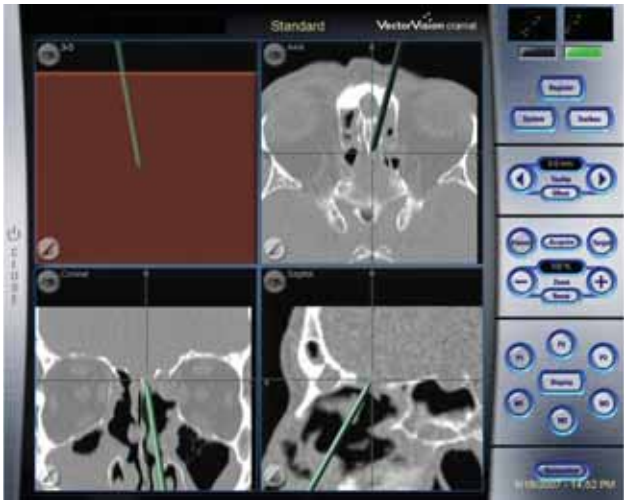


**Figure 5:** *An intra-operative BrainLab image showing coronal, axial and para-sagittal sections in a patient with post traumatic left ethmoidal CSF leak (green pointer)*

generally acquired using BrainLab® image guidance protocol so that they can be used for image navigation should surgery become necessary. Except in clear-cut cases of post-traumatic CSF rhinorrhoea, all patients also have an MRI scan to rule out further intracranial pathology (figures 2 to 5).

## SURGERY

**Intrathecal Fluoroscein.** This is used when the leak site is not readily identifiable on CT scanning or where there is concern about multiple leak sites (i.e post-traumatic cases with skull-base comminution) and in revision cases (figures 6 and 7)[13,14]. Safety of intrathecal fluorescein administration is ascertained at the time of admission for surgery with a small subdermal injection of fluorescein to test for allergy.

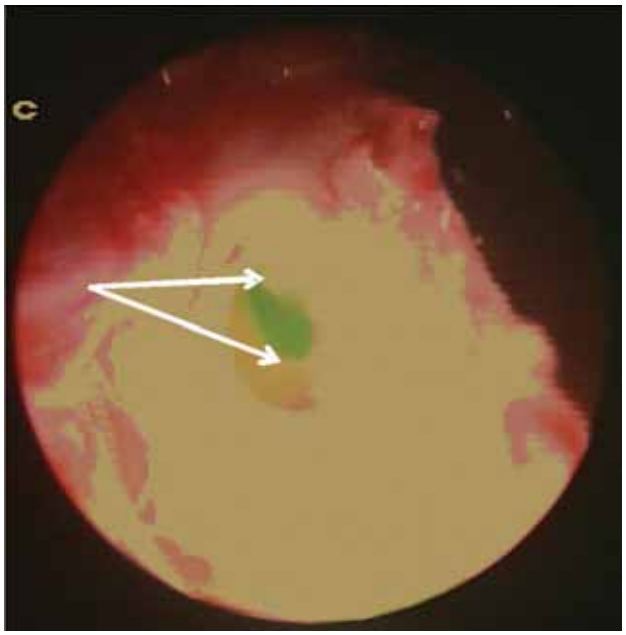


**Figure 6:** *An intra-operative photograph of <1mm defect in the left olfactory niche (arrows). This was not detected on CT but was readily identifiable using intrathecal fluorescein*

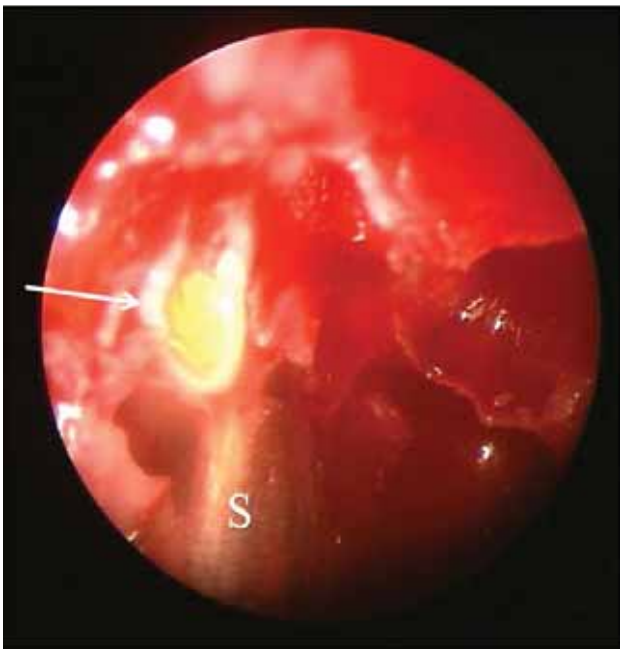


**Figure 7:** *An intra-operative photograph of 0.5mm defect in the lateral lamella of the left middle turbinate (arrow). This was not detected on CT but was readily identifiable using intrathecal fluorescein. S = suction tip*

**Access.** All patients receive nasal decongestion using Moffet's solution[15]. This is achieved using selective sinus dissection to identify the leak site. For sphenoid sinus leaks for example the ethmoid sinus and middle turbinate are not routinely disturbed whereas access to a lateral lamella or ethmoid sinus leaks requires an ethmoidectomy. Access to olfactory groove leaks usually requires partial middle turbinectomy. In special circumstances specific access techniques are necessary for example frontal sinus leaks, particularly those situated laterally or superiorly, require a modified Lathrop approach[16] while a proportion of spontaneous CSF leak via a pneumatised pterygoid require drilling down of the medial pterygoid and basisphenoid to improve access . In all cases the aim is to create a 5mm freshened mucosal perimeter around the leak site to allow the repair to proceed. We use BrainLab™ image guidance system in all cases.

**The Repair.** A variety of graft materials and methods of application have been described for endoscopic CSF leak repair. These include the use of local flaps, of which the middle turbinate osteomucoperiosteal flap or the septal

mucoperichondrial flap are the most notable and practised examples, or free grafts, which may be harvested from local nasal sites including turbinate mucosa or septal cartilage, or from distant areas such as temporalis fascia, fat or calvarial bone[6]. Alloplastic material, in the form of Hydroxyapatite cement (HAC) has been documented and collagen matrix (Duragen) is commonly used for dual repair[17]. Our standard endoscopic CSF repair consists of reducing the herniated dura or excising an encephalocele and then placing an underlay fascia lata graft into the defect. In selected cases where the leak is located at a difficult site, such as the lateral wall of the sphenoid, or in revision cases bone pate is used to reinforce the repair[18]. The repair is further closed using free mucosal graft taken from the middle turbinate as well as fibrin sealant (Tisseel). We occasionally use fat grafts for very small defects or to seal the edges of the fascial graft if there is still a leak. Once this repair is completed the nose is packed for one week with half an inch gauze pack impregnated in whitehead varnish.

**Postoperative care.** The aim of postoperative care is prevention or prompt recognition of intracranial complications and minimizing structural stresses on the repair while healing occurs. Patients are nursed in head-up position for 48 hours and regular neurological observations are performed watching particularly for signs of meningism and increased intracranial pressure. All efforts are made to avoid an increase in intracranial pressure and this consists of general measures like avoiding straining and use of laxatives[19], as well as, for patients with spontaneous leaks and revision cases, the use of CSF lumbar drains, which remain in situ for five days. There is significant variation in the use of and duration of placement of lumbar drains between different institutions[17]. Acetazolamide, which is a drug that reduces CSF production, has also been suggested in these patients[20].

## OUTCOME OF ENDOSCOPIC CSF LEAK REPAIR

**Success of endonasal endoscopic CSF leak repair.** At a pooled mean follow-up of 26 months, the overall success rate of endonasal endoscopic closure of CSF fistulae was found on a meta-analysis by Hegazy *et al* 17 to be 90% following first attempt and 97% following second attempt. Many consider referring the patient for intracranial CSF fistula closure after three failed attempts at endoscopic repair.

**Prevention of intracranial complications.** Endonasal endoscopic CSF leak repair is very effective in reducing intracranial complications. The pooled incidence of meningitis and brain abscess formation was 10% preoperatively, falling to 1% following CSF fistula closure. The composite pooled incidence of meningoceoele/encephalocoele, hydrocephalus and pneumocephalus was 24%, falling to <2% following CSF leak repair[17].

## SPECIAL CONSIDERATIONS IN ENDOSCOPIC CSF LEAK REPAIR

**Spontaneous CSF leak repair.** Patients with spontaneous CSF rhinorrhoea form a difficult subgroup, less likely to achieve successful closure of their CSF fistula with either endoscopic or open techniques with failure rates of CSF fistula closure reported to be between 25-87%[21-23] in comparison to other aetiologies where repair is successful in >90% of cases[17]. An anatomical association has also been noted between the presence of an empty sella turcica, a highly pneumatized sphenoid sinus and spontaneous CSF fistula formation[22], but most cases occur in obese middle-aged females. This is the same demographic as patients with benign intracranial hypertension[24]. In our opinion, spontaneous CSF rhinorrhoea is a primary disorder of CSF circulation, manifesting itself via a dehiscence in the skull base. As such, unless the underlying CSF pathology is investigated and treated, CSF fistula repair is likely to continue to be associated with a high failure rate. In our practice, all cases of spontaneous CSF rhinorrhoea are referred to a neurologist for further evaluation of CSF circulation, given that in selected cases this may be amenable to medical (diuretic or acetozolamide administration)[20], surgical (venticulo-peritoneal shunting)[25] or radiological (intracranial venous stenting) therapy[26]. Management of spontaneous CSF rhinorrhoea calls for a multidisciplinary approach involving an otolaryngologist, a neurologist and a neurosurgeon with an interest in disorders of CSF circulation.

## CONCLUSIONS

Endoscopic CSF fistula closure is a safe and effective operation which has become the standard of care for managing CSF rhinorrhoea. Its scope and efficacy have been enhanced through developments in endoscopic techniques, use of image guidance system and intrathecal fluorescein, but it continues to post a technical challenge particularly in areas which are anatomically difficult to access. It has a very high success rate for repairing traumatic CSF leaks abutting perhaps what can be achieved endoscopically, but has a considerably higher failure rate in treating spontaneous CSF rhinorrhoea. In our opinion this is because the latter condition is primarily a manifestation of disordered CSF circulation which, if untreated, will continue to put the patient at risk of developing further leaks. We recommend more research and a multidisciplinary approach to the management of this difficult condition.

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# The causation and treatment of nasal polyposis

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## ABSTRACT

### Aetiology
The causation of nasal polyposis is unknown in the majority of cases, but they are associated with a number of conditions, such as asthma, aspirin sensitivity and cystic fibrosis. Symptomatic polyposis occurs in up to 4 percent of the general population with the osteomeatal complex being the most common site.

### Treatment
Primary treatment consists of intranasal corticosteroids in the majority of cases. Short courses of systemic corticosteroid should be used as a medical polypectomy to alleviate severe symptoms, facilitate maintenance therapies or in conjunction with surgical interventions. Although polyp regrowth occurs after surgery, it remains a crucial tool in the management of this common but poorly understood condition. Novel treatments are discussed although most are not yet in routine clinical practice.

## KEYWORDS
Chronic rhinosinusitis, nasal polyposis, corticosteroid

### Definition:
Nasal polyps are oedematous, semi translucent, benign masses that develop from mucosal linings of the paranasal cavity *(Figure 1)*, usually originating from the mucosa in the osteomeatal complex[1], so strictly speaking should be referred to as sinonasal polyps. They protrude into the nasal cavity as grape-like structures causing nasal blockage and obstructing airflow to olfactory mucosa. Polyps consist of loose connective tissue, oedema, inflammatory cells (predominantly eosinophils), capillaries and some glands, mainly covered with respiratory pseudostratified epithelium with cilia and goblet cells. The relationship between sinonasal polyposis and chronic rhinosinusitis is much debated, but should now be regarded as part of the same disease spectrum[2].

### Aetiology:
The reason why polyps develop in some patients and not in others is unknown. It is a heterogeneous condition associated with chronic sinus inflammation. Symptomatic polyposis occurs in up to 4% of the general population[3] but there is a higher prevalence in patients with specific conditions such as asthma, aspirin sensitivity, and cystic fibrosis. Autopsy studies have demonstrated prevalence rates of 32-42% in unselected cadavers[4,5] suggesting that a large proportion of patients with polyposis remain asymptomatic.

### Associations:
**Allergy:** Chronic rhinosinusitis (CRS) can be subdivided according to the presence or absence of sinonasal polyps[2]. Mucosal inflammation in CRS without polyposis is usually neutrophil predominant, but when sinonasal

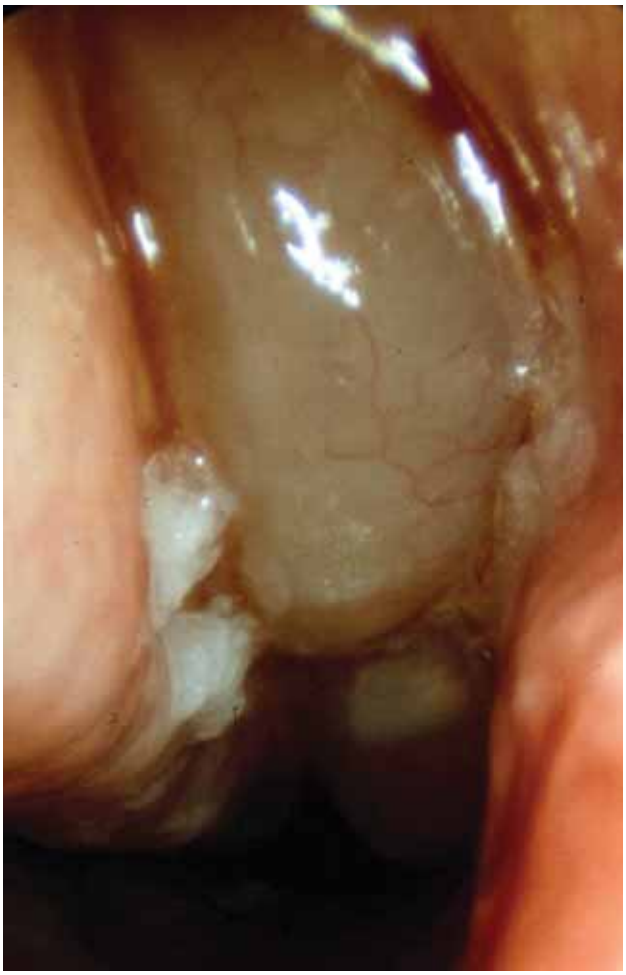

**Figure 1.** *Endoscopic view of a typical nasal polyp arising out of the right middle meatus.*

polyposis is present is eosinophil predominant. This eosinophilic infiltrate, the fact that patients commonly complain of watery rhinorrhoea with nasal obstruction, and have a degree of mucosal swelling has lead many groups to believe that allergy plays a significant role in polyp formation. However, there is no difference in the prevalence of allergy in patients with sinonasal polyposis compared to the general population, and there is no difference in prevalence of nasal polyps in patients with allergy[6-8]. Polyps are found in 0.5 to 1.5% of patients with positive skin prick tests for common allergens[6,9]. Moreover, specific treatment by allergen avoidance and/ or antihistamines have no effect on polyp size[10] and conditions associated with a high prevalence of polyposis, such as the Samter triad group, are not based on IgE mediated allergy. The exception is allergic fungal rhinosinusitis. This condition is found in up to 8% of CRS patients requiring surgery[11] and polyposis occurs in almost all patients with this condition. Specific IgE to the fungal allergen can be demonstrated in sinus mucin in 71% of this patient group[12].

**Samter's triad:** Up to 96% of patients with asthma and aspirin (or non steroidal inflammatory drug (NSAID)) intolerance develop polyposis6 demonstrating a very strong relationship. This relationship was described by Samter in 1967[13] and represents the most aggressive form of the disease, however, not all asthmatics with NSAID sensitivity develop nasal polyps. It is not an IgE mediated allergy, but rather a pharmacological intolerance due to dysregulation of prostaglandin and leukotriene metabolism. Asthmatics without an intolerance to aspirin have a prevalence of polyposis of up to 13%, which is greater than that of non-asthmatics[7,14].

Cystic fibrosis (CF), primary ciliary dyskinesia (PCD), Young's syndrome: 37% of adults with CF have nasal polyps visible at nasal endoscopy[15]. Similarly deficient mucociliary clearance and recurrent bacterial infections result in sinonasal polyposis in 40% of patients with PCD[16]. PCD is classically manifested in Kartagener's syndrome, which is inherited in an autosomal recessive manner[17]. Young's syndrome encompasses a combination of bronchiectasis, rhinosinusitis +/- nasal polyposis and reduced fertility[18]. In all three conditions nasal polyps have a lymphocyte/ neutrophil infiltrate as opposed to an eosinophilic infiltrate.

**Heredity:** There seems to be increasing evidence for a genetic role. In a study of 224 patients with sinonasal polyposis 52% had a positive family history[19]. Greisner *et al*[20] studied 50 patients with polyposis and found 14% had a positive family history with between 1-3 immediate family members having sinonasal polyposis. This compared to a matched control group in which none had a family member with polyposis. As well as shared environmental factors, the known heredity of polyp associated conditions, such as asthma and allergy, make it difficult to establish whether the findings are more than this.

## Pathogenesis

The pathogenesis of nasal polyposis are far from clear, with suggestions of them being adenoma formations[21], arising from inflammation[22,23], oedema[24], epithelial rupture[25], or pseudocysts[26]. A number of studies have proposed a role for angiogenesis[27-29] but this has also been refuted *(Figure 2)*[30]. None of these theories explain all the histopathological findings and research is now moving toward molecular biology, gene array and proteomic array technologies[31,32].

**Location:** The majority of sinonasal polyps arise from the osteomeatal complex. The reason for this is unknown but theories put forward include 'touching mucous

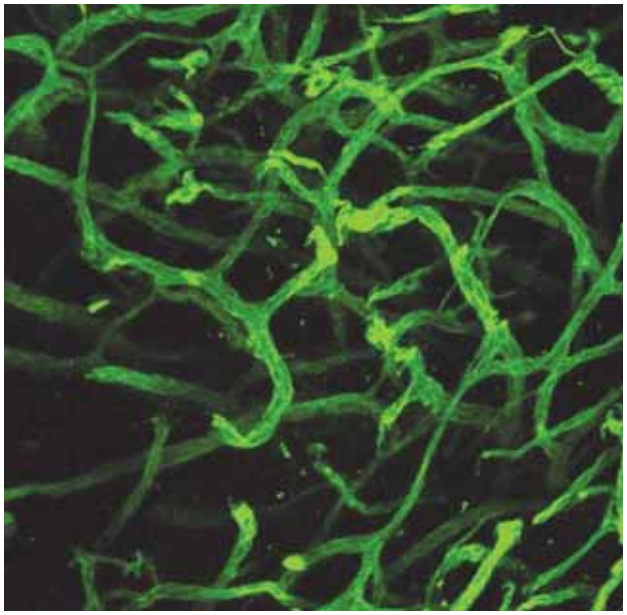

**Figure 2**. *Confocal microscopy of subepithelial capillaries running under the epithelium of mucosa of a nasal polyp.*

membranes' resulting in the release of proinflammatory cytokines, special air currents including the Bernoulli principle, in which there is internal pressure reduction with increased air stream velocity, or it may be neurogenic as nerve endings at the osteomeatal complex are thin[33] and more susceptible to cytotoxic damage.

**Neurogenic:** Sensory, autonomic secretory and vasomotor nerves cannot be identified within the stroma of polyps[33]. It is postulated that this denervation induces an abnormal vascular permeability leading to polyp formation[33].

**Histology and inflammation:** At microscopy there is marked oedema of connective tissue with prominent lymphatic dilatation[34]. Different types of epithelium have been found, most typically respiratory pseudostratified epithelium with ciliary cells and goblet cells, but low cubic or cylindric, stratified squamous non-keratinized, and transitional epithelium can also be seen. The basement membrane is often thickened and the stroma is markedly oedematous with a myxomatous appearance and contains variable numbers of fibroblasts. An associated inflammatory infiltrate is predominantly composed of eosinophils in 80% of European polyps[35]. There are also increased numbers of mast cells and T lymphocytes with their humeral products, the cytokines[36].

**Biofilms:** CRS possesses all the hallmarks of biofilm mediated disease and there is good evidence of biofilm formation in CRS[37], however, little is known about its potential role in the pathogenesis of sinonasal diseases.

**Superantigens:** Superantigens, predominantly derived from *Staphylococcus aureus*, are potent activators of T-cells, induce the synthesis of IgE in B-cells and have many direct affects on pro-inflammatory cells, such as eosinophils. IgE antibody to S.aureus enterotoxins have been described in polyp tissue, linked to both local IgE production and an aggravation of eosinophilic inflammation[38].

**Nitric oxide (NO):** Epithelial cells in CRS show a stronger expression for inducible nitric oxide synthase (iNOS) than controls, iNOS being upregulated in nasal epithelium[39]. In a prospective randomised trial in patients with CRS who failed medical therapy with nasal corticosteroids, the rise in nasal NO seen on both medical and surgical treatments correlated with symptom score, saccharin clearance time, endoscopic changes and polyp size suggesting that nasal NO provides a non-invasive measure of the response for CRS to therapy[40].

In summary, sinonasal polyposis is a multifactorial disease process with local and general patient factors determining disease progression. The precise cause and mechanism of polyposis in the majority of patients remains unknown.

## Treatment

Treatment depends upon patient symptomatology which includes nasal blockage, nasal discharge, facial pain or pressure and hypo- or anosmia. Loss of sense of smell with associated taste disturbance caused by polyp obstruction of the upper part of the nasal cavity is a common feature in many patients.

Treatment can either be medical and/ or surgical. Medical treatment consists of intranasal and/ or systemic corticosteroids.

**Intranasal corticosteroids:** Topical intranasal corticosteroid sprays have a documented positive effect on bilateral sinonasal polyposis and on their associated symptoms[41]. Nasal drops are more effective than nasal spray in symptom control and are more efficacious in improving the sense of smell[41,42]. However, this is balanced with the slightly increased systemic absorption and potential side effects. Intranasal corticosteroids have been extensively used for 30 years without any serious adverse event[43].

**Systemic corticosteroids:** Systemic corticosteroids should be used in patients with severe symptoms as a means of creating a medical polypectomy[44] to create space for intranasal corticosteroid sprays or used when topical

**Figure 3.** *Capsaicin is the active substance from hot chilli peppers.*

nasal sprays are ineffective. They are also increasingly being used in the perioperative period to reduce intraoperative bleeding and improve longer term surgical outcomes in patients with CRS with polyposis undergoing endoscopic sinus surgery[45]. A short oral course is indeed as effective as a simple polypectomy with a snare[44] and the therapeutic effect outlasts the medication for a variable period. The beneficial effect on olfaction is also most pronounced with oral corticosteroids than nasal drops or topical nasal spray.

## Novel medical treatments:

**Capsaicin:** Capsaicin is the active substance in hot chilli peppers *(Figure 3)*. It is a neurotoxin leading to long term damage of axons when repeatedly applied to the nasal mucosa. The neurogenic hypothesis in nasal polyp formation has lead to trials in capsaicin treatment for nasal polyposis that have shown potential benefit for this novel treatment[46,47]. The commonest side effect, if the nose is not topically anaesthetised, is a severe burning sensation.

**Antileukotrienes:** Leukotrienes are upregulated in asthma and nasal polyposis especially in association with aspirin sensitivity. Current evidence does not yet support the routine use of leukotrienne antagonists for sinonasal polyposis.

**Aspirin desensitization:** In CRS patients with sinonasal polyposis and aspirin intolerance, systemic aspirin desensitisation or topical lysine-aspirin treatment may protect against polyp recurrence[48,49]. Aspirin desensitisation by graded oral doses can be effective, but must only be carried out by a specialist under controlled supervised conditions.

## Surgical treatment

Due to the inflammatory nature of mucous membranes in sinonasal polyposis, surgery cannot be expected to cure the disease. In most patients sinonasal surgery is reserved for those who do not satisfactorily respond to medical treatment. The aim is to reduce the amount of inflammatory tissue, open up the nasal airway and improve ventilation of the paranasal sinuses. Although a simple intranasal polypectomy was performed repeatedly before, most patients should be referred to a rhinologist for endoscopic sinus surgery, preceded by a computed tomography (CT) scan. Endoscopic sinus surgery is well established and there are many techniques. However, the risks of minor and major complications exist and this has to be balanced with the expected result of operative verses conservative treatment. If surgery is chosen then the extent of surgery is up to the individual surgeon and will also be determined by the extent of sinus disease as well as patient symptoms. Surgery gives the greatest improvement in relieving nasal obstruction and the least improvement in sense of smell. Surgery can range from simple intranasal polypectomy to nasalisation with removal of the middle turbinate and large antrostomies in all paranasal sinuses, including a median drainage procedure for the frontal sinuses. There is as yet no convincing evidence that more radical surgery is more beneficial.

## Conclusions:

CRS with polyposis is a multifactorial disease process with local and general patient factors determining disease progression. The precise cause and mechanism of polyposis in the majority of patients remains unknown. The mainstay of treatment is corticosteroids which act on the allergic and the non-allergic inflammation. Topical intranasal corticosteroids are effective in most patients. Short intermittent courses of systemic corticosteroids are used to alleviate severe symptoms, facilitate maintenance therapies or in conjunction with surgical interventions. Although polyp regrowth occurs after surgery, it remains a crucial tool in the management of this common but poorly understood condition. Novel medical therapies are finally on the horizon.

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# Surgical Approaches to the Frontal Sinus

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## ABSTRACT
Frontal sinus is considered the most difficult sinus to address surgically in paranasal sinus surgery. Historically numerous approaches and procedures have been described and in the recent years there has been a trend from external to endoscopic approaches. The authors present their experience over 15 years and their philosophy of the role of the different approaches in the current era. The authors' suggest that the anatomy of the frontal sinus/recess and the pathology should determine the surgical approach and present a structured systematic approach to surgery in this area.

## Key words
Frontal sinus surgery, approaches, endoscopic sinus surgery.

## Introduction
The first description of frontal sinus disease probably dates to 1564 when Ambrose Pare described thick sticky mucus extruding from the frontal sinus during skull trephination 1. However, it wasn't till 1704 when Lettre first described the frontal sinus trephine technique and the first external procedure was reported by Ogston in 1884[1]. This led to a plethora of external approaches in the early 1900's including Reidel Procedure, Sewell-Boyden/McNaught procedure, MacBeth, Lynch and Lothrop procedures[1-3]. It wasn't till the introduction of the Hopkins's Rod in the 1980's, that the transnasal approach to the frontal sinus became popularised in the 1990's[4,5]. As a result, currently, many different operative procedures are utilized to manage frontal sinus disease. These range from minimally invasive balloon sinuplasty to destructive Reidel's or cranialization of the frontal sinus. The range is at the least confusing and at best confounding. The authors would go as far as to suggest that the approach most commonly used by the sinus surgeon, reflects their training, exposure and surgical repertoire rather than a structured approach. The authors, hence, present their experience and philosophy of their surgical approach to frontal sinus surgery and from there experience draw guidelines of a structured approach to the surgical management of frontal sinus disease.

## Anatomy and physiology of Frontal Sinus
A wide range of pathologies are associated with chronic frontal sinus disease including sinusitis (bacterial and fungal), nasal polyposis, mucoceles, tumours and osteomyelitis. The underlying disease process has an important role in selection of the frontal sinus approach as does an understanding of the anatomy and drainage.

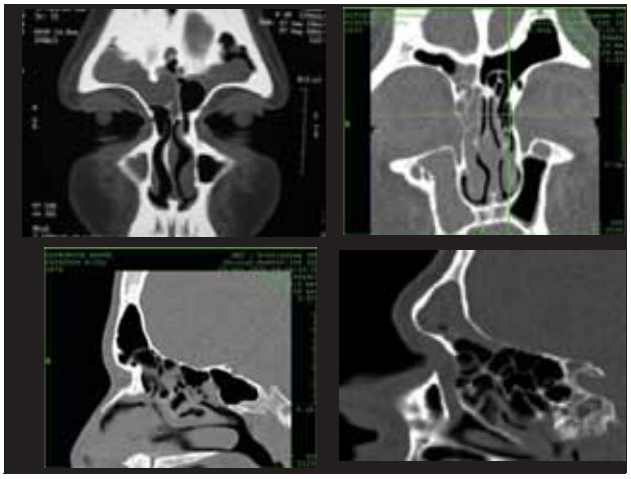

**Figure 1:** *Variations in the pnematisation of the frontal recess*

The Frontal sinus drains into the anterior ethmoidal complex via an inverted funnel shaped recess, the frontal recess. The anterior ethmoid and frontal recess probably demonstrates the greatest degree of variation in pneumatisation than any other part of the paranasal sinus complex. Van Alyea gave an extensive description of the process and variation of the pnematisation of the frontal and anterior ethmoidal bone, which led to the description of different cells like the agger nasi, frontoethmoid or Kuhn cells, supraorbital cells, septal cell and the frontal bulla cells[6,7]. The degree and variation in the pnuematisation of the frontal recess determines the location of the frontal drainage pathway. The complex and variable anatomy of this region undoubtedly contributes to the technical challenge of frontal sinus surgery, which is further compounded by the restricted operating field, the angulations and adjacent intracranial and orbital structures (Fig 1).

The frontal sinus is lined by ciliated epithelium and drains medially into the frontal recess. The ciliary beat pattern is directed from lateral to medial on the floor of the frontal sinus and along the lateral aspect of the frontal recess into the infundibulum. Messerklinger showed that mucus in the frontal sinus recirculates with only 40-60% of the mucus being cleared per circuit. There is also retrograde flow of mucus from the frontal recess back into the frontal sinus creating a potential source of infection for the frontal sinus and hence may contribute to frontal recess obstruction[8].

## Structured approach

Frontal sinus surgery is uncommon and in the UK often tertiary centre led. In the author's experience, most if not all the procedures described, had and still may have a place in the management of frontal sinus surgery. The choice of approach is determined by a) the Pathology and its behaviour and b) the Anatomy and its constraints. Over the last 15 years over 300 frontal sinus procedures were undertaken at our institution. A structured approach to the frontal sinus can be adopted ranging from minimally invasive endoscopic approaches to external osteoplastic approaches or destructive approaches like obliteration or cranialisation of the frontal sinus. Each technique has its unique applications which shall be discussed sequentially with the author's experience in a tertiary centre.

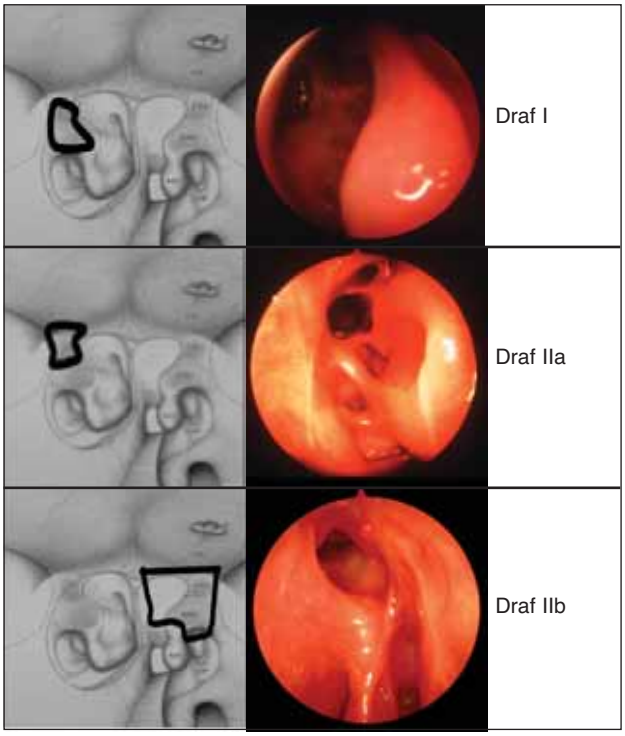


**Figure 2:** *Draf Type I and II* (Diagramatic images reproduced with the permission of Prof P J Wormold and modified by author.)

General principles should be applied when operating on the frontal recess. Frontal recess and outlet obstruction is the primary cause of chronic frontal sinus disease and hence the principle of surgery is to remove the frontoethmoid cells obstructing or narrowing the frontal drainage to create the widest mucosal lined drainage pathway possible. Strict mucosal preservation technique should be used as frontal recess mucus membrane does not regenerate with normal cilia and hence should be preserved when operating[9].

A posterior to anterior and medial to lateral dissection plane is favoured as the dissection forces are directed away from the thinner anterior ethmoidal and cribriform plate. The author prefers to adopt a bulla intact approach to the frontal sinus dissection. This protects the anterior ethmoidal artery from damage as it is in-bearably deeper than the face of the bulla. Furthermore, the face of the bulla naturally directs the plane of dissection to the frontal

recess and drainage pathway (Fig 1).

Three planner Pre operative CT imaging is paramount to understand the three dimensional anatomy of this area. Image guidance techniques can be of assistance in localisation and improving safety.

## Anterior ethmoidectomy and frontal sinustomy (Draf I) (Fig 2)

Endoscopic frontal sinusotomy accounts for a majority of frontal sinus surgery procedures in the UK to date and for 80% of the procedures in our unit. In the author's experience, the most common indication for frontal sinusotomy was nasal polyposis with mild frontal mucosal changes, infective sinusitis (bacterial and fungal), and rarely for ethmoidal inverted papilloma, trauma and surgery for dysthyroid eye disease. The principle of limited approach of anterior ethmoidectomy and frontal sinustomy is that most frontal sinus disease is secondary to frontal sinus outlet obstruction and ascending inflammation from the ethmoids. Therefore, addressing the frontal recess and sinus drainage together with the anterior ethmoidal complex should be adequate for resolution.

The author does not use Stents in the frontal ostium. Semirigid stents have been shown to lead to circumferential scarring[10]. However, the author accepts that some surgeons use soft silastic sheets rolled into non-rigid stents which are associated with reduced scarring and osteogenesis.

A relatively new and exciting technique of dilating the frontal recess using balloon sinuplasty is being popularised in United States (Fig 3). The author has limited experience with this technique and is not able to comment on the long term outcomes associated with this technology from personal experience. Weiss et al have recently reported the two year follow up of an original mutlicentre cohort and reported encouraging results[11].

## Draf II a and b

Draf II procedures are where the frontal sinus ostium is increased by removing part of the floor of the frontal sinus. In Type IIa procedures, the frontal sinus ostium is extended laterally and medially so that it extends from the lamina papricia laterally to the level of the middle turbinate medially (Fig 2). Type IIb is when this is extended to the level of the nasal septum and involves resection of the anterior part of the middle turbinate (Fig 2). Although the former can sometimes be achieved by blunt dissection in a well pneumatised frontal recess, the latter can only be achieved by drilling part of the floor of the frontal sinus. The extended approach allows greater access to the frontal sinus and any frontal pathology. Some literature suggests that Type IIb approach is insufficient as when ever a drill is applied to the frontal floor, there is significant mucosal damage and a notable scarring and stenosis of the resultant ostium. The author has used this procedure in 3% of the cases and specifically for mucoceles in a medial position, benign tumours like inverted papilloma and spindle cell tumours with a limited extension to the frontal sinus, unilateral nasal polyposis disease and rarely in infected cases. Only in one case of spindle cell tumour did the Draf IIb need to be revised and in no cases did the procedure need to be converted to Draf III or external procedure.

## Draf III/ Endoscopic modified Lothrop (Fig 4)

Lothrop's original procedure was described in 1914 and involved an external approach to remove the inter-frontal sinus septum, floor of the frontal sinus and the upper nasal septum to create a large common frontal sinus opening with out stripping the frontal mucosa[2,3]. An endoscopic trans nasal modification of the approach was described in the mid-nineties by Gross et al[12]. As the Endoscopic modification does involving drilling the lateral aspect of the frontal recess which may result in defective cilia mediated mucus clearance and stenosis and hence a trans-septal approach was described by Lanza in 2001[13].

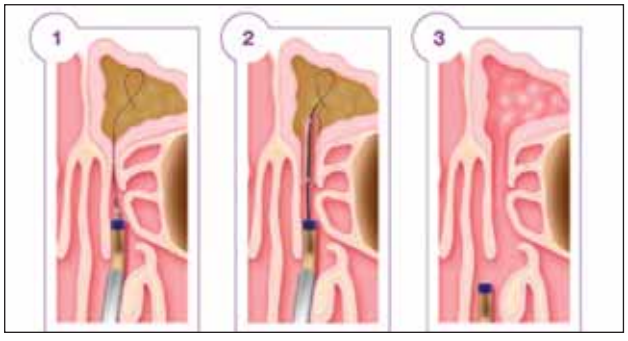


**Figure 3:** *Balloon Sinuplasty* (Reproduced with permission of Acclarent.Inc.)

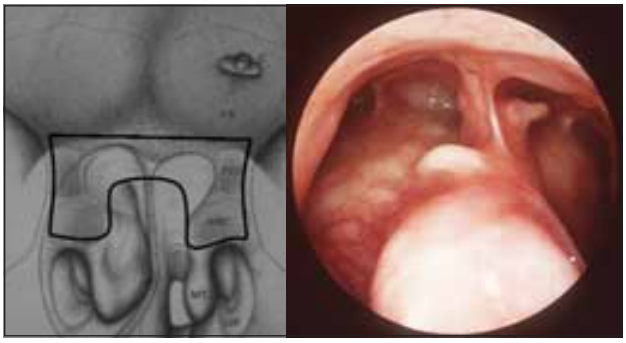

**Figure 4:** *Draf III/Modified Lothrop's* (Diagramatic images reproduced with the permission of Prof P J Wormold and modified by author.)

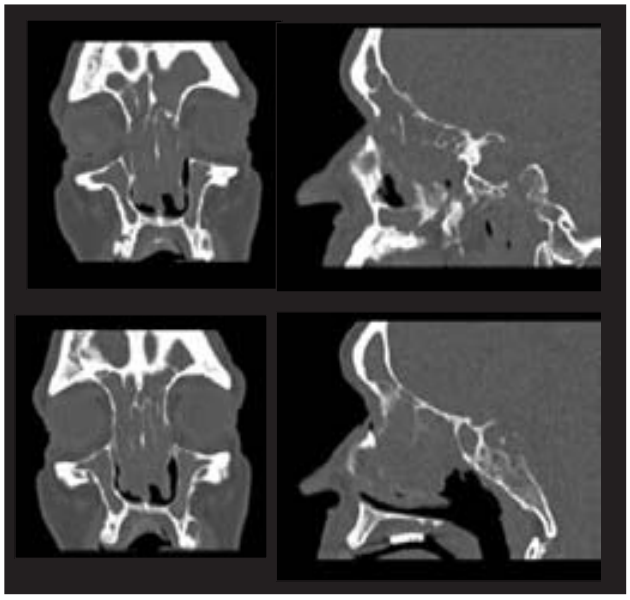

**Figure 5:** *Axial and Parasagatal CT scan of patient with SAMTER'S Triad.*

In the authors experience, Draf III or Modified endoscopic lothrop procedures comprised 3% of frontal sinus procedures performed. Over half were revision operations on the frontal sinus, including patients who were positive for Samter's triad (Asthma, Aspirin Sensitivity and nasal polyposis) (Fig 5) or had had multiple external approaches and had previous extensive bilateral disease and surgery. Inverted papilloma, large osteoma's and spindle cell tumour comprised a third of the cases. Laterally placed Mucoceles and Large Type III Kuhn cells formed the remaining. In the author's experience, benign tumours that extends beyond the vertical plane of the medial orbital wall merit a more extensive Draf III approach to ensure adequate exposure for clearance and surveillance. In patients who have had multiple external approaches using Lynch-Howarth approach, Draf III become necessary due to the extensive loss of lateral bony support at the level of the frontal recess. In the author's experience, the commonest site of recurrence of nasal polyposis in patients with extensive recurrent polyposis and Samter's triad is the anterior ethmoid and frontal recess. It is not unusual for the author to consider Draf III as a primary or second procedure in patients with these conditions.

As the procedure invariably involves the use of the drill to drill the floor of the frontal sinus, there is often circumferential damage to the mucosa, exposed bone and mild osteitis and a resultant stenosis of the antrostomy created. Therefore, this approach is likely to be unsuccessful in patients with small antroposterior dimension to there frontal ostium.

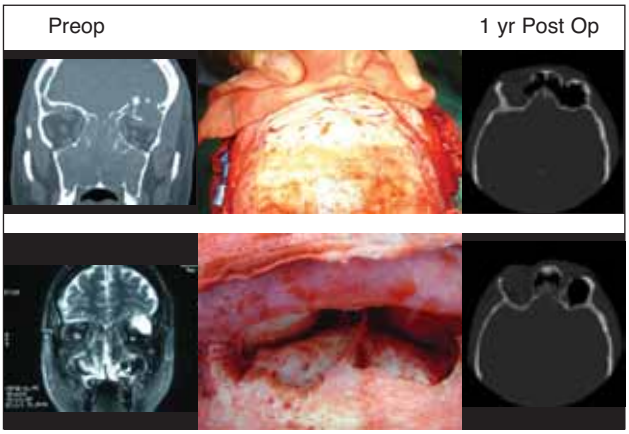


**Figure 6:** *Lateral Orbital mucocele with nasal polyposis.*

## Osteoplastic Flap +/- Combined Endoscopic approach

Many guises of combined endoscopic and external procedures have been described. Some involve a trephine[14], whilst others involve a more traditional Lynch-Howarth approach but with reconstruction called Contralateral Ispilateral Median drainage (CIM) approach. In the author's experience, these approaches do not lend any further advantage or exposure than what is available by a Draff III approach. However, an osteoplastic flap, with or without a transnasal endoscopic approach, does lend a significant advantage to endoscopic Draf III approach on its own. It is particularly valuable in cases of lateral disease which cannot be adequately accessed endoscopically, to access pathology that needs a more thorough resection and when there is CT scan evidence of significant osteoneogenisis due to chronic ostitis. Examples include lateral orbital mucocele, giant frontal osteomas, inverted papilloma with erosion of the lateral frontal sinus/orbital roof or when associated with recurrence or histological changes such as moderate to severe dysplasia.

Although the traditional belief that pathology beyond the mid-orbital vertical plane cannot be accessed by the endoscopic has long been proven to be not true, the instrumentation and access can still be limited to the lateral extremities of the frontal sinus. We present the preoperative and postoperative scans of a patient who had 16 previous operations for recurrent polyposis and referred to us with a mucocele based lateral to the orbit (Fig 6). This patient was best served by a combined Osteoplastic and endoscopic procedure as is born out by his repeat scans a year after his surgery. It is the authors belief that that if a benign tumour (e.g. inverted papiloma, spindle cell tumour etc) recurs subsequent to a

thorough resection by endoscopic approach (i.e Draf III), then using the same endoscopic approach is inappropriate and inadequate. Similarly, if the pathology you are dealing with isn't behaving in a benign fasion, such as inverted papiloma showing signs of moderate to severe dysplasia, or erosion of the lateral frontal sinus/orbital roof, it merits a more thorough resection which can only be achieved by an open osteoplastic flap approach.

## Osteoplastic flap and obliteration

Till the 1980's Osteoplastic flap approach and obliteration was considered the definitive procedure to treat chronic recalcitrant disease of the frontal sinus which had been unresponsive to endoscopic or external approaches. An external osteoplastic approach is used to access the frontal sinus, mucosa stripped, the sinus walls and mucosal remnants drilled away and the sinus obliterated with fat to prevent further disease. It is now an uncommon procedure, but still can be indicated in certain scenarios. It has been used in lateral pathology such as mucoceles, following failed median drainage procedure or stenosis of the drainage pathway following loss of lateral support post previous external procedures[15]. Fat autograft has been shown to have the best results compared to inorganic material which has been largely tested on animal models[16,17]. Obliteration, always carries the risk of a late mucocele.

Obliteration of the frontal sinus should not be performed if there is a possibility that all of the mucus membrane cannot be removed. In our practice it is reserved for patients who have failed adequate median drainage through endonasal or external approaches, and for malignant disease that needs wide resection and often drilling of the frontal sinus walls (Fig 7).

## Riedel's procedure

Riedel's procedure although may be considered an archaic procedure of historic interest only, surprisingly, can still have a role in the management of frontal sinus disease in the current era. It can be implemented when previous attempts at drainage and obliteration have proved unsuccessful leaving residual chronic frontal sinus disease. It is particularly useful in cases where the disease process is involves the anterior aspect of the frontal sinus and the posterior wall is preserved[18]. Disadvantages from this technique include the considerable cosmetic disfigurement for the patient although this can be managed by titanium prosthetic reconstruction.

In the authors experience, Riedel's procedure has a place in the modern era if the there is significant or almost complete loss of the frontal plate of the frontal sinus due to osteomylitis or another destructive process such as tumours or cancers.

The author has also used it in patients with rudimentary frontal sinuses with recurrent or recalcitrant frontal sinus disease. In such patients, most endoscopic approaches are likely to fail due to stenosis and the frontal sinuses are too small to consider open or osteoplastic flap techniques. As an example the author presents a child with recurrent osteomyelitis (2 years apart) with extensive erosion of the frontal wall and rudimentary frontal sinus which was treated with a Riedel's procedure (Fig 8). When the frontal sinuses are rudimentary, the cosmetic deformity is minimal as demonstrated by images of the child taken 2 years after his surgery (Fig 8).

## Cranialization

The converse of Riedel's is Cranialization when the entire back wall of the frontal sinus together with the mucosa is removed and the frontal sinus becomes part of the cranial cavity. Like any destructive procedure of the frontal sinus, it is paramount that all mucosa is extensively removed and the frontal walls drilled down to prevent the possibility of mucosal remnants developing into mucoceles in the future. It should therefore only be cautiously used in selective cases such as malignant disease with notable

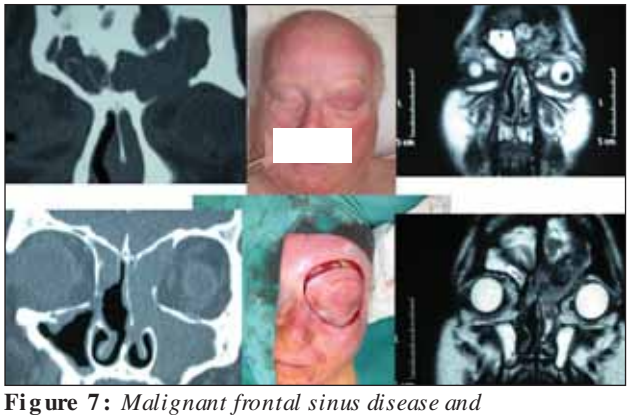

**Figure 7:** *Malignant frontal sinus disease and obliteration.*

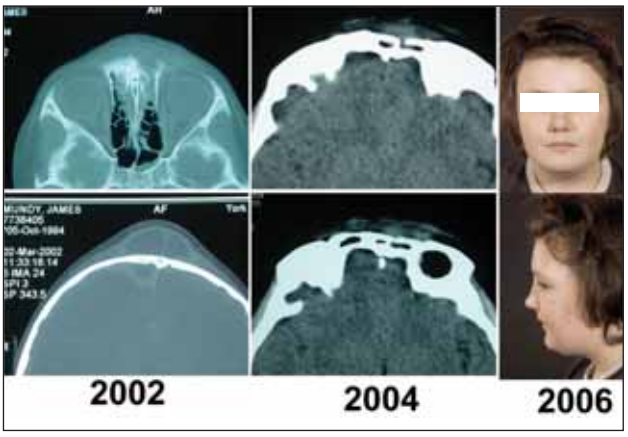


**Figure 8:** *Recurrent Acute Osteomylitis and 2 years post Riedel's procedure.*

intracranial involvement and destruction of the posterior table of the frontal sinus.

The author has only used this approach in one case of a teenage girl with extensive intracranial abscess secondary to frontal sinusitis with almost complete loss of the posterior frontal wall that was managed with a craniotomy and cranilizastion of the frontal sinus.

## Conclusions

Operating on the Frontal sinus is technically difficult due to the complex and variable anatomy, confined operating field and proximity of the orbit and intracranial structures. It can be considered as the last frontier in sinus surgery and should only be performed by the experienced rhinologist. Three dimensional imaging to assist the surgeon and an otological-style meticulous mucosal preservation technique should be employed. The literature describes a myriad of the approaches to the frontal sinus. The choice of approach and operation should be defined by the underlying pathology and anatomy of the frontal recess and not by the surgeon's preferences. A structured approach encompassing all techniques should be considered rather than the approach that "one model fits all". The authors present their experience in this area and suggest a structured sequential approach based on their experience.

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# Decision Making in the Management of the Neck in Head and Neck Squamous Cell Carcinoma

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## Abstract
Management of the neck in head and neck squamous cell carcinoma is of vital importance because of the significant impact of regional disease on survival. Occult disease in the neck not detected by clinical examination may also be difficult to identify on routine histological examination. The use of immunohistochemistry or molecular analysis in detecting cervical metastatic involvement as well as the prognostic role of micrometastasis are already established standpoints in head and neck cancer practice. The current considerations in the management of the clinically negative neck (with a parenthesis on the use of sentinel lymph node biopsy) as well as of the clinically positive neck in head and neck cancer patients, and the most recent trends on the nomenclature and classification of neck dissections are discussed.

## Key words
head and neck cancer, neck dissection, neck metastasis, squamous cell carcinoma

## Introduction
Malignancies of the head and neck refer to tumors of the upper aerodigestive tract, of the salivary glands, of the thyroid and parathyroid glands and of the skin of the head and neck. These neoplastic entities vary biologically in consideration of their histology and potential for regional and distant metastasis. This article, however, concentrates only on the decision making in the management of the neck in head and neck squamous cell carcinoma.

## Cervical metastasis
The development of regional metastasis in patients with head and neck squamous cell carcinoma is the most significant independent adverse prognostic factor. It has generally been observed that the presence of cervical lymph node metastasis reduces the 5-year survival rate by approximately 50%[1]. Additionally, the number of the positive lymph nodes, their level in the neck, the presence of central necrosis, of macroscopic or microscopic extracapsular spread of the metastatic tumor and soft tissue deposits have all been shown to have prognostic significance (for both long-term survival and recurrence-free survival) in patients with head and neck squamous cell

carcinoma[2-5]. Only by a careful pathological examination of the neck dissection specimen a potentially valuable wealth of information can be provided to the treating clinician(s).

However, the presence of lymph node metastases cannot always be detected clinically and pathologically by current routine clinical and histopathological methods. With the recent advances in diagnostic surgical pathology, increasingly sophisticated investigative methods (as, for example, immunohistochemistry and molecular analysis) have become widely used tools for the analysis of neck dissection specimens. In fact, a negative conventional pathological examination does not eliminate the possibility of occult disease in a single node or nodes. While the significance of large cervical node metastases in patients with head and neck squamous carcinomas is well established, the importance of finding regional nodal micrometastases or isolated tumor cells in those patients is less clearly understood. In the past, no definition of micrometastases existed; many published studies have used 3 mm as the upper limit of size for micrometastases, but these studies do not always specify a lower limit, which means that such studies run the risk of conflating results of finding a 3mm deposit with the results of finding only fleeting, evanescent molecular evidence of tumor cells by way of a method such a reverse transcriptase-polymerase chain reaction. As increasing numbers of investigators join the search for evidence of the value of detecting micrometastases, some uniform upper and lower size limits probably should be established and consistently employed. In the interest of continuity of tumor diagnosis, it has been suggested that the already established definition of micrometastasis from study of breast cancer patients - that is, a micrometastasis is greater than 0.2 mm and not greater than 2.0 mm in greatest dimension - be adopted.[6,7] Without a precise definition of micrometastasis, it is very difficult to evaluate both the incidence and the clinical implications (with regard to prognosis) of such a finding.

## Clinical evaluation of the neck

Since lymphatic metastasis is a common route of regional spread, a decision concerning the treatment of the neck lymph nodes has to be made in almost every patient with head and neck cancer. Therefore, pre-treatment evaluation of the nodal status of the neck is fundamental as well as it is important the assessment of the neck in the follow-up, as early detection of recurrences may have therapeutic consequences and may contribute to successful salvage treatment.

Due to the ability to detect small tumor deposits, imaging techniques (such as computed tomography, magnetic resonance imaging and ultrasound) have better accuracy, and sensitivity in particular, than palpation in distinguishing between metastasis and other causes of (palpable) masses in the neck. In addition to the detection of occult metastasis, imaging can play a role in detecting additional metastases. Conversely, the anatomical landmarks and details on (position emission tomography) PET imaging are less well evidenced than with CT or MRI. The fusion of PET images with the more anatomical information of CT has significantly improved the interpretation of the PET scans. However, the diagnostic accuracy to detect nodal metastasis does not seem to improve much by the fusion of [18F]fluorodeoxyglucose-PET (FDG-PET) with CT compared to PET alone.[8-10] Consequently, for the N0 neck a lower sensitivity ranging from 25% to 78% is reported.[11-16] It is therefore doubtful if FDG-PET will be valuable for the evaluation of the clinically negative neck, limiting its use in the already existing protocols of nodal staging. Other additional techniques like the addition of radioactively labeled monoclonal antibodies resulted again in sensitivity rates still comparable to CT and MRI.[17]

In patients who have a high risk of loco-regional recurrence, a MRI or CT may be performed 2-4 months after the initial treatment. Diffusion-weighted imaging-MRI, in particular, has obtained promising results in distinguishing residual or recurrent disease after treatment.[18] However, for the detection or exclusion of residual neck disease, PET or PET-CT is probably the most accurate technique. The interval between the end of the treatment and examination is also important. By some, an evaluation is advisable after 8-12 weeks[19-20], by others 3-4 months after therapy[21]. Anyhow, this latter suggestion seems to be justified only if there is no clinical suspicion of persistence or recurrence - in order to perform an effective salvage treatment, if necessary. Sometimes, if the PET scan is negative, further investigations (such as serial PET-CT imaging) can be undertaken and planned neck dissection after chemoradiation for head and neck squamous cell carcinoma may be deferred. Fine-needle aspiration biopsy of areas of suspicious FDG uptake can be considered prior to therapeutic neck dissection.

The use of ultrasound, ultrasound-guided fine-needle aspiration biopsy or duplex Doppler in the follow-up of the treated neck has been investigated[22-23]. When ultrasound-guided fine-needle aspiration biopsy is employed to evaluate the irradiated neck, the interpretation of the cytological aspirate may be more difficult than in the untreated necks - in particular, if the interval after treatment is short. In the case elective treatment of the clinically N0 neck is under investigation, ultrasound-guided fine-needle aspiration biopsy may be considered as a diagnostic tool for follow-up.

## Treatment of the N0 neck

Primary squamous cell carcinomas of the head and neck have a propensity to metastasize to the regional lymph nodes in the neck. It has been demonstrated that cervical lymph node metastases occur in predictable patterns in patients with head and neck squamous cell carcinoma[24-30]. The location of cervical lymph node metastases is closely linked with the site and stage of the primary lesion. The choice of surgery or irradiation for elective treatment of the clinically negative neck often depends on the treatment chosen for the primary tumor. In general, elective treatment of the neck is recommended for patients with squamous cell carcinoma of the upper aerodigestive tract when the anticipated risk of occult metastasis is greater than 20%.[31-32] However, more recently, others[33-34] believe that the level of risk should probably be lowered to 15% considering that the risk-benefit ratio has changed over the past few decades as a result of the use of more conservative procedures for elective neck dissection. Patients at risk have been identified considering the characteristics of the primary tumor.

Treatment of the N0 neck in patients with early squamous cell carcinoma of the mucosal surfaces of the head and neck is controversial. A "watchful waiting" approach has generally been used in order to avoid the morbidity of elective neck dissection or irradiation in cancer patients with low risk of neck metastases. However, the current consensus is that elective neck dissection or irradiation in patients at risk for cervical metastases results in better regional tumor control than neck treatment done when the nodal disease evolves, or becomes palpable. The salvage rate following therapeutic neck dissection is only 50% to 60%[34]. An elective neck dissection, in distinction to elective irradiation, has the advantage of staging the neck pathologically which, in turn, provides more accurate prognostic information and helps in determining whether adjuvant therapy is required, depending on the status of neck lymph nodes.[35]

## Classification of neck dissections

As stated above, neck dissection (i.e., the systematic surgical removal of lymph nodes in the neck) is one way of addressing the cervical metastatic disease in patients with head and neck cancer. The understanding of the pattern of cancer spread through the anatomy of the head and neck is fundamental when deciding upon a treatment plan for a head and neck cancer patient.

During the 1980s several surgeons[36-38] realized the importance of creating a uniform nomenclature for neck dissections in order to facilitate the analysis and reporting of treatment data, to help in planning of clinical trials and the evaluation of quality control and, most importantly, to be crucial for individual patient treatment planning. Realizing the importance for such a standardized nomenclature, the Committee for Head and Neck Surgery and Oncology of the American Academy of Otolaryngology-Head and Neck Surgery met in 1988 to address terminology problems related to cervical lymphadenectomy[39]. The resulting nomenclature became internationally accepted and the Committee for Neck Dissection Classification of the American Head and Neck Society, periodically reassessing the classification system, has already published two updates[40-41]. The updates have taken into account the American Joint Commission on Cancer (AJCC) staging system for head and neck cancer, the biology of lymph nodes metastases, the changes in selective neck dissection procedures, and the correlation of surgical landmarks with radiologic landmarks. A multidisciplinary team work between surgeons, radiologist and oncologists has, therefore, been created.

The classification of neck dissections proposed by the Committee for Neck Dissection Classification of the American Head and Neck Society[40] can be summarized as follows:

1) radical neck dissection includes removal of lymph node levels I to V, and includes removal of the sternocleidomastoid muscle, spinal accessory nerve, and internal jugular vein;
2) a modified radical neck dissection includes removal of lymph node levels I to V (as in radical neck dissection), but preservation of at least one of the non-lymphatic structures (sternocleidomastoid muscle, spinal accessory nerve, and internal jugular vein);
3) when an additional lymph node level or group or a non-lymphatic structure is removed relative to a radical neck dissection (muscle, blood vessel, nerve) the procedure is termed an extended neck dissection;
4) when one or more lymph node levels are preserved, the procedure (in its several variations) is called selective neck dissection.

Recently, the Japan Neck Dissection Study Group (JNDSG)[42] conducted a study on the standardization of treatment for lymph node metastases of head and neck cancer aiming to standardize various aspects of non-radical neck dissections, such as the extent of resection of cervical lymph nodes and non-lymphatic structures, indications for various dissections, and methods of evaluating postoperative function. Based on the classification of regional lymph nodes published by the Japan Society of Clinical Oncology[43], the JNDSG presents a new and potentially useful system for classification and reporting of neck dissections based on a system of letters and symbols. However, this radical change in nomenclature

and division of lymph node groups, departing from a classification system already employed internationally, may lack the immediate acceptance for general use. Given the advantages of the JNDSG proposed classification, the correct approach could be the integration of its revised form into the currently used terminology.[44]

## Sentinel node biopsy

The use of sentinel node biopsy in selected patients with head and neck cancer is currently under investigation. At present, there is no data supporting the use of sentinel node biopsy instead of elective neck dissection for upper aerodigestive tract squamous cell carcinoma in clinical practice, although multi-institutional clinical trials testing this approach are progressing[45]. Sentinel lymph node biopsy alone is insufficient to stage the disease adequately, as a negative sentinel lymph node biopsy does not definitely exclude the presence of positive lymph nodes within the routes of draining.

## Treatment of the N+ neck

The management of neck node metastases depends on the extent of the disease. The classic radical neck dissection has been used for advanced-stage nodal metastases from head and neck cancer followed by adjuvant post-operative radiation therapy combined or not with concomitant chemotherapy. The specific indications were patients with N3 disease, extensive soft tissue disease either appreciated clinically or demonstrated radiologically.[46] Patients with advanced N stages are currently treated initially with non-surgical methods, usually with concomitant combinations of chemotherapy and irradiation. After the introduction of "organ preservation" strategies, with various combinations using chemoradiotherapy for definitive treatment of advanced locoregional cancer of the larynx and pharynx, there is emerging trend toward performing planned neck dissection for bulky cervical lymphadenopathy. The regional disease control for patients with persistent neck disease using selective and superselective neck dissections for advanced N2 and N3 disease after concurrent chemoradiation is excellent.[47-53] There is ample evidence in the literature that concomitant or concurrent radiochemotherapy can achieve good regional control in patients with advanced neck disease. However, the development of distant metastases does remain a problem, despite the administration of systemic therapy.[47] At present, the use of Radical neck dissection (RND) has become greatly limited and this surgical procedure is no longer standard[54-55].

## Conclusions

Management of the neck in squamous cell carcinoma of the head and neck has evolved from more radical techniques to limited dissections. Surgeons of the next decade should be prepared to accept the philosophy of elective Selective neck dissection (SND) and to consider that more extensive neck dissection does not equate to more curative treatment. Modifications of the type of neck dissection have largely reduced the morbidity.

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# Chemoradiation in the Primary Management of Oropharyngeal Carcinoma

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## ABSTRACT

Oropharyngeal carcinoma refers to tumours arising in the base of tongue, tonsillar region, soft palate and pharyngeal wall. Most are squamous cell carcinomas. Advanced stage at presentation with lymph node metastases occurs in the majority of patients. Surgery and radiotherapy have been the mainstays of treatment – but these have traditionally resulted in poor functional outcome, reduced locoregional control and survival. In an attempt to improve this situation, trials have looked at combining chemotherapy to radiation. The administration of chemotherapy alongside radiotherapy (RT) is known as concurrent chemoradiation or simply chemoradiation. Chemoradiation has been investigated since the 1980s but only with emergence of new schedules and robust clinical data has its place in the treatment of oropharyngeal cancer been confirmed. The aim of this article is to provide an update on the use of chemoradiation in the primary management of patients undergoing treatment with curative intent.

## Key Words

oropharyngeal carcinoma, chemoradiotherapy, radiotherapy, chemotherapy

## Introduction

The incidence of squamous cell carcinoma of the oropharynx is rising. This is despite a decrease in the overall incidence of head and neck cancer[1,2,3]. This increase is predominantly in younger patients often without the traditional risk factors of tobacco and alcohol use. This change is thought to be related to orogenital transmission of human papillomavirus (HPV). It is the same virus subtypes 16 & 18 which are implicated in other types of malignancies, notably cervical and anal carcinomas[4,5]. HPV related oropharyngeal cancer may represent a separate disease entity. They are often poorly differentiated and of a basaloid histological subtype. Several studies have suggested that HPV related oropharyngeal cancer carries a more favourable prognosis[5,6,7] and may need to be treated less aggressively.

Advanced stage at presentation with lymph node metastases occurs in the majority of patients because of the rich lymphatic drainage of this area and the relative lack of pain fibres in areas such as the base of tongue. Approximately 70% of patients have ispilateral lymph nodes involved at presentation and up to 30% have bilateral lymphadenopathy[1]. Distant metastases at presentation are rare (<10%). The curability of oropharyngeal cancers is dependant on the stage at presentation and specific site.

Traditionally, surgery or radiotherapy (RT) have been the standards for treatment of oropharyngeal cancers. However the outcomes with these modalities have been lacking with suboptimal locoregional control and significant long-term functional deficits. Patients with early stage disease achieve local control rates in excess of 80% by RT alone. As a result, chemoradiation is not required in this patient group. Unfortunately, locoregional control in advanced disease is only achieved in 40-60% with RT alone and the risk of distant metastases rises to 30-40% compared to 10% for early stage disease[8]. Chemoradiation improves survival by 10-15% in this patient group. Over the past decade, evidence from clinical trials has emerged

supporting the use of combined platinum based chemotherapy and RT as the new standard of care for advanced stage disease. The studies have consistently and reliably shown benefit both in terms of survival and locoregional control. Despite the significant acute and late toxicity which results from chemoradiotherapy it allows for organ preservation and function. Surgery has been relegated to cases for salvage after non surgical treatment [9,10,11].

More recently, evidence has emerged supporting the use of cetuximab, an epidermal growth factor receptor (EGFR) inhibitor in combination with radiotherapy when platinum chemotherapy is contraindicated.

## The evidence supporting chemoradiation

Chemotherapy had traditionally been use for palliation only. The role of chemotherapy in curative treatment has emerged as investigators have looked to improve the poor outcomes seen with more advanced disease[2,12,13,14]. A variety of different chemotherapy agents (platinums, antimetabolites and taxanes) have been tried in the past both as single agents and in combination. Cisplatin, the platinum compound, used as a single agent has emerged as the standard for use in combination with RT[15]. Its efficacy is due to a radiosensitising effect on the tumour cells, making them more susceptible to the damage caused by the radiation on the tumour cell DNA. The damage inflicted is also less likely to be repaired thus resulting in a higher overall response to the combined treatment compared to RT alone. It can also provide a degree of systemic control (by eradication of micrometastases) especially when used at higher dose levels.

Despite the consensus for cisplatin being the chemotherapeutic agent in combination with RT there remains a debate as to the actual dose and scheduling. Within the UK, most treating centres use single agent cisplatin at a dose of 100mg/m2 every 3 weeks as their chemoradiation schedule. This appears to offer the best balance between efficacy and tolerability. This is combined with conventionally fractionated RT (70Gy at 2Gy per fraction over 7 weeks). The role of altered fractionation schedules in chemoradiation remains investigational.

For early stage oropharyngeal cancer, RT alone results in high locoregional control and cure rates comparable with surgery alone[16]. Currently there is no evidence to support the use of chemoradiotherapy for early stage (I & II) oropharyngeal cancer. RT as a single modality is the preferred treatment option where the functional consequences of surgery are high e.g. tongue base, palate or tonsil.

The management of locally advanced disease (stage III & IVa) is complex and requires multidisciplinary input to ensure the best outcome for the patient. Single modality treatment is often ineffective. The introduction of combined chemoradiotherapy has been a major advance in this group of patients resulting in improved locoregional control as well as a survival advantage. Multiple well designed phase III clinical trials involving thousands of patients have now established that combined treatment yields better results than RT alone[17-21]. The study by Denis et al[19] randomised 226 patients with locally advanced oropharyngeal caner to radiotherapy with or without chemotherapy. The results confirmed that 5 yr local control (48% vs 25%), disease free survival (27% vs 15%) and overall survival (22% vs 16%) were significantly improved with the addition of chemotherapy.

The meta-analysis looking at the role of chemotherapy for non-nasopharyngeal squamous cell carcinoma of the head and neck (SCCHN)[15] included over 60 trials and an excess of 10,000 patients further confirmed the place of chemoradiotherapy. It confirmed an absolute survival benefit of 8% at 5 years (HR 0.81, 95% CI 0.76-0.88; $p<0.0001$).

Inhibition of the EGFR in cancer cells has relatively recently emerged as an alternative treatment strategy to platinum based chemoradiation in patients who are unable to receive platinum agents. This may be secondary to poor renal function or hearing dysfunction. Cetuximab is the drug which is currently licensed for this indication in SCCHN. It is an IgG1 monoclonal antibody directed against EGFR. Within the UK it has recently been approved for use by the National Institute for Clinical Excellence[22]. It has already been approved for use in Scotland. The evidence supporting it use[23] has confirmed a statistically similar magnitude of response (local control, 47% vs 34% at 3 yrs, $p=0.005$ and overall survival, 55% vs 45% at 3 yrs, $p=0.03$) as has been shown with traditional chemoradiotherapy but without the risk of myelosuppression, severe mucositis and gastrointestinal side effects. Nevertheless it is not without adverse events and patients do experience a severe acneiform rash is most cases, especially within the irradiated volume. Unfortunately there is currently no randomised data confirming that cetuximab and radiotherapy is equivalent to cisplatin plus radiotherapy.

## Adjuvant chemoradiotherapy

There is also overwhelming evidence to support the use of concomitant chemoradiotherapy in patients who require adjuvant therapy after surgical resection of locally advanced oropharyngeal cancer exhibiting high risk pathological

features such as involved surgical margins, extracapsular extension or multiple lymph node level involvement[24-27].

## Induction chemotherapy

There has been clear progress made in improving local regional control and overall survival with chemoradiotherapy in oropharyngeal cancer. However concurrent treatment has not been shown to significantly reduce the incidence of distant relapse. Unfortunately distant relapse is being seen more frequently as better local control is achieved[28]. Despite being a chemosensitive tumour many older studies comparing platinum combination regimes in the induction setting failed to demonstrate a survival advantage[29]. Nevertheless investigators have continued to trial new regimes and include more active agents which have resulted in overall survival improvements being seen[30-32]. Recent evidence from studies support the use of taxane-based combinations in the neo-adjuvant setting (induction) for locally advanced oropharygeal cancers[30-31]. In Posner's study[31] looking at the addition of taxane based induction chemotherapy followed by radical chemoradiotherapy in locally advanced SSCHN a median overall survival of 71 months vs 30 months was achieved (62% vs 48% at 3 yrs, p =0.02). Over half of the patients in this study had oropharyngeal cancer as their primary site. Induction chemotherapy has not yet become the standard of care for patients with locally advanced oropharyngeal carcinoma – but work is ongoing.

## A "toxic cure" - prerequisites for patients undergoing chemoradiation

Chemoradiation is associated with substantial acute and long term toxicity. Good patient selection is essential and chemoradiation is only suitable for the fitter patients (WHO performance status 0-1) as frailer patients risk not completing the entire treatment duration or requiring interruptions in their RT schedule which is associated with poorer outcomes.

Supportive care before, during and after treatment is demanding and must involved the relevant allied health professionals (speech and language therapists and dieticians) if outcomes are to be optimised. Over an above the side effects experienced by patients undergoing radical radiotherapy alone there is an extra burden of more severe and prolonged mucositis, nausea and vomiting, neurological complications (ototoxicity, peripheral neuropathies), renal dysfunction and myleosuppression to name a few. In the study by Denis et al[19] rates of significant mucositis (grade 3 & 4) were nearly double that seen when patients did not receive the chemotherapy (71% vs 39%). The early effects are already well recognised however the long term effects are still to be charted.

Wherever possible the following should be considered prior to commencing treatment.

**Nutritional support** – despite the fact that weight loss prior to diagnosis is rarely a problem in this patient group, consideration should be given to placing a gastrostomy tube prior to commencing treatment. The addition of chemotherapy to radiotherapy is associated with severe mucositis within the irradiated area which will have a significant impact on the patient's nutrition during treatment. Weight loss of over 10% of a patients total body weight is associated with reduced treatment outcomes[33-36]. Whilst receiving treatment it is essential that there is regular dietician assessment to ensure prompt action when oral nutrition becomes a problem and to commence gastrostomy feeding. It is important to counsel the patients on the risk of long term gastrostomy dependence.

**Dental assessment & treatment** – xerostomia is a sequlae of treatment to the oropharynx because of the relative radiosensitivity and position of the major salivary glands to the target region. Often the treatment involves irradiating a proportion of the mandible and the late effects of this combined with xerostomia make patients at increased risk of dental decay and osteoradionecosis. Often patients present with poor dental health and this exacerbates the long term effects. For these reasons it is important to maximise a patient's dental health prior to commencing chemoradiotherapy even if this means dental clearance and a delay in commencing therapy.

**Speech and language assessment –** for education and advice regarding exercises to prevent reduced mouth opening and trismus following treatment. Assessment of swallowing competency may also be relevant in some patients with oropharyngeal malignancies. Following treatment early involvement to maximise rehabilitation is essential.

## Metastatic (stage IVb) disease

Despite being incurable by definition, in select patients chemoradiation can be useful at achieving disease control and significantly improving local regional disease control.

## Conclusion

Chemoradiation (using single agent cisplatin 3 weekly during conventionally fractionated RT) has become the standard of care for patients with locally advanced (stage III & IVa) squamous cell carcinoma of the oropharynx. Its use has been validated with evidence from numerous clinical trials and the benefits in terms of survival and loco

regional control have been subject to a meta-analysis15. Where there have been significant advances in locoregional control the survival benefits achieved have been more modest. The survival benefit seen is primarily due to improved locoregional control rather than a reduction in distant metastases8. The reduction of distant failure and thus potential for better survival currently lies in the remit of using induction chemotherapy alongside chemoradiation. HPV-positive squamous cell carcinoma of the oropharynx is likely to represent a distinct disease entity with improved prognosis. Whether this means that less aggressive treatment without chemotherapy is required remains to be seen and requires evidence from clinical trials.

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# Diagnosis and management of thyroid nodules

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## Introduction

In this article, we shall review the current evidence and guidelines for the diagnosis and management of thyroid nodules in the UK, especially in view of the recent publication of the 2nd edition of the British Thyroid Association guidelines for the management of thyroid cancer[1]. We will also discuss areas of controversy routinely experienced in clinical practice and present evidence-based proposals to address them.

## Aims

1. to understand the epidemiology and natural history of thyroid nodules
2. to present an evidence based strategy for the investigation of thyroid nodules
3. to review the latest guidelines on the management of thyroid nodules

## Epidemiology and Natural History

Palpable nodules occur in 4-7% of the adult population[2]. However with the advent of high definition ultrasound, nodules and nodular thyroids can be detected in up to 50-70% of the adult population[3]. Whilst traditional teaching is that the risk of malignancy in thyroid nodules varies between 10 and 30%[4], this applies to solitary cold nodules and is therefore a selected, high-risk population. It should be noted however, that the overall of risk of malignancy for a thyroid nodule identified on ultrasound is much lower - reported to be between 4 and 7%[5].

## Referral by primary care physicians

The British Thyroid Association[1] has included, in its recent guidelines, a section on the urgency of referral of thyroid lumps by primary care physicians to secondary care. The guidelines suggest that most solitary nodules and goitres should not be referred as an urgent two-week wait referral. Instead, it is recommended that they should be referred through routine mechanisms to a specialist clinic. The guidelines recommend that those patients are seen within 4 weeks (level 4 evidence, grade C recommendation). Indeed, the guidelines suggest that patients with a history of nodule or goitre that has not changed for many years and that have no other worrying features or risk factors ( table 1) should be managed in primary care with no need for referral to secondary care.

*Table 1: High risk factors for thyroid cancer*

| |
|---|
| History of irradiation to the neck |
| Exposure to high environmental radiation |
| Family history of thyroid cancer |
| Child with thyroid lump |
| Thyroid lump with associated stridor, hoarseness, lymphadenopathy or rapid enlargement over weeks |

The British Thyroid Association guidelines recommend urgent two week referral for patients with thyroid lumps who also have hoarseness, cervical lymphadenopathy or rapid enlargement over a period of weeks, or who are children. They also recommend immediate same day referral in patients who have stridor associated with a thyroid lump (grade C recommendation).

## Assessment of the thyroid lump

We recommend the following for the assessment of any thyroid lump

1. **Thyroid function** tests to exclude a thyrotoxic nodule.
2. **Ultrasound of the thyroid and neck.**

High definition ultrasound can provide valuable information regarding the characteristics of the nodule and its potential risk for malignancy, which can help guide clinical decision making. (see table 2). It also can aid the selection of the most suspicious nodule to biopsy in a multi nodular goitre. Furthermore, it is possible to perform serial assessments of growth more accurately when using an ultrasound. Ultrasound guidance of fine needle aspiration or core biopsy can also decrease the rate of inadequate samples[6]. These issues will be discussed below in more detail.

To obtain the full benefit from ultrasonography, it is important that the operator is experienced in thyroid scanning. It is also important that there is an agreement between the radiologists and the clinicians on the characteristics that will be assessed and reported on, so that there is consistency in the techniques and reports. This is

*Table 2: Ultrasound features suggestive of thyroid malignancy - adapted from Ahuja et al [19].*

| Ultrasound feature | Risk of malignancy |
|---|---|
| Coarse calcification | Very low |
| Comet tail sign | Very low |
| Hypoechoic | Moderate |
| Halo absent or indistinct margin | Moderate |
| Intranodular blood flow on colour doppler | Moderate |
| Microcalcification | High |

especially important where the ultrasonography is performed by several radiologists and radiographers. We have agreed with our radiologists that they report on all the characteristics that were present, but also expressly state the characteristics that were not present so that we can assess the adequacy of the ultrasound report.

### 3. Fine Needle Aspiration Cytology (FNAC)

We recommend that FNAC is done under ultrasound guidance for increased accuracy. Thyroid cytology specimens should be reported by an experienced cytopathologist with a special interest in thyroid disease[1]. Aspiration maybe performed by a surgeon, cytopathologist, radiologist or an oncologist. They should be trained and follow good practice and perform sufficient numbers to maintain their expertises[1].

The technique that we follow involves localising the nodule between fingers or using the ultrasound probe, then directing a gauge 25 needle into the solid part of the nodule. Several passes are made whilst rotating the needle between the finger and thumb, and is performed under aseptic technique. Aspiration is only performed if fluid is obtained to remove the cyst contents. In the case of a cyst, once the fluid component is removed, the nodule is re-assessed by palpation or ultrasound, and any residual mass undergoes a second aspiration. Care should be taken to avoid contaminating the samples with the ultrasound gel when using ultrasound guidance.

The sample can then be directly smeared on to glass slides, or emptied into a liquid preservative, eg Cytolyte, if your local laboratory uses liquid based cytology. When lymphoma is suspected, sending a sample in a cell culture medium for flow cytometry may be very helpful in obtaining the diagnosis.

If FNAC diagnosis cannot be not obtained after two biopsies, and it was felt that it would alter management (mainly in the case of a thyroid lymphoma), then a core biopsy with or without ultrasound guidance is recommended[1]. Open biopsies of the thyroid gland should rarely be performed.

### Other investigations for the assessment of a thyroid nodule.

i. MRI or CT scan imaging can be performed for the following indications:
   a) Cervical lymphadenopathy to assess extent and distribution. This is best done using MRI, as non contrast CT scan is not as effective due to the lack of contrast . Iodine-based contrast CT scanning is best avoided in the context of suspicion of thyroid cancer as this can interfere with efficacy of radio iodine ablation post operatively and can therefore delay the institution of this management option.
   b) Fixed thyroid gland clinically to assess fixation and invasion of trachea and other structures.
   c) Suspicion of retrosternal extension to assess extent for surgical planning
   d) In the case of a diagnosis of thyroid cancer, to exclude mediastinal nodal involvement and lung metastases.

ii. Flow volume loop studies.
   These can be performed to assess the extent of airway compression caused by a large compressive goitre. The studies provide an objective measure of the degree of compression which can aid decision making and follow-up. This may be especially useful clinically in moderately sized or large goitres which are only causing the patient minimal compressive symptoms. If the flow volume loop studies show compression, then we recommend surgery.

iii. Thyroid auto-antibodies.
   These should be performed if thyrotoxicosis or hypothyroidism is identified to exclude a diagnosis of autoimmune disease such as Grave's disease.

iv. Radioiodine isotope scan.
   The role of radioisotope scanning is of very limited value in the diagnosis of thyroid cancer[8]. The American Thyroid Association recommends it in the context of follicular cytology for a solitary thyroid nodule on FNAC. They recommend follow-up in this context, as it is very unlikely that the thyrotoxic nodule will be cancerous[7].

v. Serum thyroglobulin and Calcitonin
   Thyroglobulin has no role and should not be performed in the context of diagnosis. There is currently insufficient evidence to recommend routine use of

calcitonin for screening for medullary cancer[7,9,10]. Calcitonin should however be performed if medullary thyroid cancer is diagnosed to aid post-treatment follow-up.

## Controversies surrounding ultrasound FNAC

They are several controversies and myths surrounding the use of ultrasound and FNAC in the work-up of a solitary nodule. It can sometimes result in disagreements between surgeons and radiologists regarding the indication for performing these investigations. We will review some of these below and provide the evidence base for our suggested solutions.

### 1. 'Multi nodular goitres have a low risk of malignancy and therefore do not need FNAC'.

It is often the case that radiology reports will state that there is a multi nodular goitre and therefore no FNAC was performed as they were no solitary nodules. However the evidence in the literature does not support this point of view. June et al[11] reported on 68 consecutive papillary thyroid cancers. 48% were in multi nodular thyroids and 52% were solitary nodules. Papini et al[12] showed that the rate of malignancy for solitary nodules was 9.2% (18 of 195),, whereas the incidence of cancer in multi-nodular thyroids was 6.3% (13 of 207). in the same series This would therefore strongly suggest that the risk of cancer in a multi nodular goitre is very similar to that of a solitary nodule.

We recommend that in a multi-nodular thyroid setting, ultrasound characteristics are used to select the most suspicious nodule (regardless of size) for fine needle aspiration cytology. If there are no suspicious characteristics, then we would suggest that the FNAC is performed on the dominant nodule.

### 2. 'Small nodules do not need FNAC'.

Some suggest that nodules under a certain size (usually 1 or 1.5cm) do not need to undergo biopsy because the risk of malignancy in these nodules is perceived to be very low. However the literature does not support this. Sahin[13] reported on 472 ultrasound guided FNAC biopsies. The risk of malignancy in nodules less than 1cm was 21% (31 out or 145 FNACs) in comparison to the risk of malignancy in nodules over 1cm, which was 17% (55 out of 327 nodules). They also noted that the accuracy of ultrasound FNAC was the same for nodules that were <1cm as those that were more than 1cm in size. Papini12 found that if they selected nodules for FNAC by size criteria alone (over 1cm) they would have detected 61% of the total thyroid cancers identified by US guided FNAC, However, if they selected nodules by ultrasound characteristics alone they would have detected 87% of the cancers identified in their series.

Others feel that investigating nodules that are less than 1cm in size is not necessary due to the perceived low mortality and complication rate from this subgroup of patients. However, the literature reveals that small thyroid cancers can behave aggressively. Nam-Goong et al[14] found that 69% of occult thyroid tumours identified had extra-capsular extension or nodal spread and 89% of them were multi focal. Papini et al[12] found that 35% of incidental tumours (defined as 8-15mm in their study) had extracapsular extension and 19% had nodal involvement. Both these features significantly affect the staging and hence potentially can negatively affect prognosis.

### 3. 'Assessment by interval growth with no FNAC'

In the multinodular setting and for small tumours, some radiologists suggest assessment of interval growth by serial ultrasound instead of FNAC. However Alexander et al[15] found that 90% of benign nodules grew 15% or more in 5 years. Therefore, interval growth on its own cannot confirm or exclude malignancy. An increase may be helpful if there is rapid growth but in that instance, ultrasound serial scanning is not necessary as the growth is usually clinically evident. Indeed, detection may have occurred earlier if an FNAC had been performed at the initial ultrasound.

### 4. No need for serial investigation

Evidence would suggest that serial investigation is very effective and clinically helpful. Oertel et al[16] performed ultrasound FNACs on 7394 patients, 1564 of whom had repeated FNACs. The probability of a benign lump being accurately diagnosed with one benign FNA was 90% of 560 patients. However the probability increased significantly to 98% (124 out of 126) in patients who had two benign FNACs

For a cohort of 235 patients with one benign FNAC result, Chehade et al[17] found that a repeat FNAC decreased the false negative rate from 5.2% to 1.2%. This would result in the detection of 4 additional patients with thyroid cancer for every 100 patients with cancer.

### 5. 'Ultrasound guidance for FNAC is not useful'.

The literature clearly demonstrates that ultrasound guidance decreases the rate of inadequate FNACs[6]. Furthermore, ultrasound guidance increases the accuracy of FNAC from 85% to 95%[18].

*Table 3: Management of thyroid nodules according to cytology results using the Thy classification ( adapted from the British Thyroid Association guidelines*[1]*.*

| Diagnostic Category | Actions |
|---|---|
| THY1 - non diagnostic | FNAC should be repeated with ultrasound guidance. |
| THY1 – cyst | If the aspirate contains colloid and histiocytes only in the absence of epithelial cells, the THY1 category should be clearly identified as cyst. In this case if the cyst as been aspirated completely with no residual mass, a repeat ultrasound alone maybe sufficient, with FNA only if cyst recurs |
| THY2 – non neoplastic | Repeat FNA in 3 – 6 months<br>The recent BTA guidelines suggest that in some cases a reliable benign diagnosis can be achieved with one single aspirate only.<br>Furthermore in high clinical risk patients a decision maybe taken to proceed to lobectomy even with a THY2 diagnosis |
| THY3 (i) - Follicular lesion-suspected follicular neoplasm | Discuss at MDM then proceed to lobectomy |
| THY3 (ii) –There are a small number of other cases where cytological finding are worrying but do not fit in the THY2 or THY4 categories | Discuss at MDM to decide appropriate course of action |
| THY4 - Suspicious but non diagnostic of papillary, medullary, anaplastic carcinoma or lymphoma | Discuss at MDM.<br>Ensure that immuno histochemistry has been performed for medullary carcinoma or flow cytometry for lymphoma.<br>Proceed to surgery if appropriate - lobectomy or total thyroidectomy |
| THY5 – Diagnostic of malignancy | Discuss at MDM – surgical intervention for differentiated thyroid cancer and medullary thyroid cancer as indicated. Other cancers should be treated appropriately. |

**6. 'No need for FNAC if an ultrasound scan is normal'.**

Some radiologists advocate that diagnosis of thyroid cancer can be excluded solely on the basis of ultrasound scan. Papini et al[12] found in a cohort of 402 thyroid nodules, selection by ultrasound characteristics alone identified only 87% of the cancers identified by a combination of ultrasound and FNAC. This confirms the superiority of ultrasound FNAC over ultrasound alone.

## Management of the thyroid lump

The management of the thyroid nodule is currently determined by the FNAC results. There are several different cytological classifications, which can be used to base clinical management on. These cytological classifications categorise the FNAC sample according to the number, morphology and type of cells on examination of the FNAC sample[1].

Table 3 summarises the Thy classification categories and the management as recommended by the British Thyroid Association guidelines (for more details please refer to the BTA guidelines[1]. It should be remembered however that FNAC is a diagnostic tool that is prone to error. Therefore, the clinical and ultrasound features should also be taken into consideration when deciding on further management, as discussed previously.

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# Malignant Tumours of the Submandibular Salivary Gland

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## Abstract
We present an overview of malignant submandibular tumours, which includes incidence, classification, features in the paediatric and adult population, diagnostic tools, treatment principles, treatment outcomes and future directions.

## Key Words
Submandibular gland, Salivary, Neoplasm, Malignant

## Introduction
In the following article we review the recent English language literature (obtained by searches on Medline and a survey of research at the 7th International Conference on Head and Neck Cancer, American Head & Neck Society 2008) of malignant submandibular tumours in order to provide the reader with a general overview.

## Incidence
Salivary gland tumours are relatively rare and account for about 3% of all head and neck cancers. The national cancer database in the United States records that 0.3% to 0.9% of cancers are of salivary gland origin with 10% of these occurring within the submandibular gland (SMG)[1]. According to the national cancer statistics for England, incidence of non-parotid (and unspecified) major salivary gland cancer is 0.4 per 100,000 population (this compares with 1.4/100,000 for parotid cancer). There is equal incidence between males and females. The incidence increases with age, with no recorded cases under the age of 10 years and most cases occurring above 40 years of age[2].

## Classification and Staging
There is a diverse range of salivary tumours which exhibit considerable clinical heterogeneity. The World Health Organization classification of 2005 (see table 1) groups both benign and malignant tumors into epithelial and non-epithelial categories[3].

In general, tumours of the major salivary glands are staged according to size, extraparenchymal extension, lymph node involvement and presence of metastases. Tables 2 and 3 illustrate the American Joint Committee on Cancer staging for major salivary gland cancer[4].

## Clinical Assessment

**Table 1**

| | |
|---|---|
| 5.2.00 | Malignant epithelial tumors |
| 5.2.01 | Acinic cell carcinoma |
| 5.2.02 | Mucoepidermoid carcinoma |
| 5.2.03 | Adenoid cystic carcinoma |
| 5.2.04 | Polymorphous low-grade adenocarcinoma (terminal duct adenocarcinoma) |
| 5.2.05 | Epithelial-myoepithelial carcinoma |
| **5.2.06** | **Clear cell carcinoma** |
| 5.2.07 | Basal cell adenocarcinoma |
| 5.2.08 | Sebaceous carcinoma and sebaceous lymphadenocarcinoma |
| 5.2.09 | Papillary cystadenocarcinoma |
| **5.2.081** | **Low-grade cribriform cystdenocarcinoma** |
| 5.2.09 | Mucinous adenocarcinoma |
| 5.2.10 | Oncocytic carcinoma |
| 5.2.11 | Salivary duct carcinoma |
| 5.2.12 | Adenocarcinoma, not otherwise specified |
| 5.2.13 | Malignant myoepithelioma (myoepithelial carcinoma) |
| 5.2.14 | Carcinoma in pleomorphic adenoma (malignant mixed tumor) |
| 5.2.15 | Squamous cell carcinoma |
| 5.2.16 | Undifferentiated carcinoma |
| 5.2.16.1 | Small cell undifferentiated carcinoma |
| 5.2.16.2 | Large cell undifferentiated carcinoma |
| 5.2.16.3 | Lymphoepithelial carcinoma |
| 5.3.00 | Benign epithelial tumors |
| 5.3.1 | Pleomorphic adenoma |
| 5.3.2 | Myoepithelioma (myoepithelial adenoma) |
| 5.3.3 | Basal cell adenoma |
| 5.3.4 | Warthin tumor (adenolymphoma) |
| 5.3.5 | Oncocytoma (oncocytic adenoma) |
| 5.3.6 | Canalicular adenoma |
| 5.3.7 | Sebaceous adenoma and sebaceous lymphadenoma |
| 5.3.8 | Ductal papilloma |
| 5.3.8.1 | Inverted ductal papilloma |
| 5.3.8.2 | Intraductal papilloma |
| 5.3.8.3 | Sialadenoma papilliferum |
| 5.3.9 | Cystadenoma |
| 5.3.9.1 | Papillary cystadenoma |
| 5.3.9.2 | Mucinous cystadenoma |
| **5.3.10** | **Sialoblastoma** |
| **5.3.11** | **Keratocystoma** |
| **5.3.12** | **Lymphadenoma** |
| 5.4 | Soft tissue |
| 5.5 | Hematopoetic |
| 5.6 | Secondary tumors |
| 5.7 | Salivary cysts |

*Diagnoses in bold represent new additions with respect to the 1992 World Health Organization classification

Most malignant salivary tumours present as a slow-growing painless lump. Pain and rapid growth are suggestive of malignancy. Assessment of the SMG should include bimanual palpation of the gland, looking for involvement of the floor of the mouth and establishing the relationship of the tumour to the mandible. Sensation and mobility of the tongue should be assessed. Although nerve involvement is suggestive of malignancy it is a late sign.

## Paediatric Submandibular Gland Tumours

These present typically as a painless slow growing lump which may be focal or diffuse. Tumours fall into 3 histological groups: benign, low grade or high grade malignant. Malignancy of the SMG is very rare in the paediatric population, but when found usually occurs in older children (over 10 years old) and is usually low grade. Malignant tumours occurring in children under 10 years of age are more likely to be high grade and have a poor prognosis[5,6]. Mucoepidermoid carcinoma (MEC) is the most common malignancy of the SMG in children and accounts for approximately 50% of malignant SMG tumours in this age group[5].

**Table 2**

| T stage | |
|---|---|
| TX | Primary tumour cannot be assessed |
| T0 | No evidence of primary tumour |
| T1 | Tumour 2cm or less in greatest dimension without extraparenchymal extension* |
| T2 | Tumour more than 2cm but not more than 4cm in greatest dimension without extraparenchymal extension |
| T3 | Tumour more than 4cm and/or having extraparenchymal extension* |
| T4a | Tumour invades skin, mandible, ear canal and/or facial nerve |
| T4b | Tumours invades skull base, pterygoid plates and/or encases carotid artery |

*Extraparenchymal extension is clinical or macroscopic evidence of invasion of soft tissues. Microscopic evidence alone does not constitute extraparenchymal extension for classification purposes.

N stage: Nodal stage is as for squamous cell carcinoma of the head and neck.

Bull reports on 10 cases of salivary neoplasia accumulated over a 20 year period (approximate incidence 0.5/million/year). Of these, 3 were arising form the SMG. One of these was malignant (adenoid cystic carcinoma). Because of the rarity of salivary neoplasia in the paediatric population, Bull warns that one should be wary of the risk

**Table 3**

| | |
|---|---|
| Stage I | T1,N0,M0 |
| Stage II | T2,N0,M0 |
| Stage III | T3,N0,M0<br>T1,N1,M0<br>T2,N1,M0<br>T3,N1,M0 |
| Stage IV | T4a,N0,M0<br>T4a,N1,M0<br>T1,N2,M0<br>T2,N2,M0<br>T3,N2,M0<br>T4a,N2,M0 |
| Stage IVb | T4b,AnyN,M0<br>AnyT,M3,M0 |
| Stage IVc | AnyT,AnyN,M1 |

of misdiagnosis[7].

A review of all major salivary gland malignancies in children over a 13-year period, recorded on the Surveillance Epidemiology and End Results (SEER) database (which covers approximately 26% of the population of the USA), found 10 of the 113 cases arose from the SMG. The primary histologies were acinic cell carcinoma (n=3), adenocarcinoma (n=2) and MEC (n=2)[6].

Treatment of salivary carcinoma in children is primarily surgical. There is some debate regarding the value of adjuvant radiotherapy. It has been advocated in some datasets, but not shown any long-benefit in others6. Bull writes that salivary gland disease is less aggressive than in adults and that unless the histology is overtly aggressive, radiotherapy should be avoided in order to prevent complications such as retarding bone growth and radiation induced malignancy[7].

## Imaging

The role of imaging is to define the location of the tumour (intra- vs extra-glandular), to look for radiological features suggestive of benign vs. malignant disease, assess local extension/invasion and detect metastases (both regional and distant)[8].

For lesions in the SMG, ultrasound is an ideal tool for initial assessment. High resolution ultrasound provides excellent tissue characterisation, multiplanar information and vascular pattern (Doppler technique). It can also assess for cervical node involvement and can also be combined with fine needle aspiration cytology (FNAC). However, it's accuracy is dependent on the operator[8]. Ultrasound is able to distinguish benign from malignant tumours in 80% of cases[9].

If malignancy is confirmed on cytology or there is high clinical suspicion for malignancy, then further imaging should be performed. MRI is superior to CT in soft tissue differentiation and is especially useful in detecting deep tissue extension, marrow infiltration and perineural spread. Because of this, the role of CT in evaluation of salivary gland tumours is limited. However, compared with CT, MRI is more costly, more susceptible to motion artefact and has poorer cortical bone delineation.

The disadvantage of CT is the artefact created by dental restorations. When bone involvement is a concern, CT may be required. Both MRI and CT can assess similar features such as enhancement pattern, ill-defined edge, extraglandular extension and presence of adjacent involved lymph nodes[8]. In addition CT scanning of the chest is recommended in patients with malignant tumours to exclude lung metastases.

## Fine Needle Aspiration Cytology (FNAC)

This is a useful, cheap and relatively simple outpatient investigation that is used routinely by the senior author. However there are limitations and results of FNAC must always be used in conjunction with clinical findings and other investigative findings. Due to the diverse histological types of salivary tumours, an experienced histopathologist is essential to ensure accurate and appropriate reporting of results. The procedure is safe with no evidence of seeding if a needle smaller than 20G is used[10].

The accuracy of FNAC is dependent on the cytologist and type and quality of the sample. Reported sensitivity and specificity is 88-93% and 75-99% respectively[8]. There are significant false-negative rates (i.e. malignant tumours in which cytological diagnosis was benign or insufficient). Thus, diagnosis with FNAC can only be made when the cytologic findings fit the clinical picture.

FNAC is particularly useful to confirm the benign nature of a tumour (when the probability of malignancy is low) and to exclude lymphoma, inflammation and secondary malignancies. However there are limitations of FNA for example cystic lesions may collapse after FNAC which may make subsequent surgery and diagnosis more difficult; the FNA may miss the carcinomatous part of carcinoma ex-pleomorphic adenomas; differentiating between certain histological types can be difficult (e.g. basaloid neoplasms and basal cell carcinomas, adenoid cystic carcinoma and pleomorphic adenoma).

Data on FNAC in children is sparse. Several small series report similar sensitivity and specificity to adults[11]. Obviously, in order to carry out this investigation, the patient should be able to tolerate it, so clinical judgement will determine which children are suitable.

## Pathology

As mentioned there are many types of malignant tumours that can occur within the submandibular salivary gland and it is beyond the scope of this article to discuss all of the types in detail. Of all submandibular tumours approximately one third will be malignant. Wahlberg reported 403 patients with malignant submandibular tumours, details of which were obtained from the Swedish Cancer registry which showed adenoid cystic carcinoma to be the most common type (45%), followed by MEC (16.5%), adenocarcinoma (13%), carcinoma ex-pleomorphic adenoma (11.5%), undifferentiated carcinoma (10%) and acinic cell carcinoma (4%)12. Andreu et al from Toronto in Canada reported 68 cases in which

**Table 4**

| Stage of disease | | Tumour grade |
|---|---|---|
| **Treatment** | | |
| Stage 1 | Low grade | Surgery alone |
| | High grade | Surgery +/- adjuvant radiotherapy |
| Stage II - IV | Low grade | Surgery +/- adjuvant radiotherapy |
| | High grade | Surgery + adjuvant |

**Table 5**

| | |
|---|---|
| **Indications for adjuvant radiotherapy to primary site** | High grade tumours |
| | Locally advanced tumours |
| **Indications for adjuvant radiotherapy to neck** | Recurrent disease |
| | Residual neck disease |
| | Extra-capsular spread |
| **Indications for definitive radiotherapy** | Patient unfit for surgery |
| | Recurrent disease |
| | Unresectable disease |

mucoepidermoid carcinoma was the most common (23%)[1].

In the U.K. adenoid cystic carcinoma (ACC) is the most common malignant salivary tumour affecting the SMG. It is a slow growing and aggressive tumour with a propensity for perineural invasion. Three growth patterns have been described: cribriform, tubular and solid. The latter is associated with worse prognosis due to advanced stage and distant metastases. Mucoepidermoid carcinomas are classed as low, intermediate or high grade. The low grade tumours are cystic with an orderly production of mucus, intermediate tumours are mostly solid and high grade are solid tumours with a poor prognosis. Adenocarcinomas are tumours of glandular or ductal differentiation and are classed as low, intermediate or high grade depending on the cytomorphic features.

## Treatment options (Table 4)

### Surgery

#### (i) Primary tumour

Surgery is the main treatment modality but the extent of excision remains a controversy. In principle wide local excision should be considered as recurrence rates are higher in incompletely excised tumours. Since most malignant SMG tumours are confined to the gland, resection of the SMG and surrounding lymphatics is the treatment of choice. All nerves are preserved unless they are involved with tumour. Extended resection is required for tumours with extraglandular extension and this may include resection of involved skin, muscles and nerves. Rarely, if tumour is adherent to the mandible, the periosteum may need to be stripped or segmental mandibulectomy performed if there is bony involvement. In cases of incomplete excision or of close margins of the resected specimen further surgery to ensure clearance of tumour should be considered.

#### (ii) Role of Neck Dissection

There is some debate as to whether or not elective neck dissection should be carried in cases where there is a clinically negative neck. Most agree that supraomohyoid neck dissection is helpful to in assessing the first echelon lymph nodes (levels I-III) in cases where there is high risk of metastasis (in locally advanced and high-grade tumours). In cases of small, low grade tumours (such as acinic cell tumours) neck dissection may not be necessary. For palpable or radiologically evident disease a modified radical neck dissection should be performed.

## Role of radiotherapy (RT) (see table 5)

#### (i) Post-operative Radiotherapy

Adjuvant RT following surgery is recommended for all malignant tumours except in cases of low grade tumours that have been completely excised.[13] Indications for post-operative RT include high grade tumours, close or incomplete resection margins, advanced tumours (T3, T4), bone involvement and recurrent cancer. The total radiation dose may be adjusted according to resection margin status. Greater control has generally been seen with doses >60 Gy, for incomplete resection >65 Gy and for gross residual disease >70Gy is recommended[14]. Sparing of critical normal tissues (e.g. spinal cord, healthy salivary glands) is best achieved using intensity modulated radiotherapy (IMRT). However this is not widely available in the U.K. and it is an expensive, time consuming process requiring complex fields and treatment algorithms. The loco regional control rate for SMG tumours is significantly increased by post-operative radiotherapy. In patients with high risk features (perineural or vascular spread, positive margins, extra glandular spread, positive lymph nodes, locally recurrent disease and high grade tumours), there is an 88% 10 year loco regional control vs. 50% for those treated by surgery alone.[15] Thus RT to the neck is recommended in high grade tumours, positive neck

nodes (multiple or extra capsular spread) and tumours with poor prognostic features[13].

**(ii) Primary RT**

Treatment by surgery is the mainstay of treatment with post operative RT if necessary. Primary RT is indicated in cases where the tumour is deemed unresectable or in patients who are unfit or unwilling to have surgery[14]. Surgery and postoperative RT has been shown to have better results than primary RT in adenoid cystic carcinoma[16].

Because of the slow regression rate after radiotherapy, salivary gland cancer is a favourable target for neutron therapy which allows high energy deposits more rapidly than conventional RT with a higher dose delivery. Neutron radiotherapy (as compared with conventional photon or electron therapy) has been shown to improve locoregional control in patients with inoperable or recurrent disease[17]. It is not available in many centres due to cost and limited evidence for its efficacy as side effects are greater than with conventional RT with late toxicity being a significant problem[14].

## Treatment of recurrent disease

In cases of recurrent disease a full clinical assessment with CT/MRI imaging and review of the original pathology is essential[13]. If gross disease is present then wide surgical resection followed by radiotherapy (either external beam or brachytherapy) is recommended. If recurrence is deemed unresectable, high dose irradiation is recommended. As most patients will have been irradiated as part of treatment of the tumour initially, re-irradiation should be discussed with the radiation oncologist.

## Treatment outcomes

Long term survival is poor in many cases. Factors influencing survival can be seen in table 6.

In their review of 62 patients with SMG carcinomas (19 adenoid cystic carcinoma, 11 MEC, 10 salivary duct carcinoma and 8 carcinoma ex-pleomorphic adenoma), Roh et al reported 5-year loco regional control of approx 70% and survival of 57%. All patients had wide excision of the SMG and 40 patients also underwent neck dissection with 41 patients undergoing post-operative radiotherapy. Multivariate analysis showed that tumour stage and resection margin remained significant prognostic factors for loco regional control[15].

Sykes et al reported on 30 patients who had surgery and adjuvant radiotherapy for malignant SMG tumours. Most patients had early stage (stage I/II) disease and the most frequent histological type was ACC (63%). Local control was 85% and cancer specific survival 79% at five years. At

**Table 6**

| Factors influencing survival |
|---|
| stage |
| histological grade |
| perineural invasion |
| vascular invasion |
| extraglandular spread |
| lymph node status |
| excision margins |
| age |

**Table 7**

| Pathway/receptor | Description |
|---|---|
| KIT | KIT, a transmembrane glycoprotein which is a member of the tyrosine kinase receptor family. KIT activation leads to a signal cascade that contributes to cell growth and differentiation. It has been found to be expressed in adenoid cystic carcinoma |
| EGFR | EGFR, epidermal growth factor receptor, is often overexpressed in adenoid cystic carcinoma and mucoepidermoid carcinoma. |
| ErbB2 (HER2-neu) | ErbB2 (also known as HER-2/neu) is a receptor with great similarity to EGFR. It has been found to be over-expressed in mucoepidermoid carcinoma, salivary duct cancers, adenocarcinoma and to a variable extent in adenoid cystic carcinoma. |
| NF-kB | NF-kB is a protein which promotes tumour growth and spread. It is expressed in some adenoid cystic carcinoma. |
| VEGF | Vascular endothelial growth factor (VEGF) plays a central role in angiogenesis and tumour growth and metastasis. Expressed in majority of malignant SMG tumours. |
| Oestrogen and Progesterone | Receptors for these hormones have been found to a varying degree in adenoid cystic carcinoma. A partial response of parotid ACC has been reported with tamoxifen |

ten years the figures were 73% and 57% respectively (the continuing decline is attributed to late relapse in patients with adenoid cystic carcinoma)[18].

Wahlberg et al analysed survival in patients reported to the Swedish cancer registry for 1960 to 1995 in which 403 patients had malignant SMG tumours. Early-stage, low grade tumours were treated by surgery alone, whereas more advanced, higher grade tumours were treated with surgery and adjuvant radiotherapy. Radiotherapy alone was used for unresectable disease or where the patient was unfit for surgery. At 10 years, survival for ACC, carcinoma ex-pleomorphic adenoma and MEC were 73, 62 and 53 per cent respectively. MEC had a significantly worse prognosis than ACC of the SMG and a worse prognosis compared with parotid MEC[12].

## Follow-Up

Patients should be reviewed regularly following treatment. Follow-up should be every month for the first year, every two months for year 2, every 3 months for year 3, every 4 months year 4 and every 6-12 months thereafter. The frequency of follow up will vary between centres but in principle long term follow up is to be recommended, as recurrence of disease can occur after many years.

## Future directions

In a review of chemotherapy and molecular therapies for use in ACC, Dodd et al conclude that response rates to chemotherapy are varied, inconsistent and generally poor and the duration of response to combination chemotherapy is short, lasting only months. In addition, the effectiveness of various molecular targets have been disappointing. They conclude that at present there is little evidence that systemic therapy for adenoid cystic carcinoma alters its course[19].

Several agents (mostly growth factors or hormone receptors) are currently being tested that target molecular signalling and cancer cell biology. These pathways are illustrated in table 7. In the future there may be a role for these agents as biological markers of prognosis and also as an aid to guide treatment, including treatment of locally advanced, recurrent or metastatic disease. However more research is needed as most of the reported trials in the literature are of a small sample size reflecting the fact that these are uncommon tumours.

## Conclusion

Malignant tumours of the submandibular gland are rare. The histological types can vary greatly as can clinical behaviour. Most present as painless masses usually in older adults, the diagnosis usually being confirmed by a combination of cytology, imaging or histology. Multimodality treatment (surgery and radiotherapy) is required for best locoregional control. It is for this reason that management should be performed by an experienced multidisciplinary team. Late relapse may occur especially with adenoid cystic carcinoma; so long term follow up is necessary. Research into molecular targets is ongoing but as yet has not produced a clinically useful therapy.

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# Papillary Thyroid Carcinoma: Surgical Decisions

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## Introduction

In the United Kingdom, just over 2500 patients are diagnosed with thyroid cancer a year. Of these over 80% are differentiated thyroid cancers and over 90% of these will be papillary thyroid carcinomas (PTC)[1-2]. Risk factors associated with its development include previous radiation exposure and a positive family history of medullary thyroid carcinoma or multiple endocrine neoplasia[1-2]. Over 60% of thyroid carcinomas present as a solitary thyroid nodule. However they can present as a dominant nodule in a long-standing multinodular goitre, as diffuse thyroid masses, as a lateral cervical mass or develop within a thyroglossal duct cyst[1-3].

The investigation of thyroid nodules and masses is now well established and has been well addressed in several national and international consensus guidance documents[4-6]. These should include thyroid function tests, FNAC with or without ultrasound scanning (USS), and thyroid scintigraphy in selected cases as initial investigations. Computerized Axial Tomography (CT), Magnetic Resonance Imaging scanning (MRI) and Positron Emission Tomography scanning (PET) are usually reserved as staging investigations or to assess the anatomy of large and complex thyroid masses with our without cervical lymphadenopathies[4-8].

The current investigation protocols have minimized the need to perform unnecessary surgery especially in individuals with solitary thyroid masses. These also allow adequate planning in patients requiring oncological surgery.

The treatment of PTC should include a total thyroidectomy with level VI selective neck dissection in the majority of diagnosed patients. This is usually followed by radioiodine ablation and TSH suppression and post-operative adjuvant external beam radiotherapy in selected cases of locally invasive PTC. Only a small group of patients may benefit of less than a total thyroidectomy and these include low risk patients ñ female gender under 45 years of age ñ and low risk tumours ñ T1 unifocal lesions.

National Institute of Clinical Excellence guidance issued by the DOH have also ensured that all patients with cancer in the UK and PTC is no exception, should be treated in a multidisciplinary team setting. All management decisions should be discussed prior to the treatment of these patients. The decisions are adequately recorded and the patient informed about the outcome so they can made an informed decision regarding their planned treatment.

However and despite improvements in the pre-operative assessment of patients with suspected of PTC and the prior decision made in the MDM, the individual surgeon dealing with PTC is usually faced with a number of intra-operative decisions that adequate investigations and planning may have failed to address.

The aim of this review is to discuss the surgical management and a number of surgical decisions that may have a bearing on the outcome for these patients that the surgeon can be faced during surgery for PTC.

## Key Words
Papillary Thyroid carcinoma, epidemiology, presentation, management.

## Epidemiology and clinical presentation of PTC.
Papillary thyroid carcinoma accounts for over 80% of thyroid malignaces. They have a distinct propensity for multifocal involvement and regional lymph node metastasis but they have an overall excellent prognosis although up to 15% of PTC may display an aggressive behaviour.

Over 60% of PTC present as solitary thyroid nodules (STN), 10% as multinodular goitres (MNG), 10% as a lateral cervical lymphadenopathies in the absence of a palpable thyroid nodules and 10% as distant metastatic disease. A thyroid mass presenting in association with dysphonia due to vocal cord paralysis, dysphagia, airway obstruction, family history of thyroid cancer, multiple endocrine neoplasias or previous exposure to irradiation should be treated as suspicious of malignancy until otherwise proven.

## Investigations.
Patients should be investigated with a thyroid function tests, thyroid autoantibodies levels together with the USS guided FNAC. Additionally, patient may be advised to have a thyroid isotope scan when indicated. This scan is sometimes helpful in patients with suppressed TSH suggesting hyperthyroidism or MNG with dominant nodules[4,7,8].

For investigation of STN or dominant nodules within a MNG, USS with FNAC is the investigation of choice. USS gives excellent characterisation of thyroid nodules. Features suggestive of malignancy are hypoechogenicity, irregular margins, absence of through transmission, microcalcification and size of greater than 3cm. Current guidelines recommend FNAC of all solitary or dominant thyroid lesions. If thyroid cancer is diagnosed, staging of local disease should be with MR or non-contrasted CT, the former being more sensitive (Figure 1). The iodinated intravenous contrast media used in CT scanning is taken up by thyroid tissue and blocks uptake of radio-active iodine for 3-6 months. It should therefore be avoided in patients with thyroid cancer[7-8].

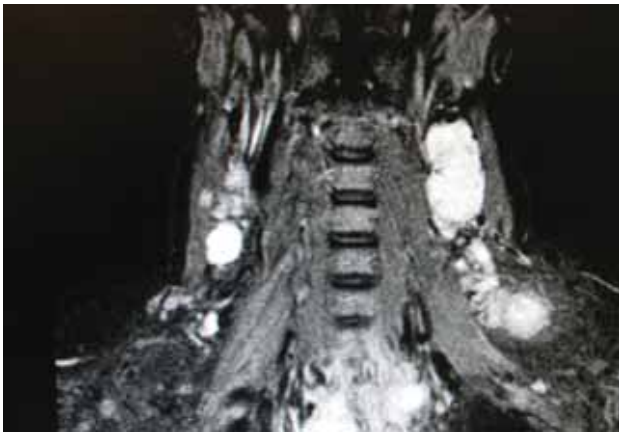

**Figure 1.** *MRI scanning of a patient with a T4N1bMx PTC with bilateral metastatic lymphadenopathy.*

When assessing cervical lymph nodes in suspected thyroid cancer, the whole neck is examined in a systematic way. The following characteristics are looked at:

1. Shape, normal nodes have an elliptical configuration, whereas metastatic nodes often become round.

2. Size. when assessing size the short axis, ie the shortest measurement possible is taken this is a much more reliable indicator of pathology than the long axis. The upper limit of normal in the neck is 10 mm although the average size of lymph nodes does vary from region to region within the neck.
3. The echo-texture of the node, this is the brightness of the node and the evenness of its appearance, if the lymph becomes dark it suggests necrosis and malignant transformation should be considered.
4. The vascularity can be assessed by using colour flow Doppler. In pathological nodes the vascular supply is much enhanced and multiple peripheral vessels become prominent.
5. Echogenic hilum the central part of the node may have a bright appearance this is known as echogenic hilum. It is present in only 50% of normal nodes but when present is a good sign of benignity as it indicates that there is no disruption to the internal architecture of the node. If the node appears abnormal a FNAC is performed[8].

The results of the FNAC should be reported according to British Thyroid Association (BTA) guidelines and the current categorization with indicated management is shown in Table 1.

**Table 1. BTA FNAC diagnostic categories and management action required.**

| | |
|---|---|
| Thy 1: Non-diagnostic | Action: Repeat FNAC under USS guidance |
| Thy 2: Non-neoplastic | Action: Two diagnostic benign results are required 3 to 6 months apart to exclude neoplasia |
| Thy 3: Follicular lesion | Action: Diagnostic lobectomy |
| Thy 4: Suspicious of malignancy | Action: Diagnostic lobectomy |
| Thy 5: Diagnostic of malignancy | Action: Total thyroidectomy |

The history, clinical and all relevant investigations findings should be discussed at the MDT meeting where a decisions should be made as to the best optimal management for an individual patient[4].

## Pre-operative considerations

Pre-operative planning is essential in order to minimize inadequate intra-operative decisions. These include:

1. All patients should be discussed at MDM and the decision recorded accordingly.
2. All patients should be euthyroid.
3. Assessment of the vocal cord function should had been done and documented
4. Evidence of FNAC and adequate imaging including USS, CT and MRI should be available in the operating theatre.
5. The patient should be adequately consented and any potential intra-operative events addressed.
6. The patient should have general anaesthesia with endotracheal tube which should be positioned over the head of the patient so it does not interfere with the surgical field.
7. Local anaesthetic is advisable pre-operatively as it will help haemostasis whilst raising the flaps and to aid analgesia in the post-operative period.
8. Nerve monitor should be available in theatre whenever possible
9. Surgical aids such as loops, microscope, fine bipolar forceps, ligaclips and harmonic knifes are very useful and should be available and encouraged.
10. Mild hypotensive anaesthesia should be used.
11. Other surgical teams such as plastic surgery or thoracic surgery should be available in appropriate cases.

## Surgical principles for the treatment of PTC.

1. Surgery is the mainstay of thyroid cancer treatment and total thyroidectomy or near-total thyroidectomy should be performed in the majority of patients. Subtotal thyroidectomy is usually a substandard operation and should not be performed whenever possible[4,9,10,11].
2. In all cases of proven PTC, a level VI selective or central compartment neck dissection should be performed[4,9,10,11].
3. Adequate incision and approach should be employed
4. Careful tissue handling is paramount as the thyroid gland is one of the most vascular glands in the body and the presence of thyroid cancer enhances its vascularity.
5. The recurrent and superior laryngeal nerves should always be identified and preserved.
6. Parathyroid glands should be identified and preserved whenever possible. If however a parathyroid gland is removed during surgery or its blood supply is lost, frozen section to confirm the nature of the tissue should be performed and if proven, it should be re-implanted in a pocket made in the sternocleidomastoid muscle[12].

## Intra-operative Management of PTC.

The mainstay of the treatment of PTC is adequate surgery. Adequate surgery means the complete removal of any thyroid tissue and any involved either microscopic or macroscopic metastatic lymphadenopathy.

## Extent of the surgery.

The extent of the surgery has been and still is a subject of controversy. However all consensus documents advise that all patients with PTC should be offered a total thyroidectomy with central compartment neck dissection (Level VI) except those low risk patients e.g. female patients under the age of 45 years with T1 tumours which don't appear to be multicentric at initial lobectomy. If the tumour is found to be multicentric then a completion thyroidectomy should be recommended[1,2,4,9,10].

## Total thyroidectomy for PTCa.

Complete surgery is the mainstay of the treatment of PTCa and leaving large tissue remnants will lead to poor local control, multiple radioiodine treatments, risk or recurrence and poor disease specific survival. Therefore attention to detail is necessary to ensure that all macroscopic glandular tissue is excised. Common pitfalls include leaving the pyramidal lobe and thyroglossal tract, inadequate management superior and inferior pole and Berry's ligament1[4,9-10].

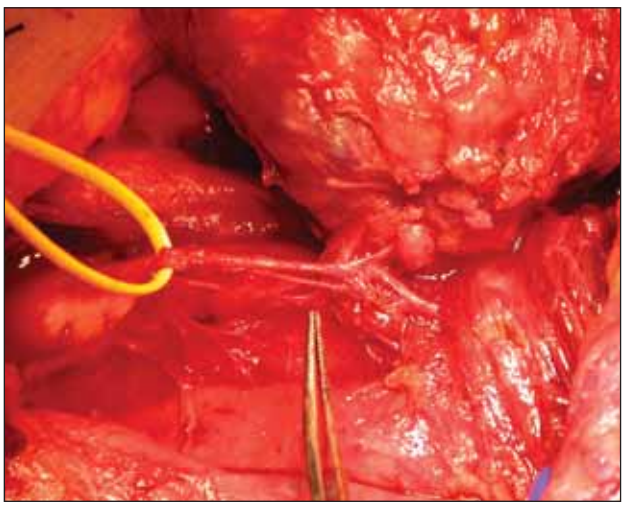

**Figure 2.** *Intra-operative photograph of left RLN at Berry's ligament with disease at the cricothyroid junction.*

Pyramidal lobe and thyroglossal tract. It is imperative that the pyramidal lobe and any obvious thyroglossal tract is identified, dissected and excised. This is accomplished by raising the subplatysmal flaps up to the level of the hyoid bone so adequate exposure can be achieved[3].

Identification and division of the vascular pedicles. This is an essential but often undervalued step of the surgical procedure. Individual vessels should be carefully dissected, identified, ligated and divided. This is best done with a curved dissector such a Lahey or a Mixter dissector. This will allow adequate haemostasis reducing the risk of post-operative haemorrhage, will reduce the risk of injury to the superior laryngeal and will reduce the risk of leaving large glandular remnants that invariably exists between the vessels[2,13].

Berry's ligament. The dissection of the Berry's ligament is one of the most delicate aspects of the thyroidectomy for PTCa. The RLN is adjacent to the ligament, and its relationship is variable. The RLN can run lateral, through or medial to the ligament. The terminal branches of the ITA run across the ligament and there is often glandular tissue in it. Therefore it is imperative to try to dissect the ligament from the nerve without leaving any glandular tissue that may contain carcinoma and this is particularly difficult if there is gross disease. In the dissection of the Berry's ligament (Fig 2), the use of magnifying loops and nerve stimulator or monitor are invaluable[2,13].

Superior Laryngeal Nerve (SLN). The external branch of the superior laryngeal nerve should be identified whenever possible. This is done at the sternothyrolaryngeal or Joll's triangle which is delimited by the superior thyroid pedicle and upper lobe of the gland, the cricothyroid muscle and the lower edge of the thyroid cartilage[2,13].

Recurrent Laryngeal Nerve (RLN). The nerve should always be identified and this is done in the Bearh's triangle in the lower part of neck. This triangle is defined by the inferior thyroid artery superiorly, the trachea medially and the common carotid artery laterally. In the opinion of the authors, this is the safest way of identifying the RLN. Once the nerve is identified this should be dissected in cranial direction tunnelling the tissue sorrounding the nerve with a mosquito fine-tip dissector. The tissue above the tunnel is judiciously diathermized with bipolar diathermy, and divided. However, if there is gross tumour in the central or inferior aspect of the lobe the Beahr's triangle may be difficult to be exposed. In this situations, the nerve can be identified at the level of the cricothyroid junction at its entry in the larynx and then followed in a caudal direction instead[2,13].

Parathyroid glands. The parathyroid glands should be identified whenever possible. The position of the glands can be variable and in 25% of necks they may not be in the position that there expected to be. This can be particularly difficult if there is gross tumour, extracapsular extension or large volume metastatic lymphadenopaties at level VI. Once the thyroid gland has been mobilized medially, the superior parathyroid gland should fall in a posterior position from the nerve and the inferior parathyroid gland in an anterior one. Once identified the tissue handling needs to be very precise and delicate so the gland can be dissected with its own blood supply. If this is not possible, a frozen section should be performed when treating patients with thyroid cancer. If parathyroid tissue confirmed then implantation of the glands should be performed in a pocket made in the sternocleidomastoid muscle[2,12-13].

## Management of the Neck

The management of the neck is essential in the management of PTC. As up to 60% of these cases may have either macroscopic or microscopic deposits in the draining lymph nodes. The dissection of the central compartment or level VI should be part of the procedure of total thyroidectomy for proven PTCa. If there are proven macroscopic lymphadenopathy in the lateral compartment of the neck, a lateral neck dissection should be performed. This has lead to the concept of 'wide-field total thyroidectomy', which consists in a complete total thyroidectomy in continuity with a level VI selective neck dissection and when necessary either a unilateral or bilateral selective, modified radical or radical neck

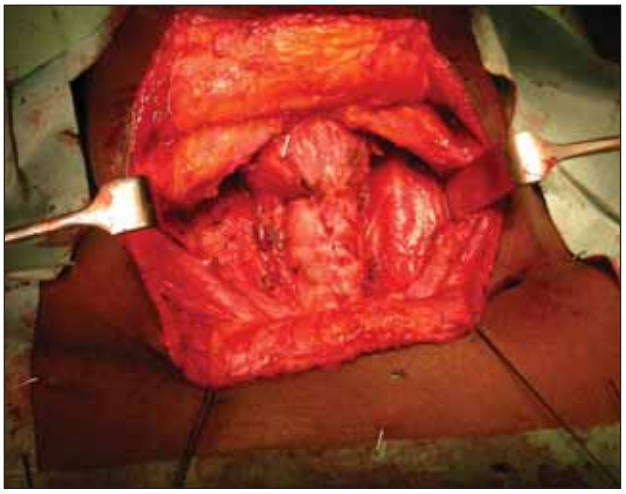

**Figure 3.** *Surgical field after a 'wide-field total thyroidectomy' demonstrating intact RLN and superior*

dissection[1,14-16] (Figure 3).

## Management of the N0 neck.

In patients with N0 necks, level VI should always dissected and levels II, III, Vb, and VII palpated at the time of surgery. Any suspicious nodes should be biopsied and sent to frozen section analysis. Positive metastatic disease will obviate the need for a selective neck dissection of levels II, III, IV and VII. Controversy exists on what should be done when a diagnostic lobectomy is performed for a follicular thyroid neoplasm (THY III). In this situation it is recomende that, the ipsilateral level VI should be explored and any suspicious lymphadenopathies excised for histological evaluation[1,14,15].

Management of the N+ neck. Clinically palpable or radiological evident metastatic lymph nodes indicates the need for a selective neck dissection. The extent of the neck dissection will be determined by the levels involved but should include at least levels II, III, IV and Vb. Level I involvement is rare and should only it be dissected if there is disease present or there is gross involvement of level II adjacent or above the digastric muscle. The same principle applies for level Va. In cases where there is radiological involvement of any of the non-lymphatic structures or any of these appear to be involved intra-operatively, then a modified radical, radical or an extended radical neck dissection if there is gross level VII metastatic disease may be necessary[1,10,14,15].

## Locally invasive PTC

Locally invasive thyroid carcinoma account for up to 15% of PTC. Adequate imaging investigations including CT and MRI scanning should assess the potential site and extent invasion of the surrounding anatomical structures of the thyroid gland. However, there will be occasions were even high resolution imaging techniques will not demonstrate invasion and therefore the surgeon will be forced to make challenging intra-operative decisions. It is generally accepted that leaving microscopic disease should not influence the outcome providing that adequate adjuvant therapy with radioiodine ablation and post-operative radiotherapy[4,17,18].

Strap muscle invasion. Direct tumour invasion to the strap muscles is the most common form of extra-thyroidal extension due to its close relationship with the gland but it is usually not considered an adverse prognostic factor. This is usually dealt with the resection of the involved muscle which is left over the affected thyroid lobe to obtain an adequate surgical margin[4,17,18].

Recurrent laryngeal nerve invasion. The management of the involved RLN still generates considerable controversy. Invasion of the nerve can arise from direct tumour extension or extracapsular spread of the involved paratracheal lymph nodes. It is generally agreed that if the RLN is paralized pre-operatively, the nerve should be sacrificed. However if the nerve is functioning but involved, the decision to sacrifice is very difficult. In this situation, the extent of the involvement should be taken in consideration. If there is gross involvement of the nerve then it is possibly justified to resect the nerve, however if there is only minimal invasion then preserving the nerve an leaving microscopic disease on the nerve sheath it would be advisible. This is justified by the fact that leaving a microscopic remnant does not affect prognosis if adequate adjuvant treatment is used[4,17,18].

Laryngeal invasion. The mechanism of laryngeal invasion can occur through the thyroid lamina, the cricoid cartilage or the cricothyroid ligament. Controversy exist regarding the extent of the resection and as to whether to perform a shave excision versus a complete resection. Shaving is generally acceptable if there is cartilage invasion but no involvment of the inner perichondrium or intraluminal invasion. However local resection in form of partial or total laryngectomy may be necessary[4,17,18].

Tracheal invasion. Tracheal invasion is more common than laryngeal invasion due to the position of the thyroid gland. Invasion of the trachea usually results as a consequence of direct extension either anteriorly or posterolaterally. The same controversy exists with tracheal invasion as there is with laryngeal involvement, and therefore the same principles should be applied. If there is tracheal ring cartilage invasion but no involvment of the inner perichondrium or intraluminal invasion shaving should be adequate however if the latter occurs, local excision should be considered[4,17,18].

## Pharyngeal and oesophageal invasion

Invasion of the oesophagous and pharynx is usually confined to the muscularis layer. The extension into the mucosa and submucosa is rare as the muscularis layer is thick and therefore resistant to direct invasion. If the muscularis layer is involved then resection of the segment is advisable to obtain a negative margin. Care should be taken not to tear the mucosa and if this occurs adequate repair should be undertaken. However if there is intraluminal invasion by PTC, then an adequate resection should be undertaken. The extend of the resection will depend of the extend of the disease and requires an experienced surgical team familiar with laryngo-pharyngo oncological resections and adequate reconstruction techniques[4,17,18].

## Conclusions

Surgical management of PTC is still controversial. Adequate pre-operative investigations and discussion of patients in the thyroid oncology MDT planning meeting can help to identify high-risk patients and aid surgical management. However, surgical decisions still need to be made and these are particularly difficult and challenging in locally advance disease or with gross lymph node metastatic disease.

Surgery is the mainstay of thyroid cancer treatment and total thyroidectomy or near-total thyroidectomy should be performed in the majority of patients. Subtotal thyroidectomy is usually a substandard operation and should not be performed whenever possible. In all cases of proven PTC, a level VI selective or central compartment neck dissection should be performed. Wide-field total thyroidectomy, consisting in a complete total thyroidectomy in continuity with a level VI selective neck dissection and when necessary either a unilateral or bilateral selective, modified radical or radical neck dissection is the treatment of choice in locally advanced disease with proven metastatic lymphadenopathies. Locally advanced PTC, requires the complete resection of macroscopic disease, however leaving microscopic disease in selected cases may help to preserve functioning structures and does not affect survival if adequate adjuvant treatments are used.

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# Current Options In The Management Of Early Primary Laryngeal Cancers

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## Introduction

Strictly speaking, early primary laryngeal cancer is defined as an invasive carcinoma confined to the lamina propria, not invading the adjacent muscles and cartilages[1]. However, in the literature the term is generally used for Tis, T1, T2 lesions as one group. Most authors tend to make a distinction between Tis, T1 and T2 so as to better compare local control rates and voice outcomes between different studies. Because of the early occurrence of symptoms such as hoarseness and the paucity of lymphatic drainage, glottic cancers in an early stage are highly curable indifferent of the chosen treatment. Supraglottic and subglottic cancers can spread more easily and give rise to a higher incidence of cervical metastases. Especially subglottic tumours, which fortunately are seldom, can reach an advanced stage before they are detected and therefore need more extensive treatment. In general there are three options to treat early laryngeal cancer, namely endoscopic excision, external beam radiotherapy (EBRT) and external surgery. We agree with recent guidelines[2] that, regardless of the chosen treatment option, all patients with T1 or T2 larynx cancer should be treated, at least initially, with intent to preserve the larynx.

## Endoscopic surgery

Endoscopic microsurgical resection can be done using cold instruments, but is nowadays more and more often performed with the use of the carbon dioxide laser. Since its first description by Strong it has gained widely spread acceptance in the treatment of early glottic cancer[3]. An adequate exposure is a prerequisite for successful surgery and therefore patient selection and the right instruments are essential. Endoscopic resection has several advantages; a low morbidity, namely less need for tracheotomy and nasogastric feeding and less complications. It can also be easily repeated and if local recurrence occurs, more re-treatment options are available as compared to initial radiotherapy or open surgery. Some authors advise a "wait and see" policy with close follow-up of patients with positive or suspicious margins as an alternative to further routine treatment because they saw a low rate of recurrences[4,5]. There is however a general tendency, which we agree with to perform a second resection in case of positive margins and when frozen section is used, this can be done during the same anaesthesia.

Many authors reported very good results with regard to oncological and functional outcomes; however there was a lack of uniformity between the classifications of cordectomies regarding the extent of resection among the various authors. Therefore the European Laryngological Society (ELS) proposed a new classification of endoscopic cordectomies which comprised six different types[6,7]. In most of the recent publications this ELS classification is used[4,5,8-12]. For Tis and T1a lesions, performing an excision biopsy by cordectomy type I and II can be considered a first line treatment with "en bloc" removal of the lesion8. For more advanced tumours, some authors recommend the piecemeal technique rather than "en bloc" resection because they feel in that way they can more precisely evaluate the deep extension of the tumour[13-16].

In **figure 1** the ELS classification of endoscopic cordectomies is shown.

Concerning the endoscopic supraglottic laryngectomies, the ELS just recently also proposed a new classification which has been submitted for publication. This is shown in **figure 2**.

Subglottic extension up to one centimetre under the glottis can be treated endoscopically if adequate exposure is possible and if the surgeon has the required experience. Otherwise, subglottic cancers are best treated by an external approach, with or without post-operative EBRT, and treatment of the neck.

A new development in the endoscopic approach is the transoral robotic surgery (TORS) for laryngeal cancers. Weinstein successfully used the da Vinci Surgical Robot to perform a supraglottic partial laryngectomy in 3 human patients with supraglottic carcinoma[17]. Adequate exposure is paramount. Although further development of TORS is required, it may evolve into a generally accepted treatment

**Figure: 1** *European Laryngological Society (ELS) classification of endoscopic cordectomies*

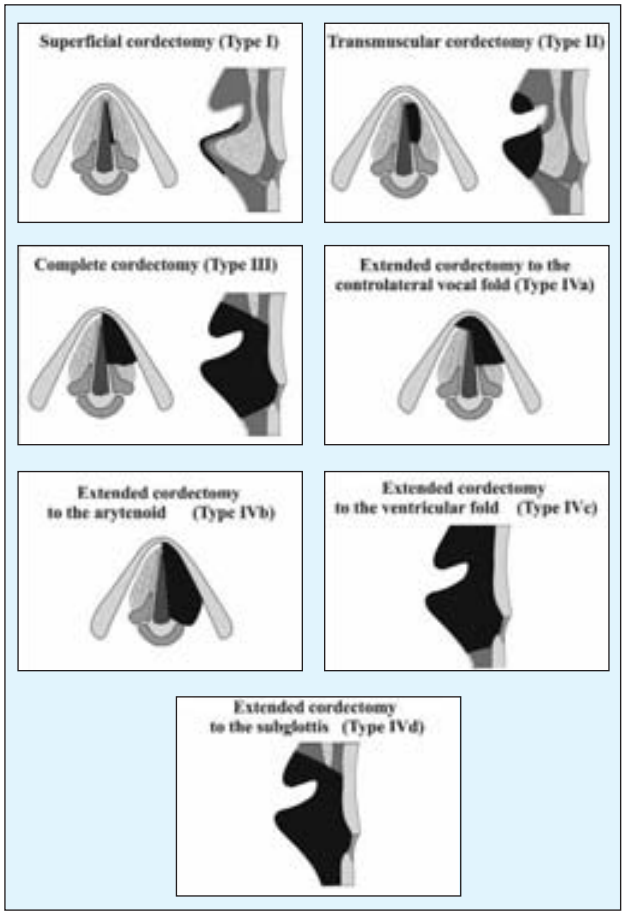
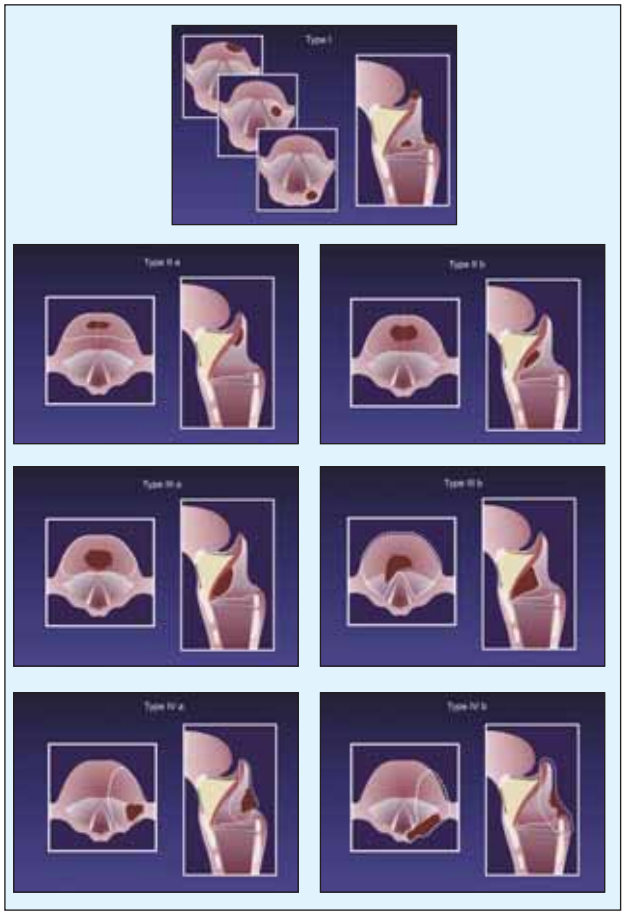



**Figure 2:** *European Laryngological Society (ELS) classification of endoscopic supraglottic laryngectomies.*



option for early laryngeal cancers.

## External "open" surgery

Cordectomy, median thyrotomy or laryngofissure is indicated for a tumour strictly limited to the vocal fold without deep infiltration and is nowadays reserved for those cases where endoscopic exposition is impossible. Frontolateral laryngectomy is performed in cases of tumours of the entire vocal fold reaching up to the anterior commisure but no further.

Hemilaryngectomy is indicated for cancer of the mobile vocal cord reaching the vocal process without invading the arytenoid cartilage. Frontal anterior laryngectomy with epiglottoplasty or Tucker intervention for glottic cancers which extend to both vocal folds and limited paraglottic extension.

Supracricoid laryngectomy with cricoidopexy is indicated for tumours of the ventricle, of the ventricular fold with glottic extension or anterior commisure cancers with risk of extension to the lower part. Supracricoid laryngectomy with crico-hyoido-epiglottopexy is indicated for glottic cancers with immobile vocal fold but mobile arytenoids, bilateral glottic cancer, glottic cancer with superficial extension to the anterior commisure or bottom of the ventricle.

Supraglottic horizontal laryngectomy is indicated for tumours of the ventricular folds with invasion of the epiglottis or in tumours on the laryngeal side of the epiglottis. In cases of subglottic cancer or extension of more than one centimetre below the vocal cords, total laryngectomy with thyroidectomy and treatment of the neck with post-operative EBRT is usually recommended[18].

## External beam radiotherapy

Small glottic cancers, due to the paucity of lymphatic drainage, are usually irradiated using two equally weighted parallel-opposed fields. The dose delivered to the primary tumour varies between 60 and 70 Gy depending on the clinical stage for a classic fractionation and varies between 70 and 80 Gy in case of multi- fractioning. A commonly used dose-fractionation schedule is 66 Gy for T1 lesions and

70 Gy for T2 cancers given in 2-Gy fractions19. The EBRT is spread over a period of six to eight weeks. In case of supraglottic extension, the cervical adenopathies in level II, III and IV of the neck have to be included. When there is subglottic extension, region II, III, IV and VI need to be irradiated together with the larynx. For the neck it ranges from a prophylactic dose of about 50 Gy, if there are no clinical lymph nodes, up to 60-70 Gy for the regions with positive lymph nodes. Concerning supraglottic larynx carcinoma, radiation dose is similar to those for glottic tumours, but due to a richer lymphatic drainage, it is recommended that all patients with supraglottic cancer should have elective neck treatment of level II, III and IV. For the clinically N0 neck, selective neck dissection or radiotherapy is recommended. In case of positive cervical nodes a neck dissection with or without post-operative radiotherapy is advised. The addition of a neck dissection usually increases the risk of temporary lymphedema and surgery specific morbidity; however, it is preferable in terms of tumour control and complications to the higher doses of irradiation required to control large neck nodes[20].

There appears to be a significant dose-response curve for EBRT in T1 glottic cancer where there is a significantly lower probability of local tumour control at total doses below 61 to 65 Gy[21-23]. A shorter duration of EBRT and increasing the dose administered per fraction may also improve outcome[22].

Intensity modulated radiation therapy (IMRT) is not routinely indicated for early laryngeal cancers, especially early glottic cancers. This due to the fact that its advantages, especially salivary gland sparing with less xerostomia, play no major role since the fields used in conventional techniques are usually small and the salivary glands do not receive a clinically significant dose[24].

## Chemotherapy

Both induction and concomitant chemotherapy have been investigated in clinical trials, but are generally not regarded as a standard treatment for early laryngeal cancer.

## Discussion

Given the fundamental role that the larynx plays in human speech and communication, determining the optimal management of laryngeal cancer must consider both survival and the functional consequences of the chosen treatment approach. Although different options for voice rehabilitation exist, many patients express dissatisfaction with the results, and social isolation, job loss, and depression are common sequelae[25]. As a result, much effort has focused on larynx-sparing approaches such as radiation therapy, alone or in combination with chemotherapy, and function-preserving partial laryngectomy procedures. In 2006 the American Society of Clinical oncology published treatment guidelines in which they recommend that all patients with T1 or T2 laryngeal cancer should be treated, at least initially, with intent to preserve the larynx2.

The oncologic outcome of surgery, endoscopic or external, versus radiotherapy is equal[8,13,14,26-32]. The most recent published studies of endoscopic resection of Tis and T1 lesions shows definite local control rates between 83 and 100% and laryngeal preservation rates between 90 and 100%[8,13-16,26-30,33,34]. Concerning T2 lesions, in a review of the most recent literature, definite local control rates vary between 84 and 91% and laryngeal preservation rates of approximately 90 %8,[13-16,27]. Results after external beam therapy show local control rates around 90% for T1 lesions and 70 to 80% for T2 lesions[19,21,28,30]. In a recent article patients undergoing laser or conventional surgery for a T1a carcinoma were found to have a significantly lower incidence of locoregional recurrences and longer disease-free intervals when compared to those treated by radiotherapy[30].

Anterior commisure involvement was sometimes considered as a contraindication for endoscopic surgery. Some authors found a lower control rate (79 vs. 96%) and larynx preservation rate (96 vs. 100%) in cases with anterior commissure involvement[35]. Several authors however observed that anterior commissural involvement does not negatively influence oncological outcomes after endoscopic resection[36]. For the majority of authors, tumoral infiltration of the thyroid cartilage is a contraindication to endoscopic approach. In this case an open neck partial laryngectomy can be indicated.

Tumours of the base of the epiglottis can easily spread to the pre-epiglottic space and consequently be more difficult to control. In a recent review article of salvage conservation laryngeal surgery for recurrent early glottic cancer after irradiation failure, the reported local control rates using the external or the endoscopic laser approach were 77% and 65% respectively[37]. So the authors concluded that local control could be achieved with laryngeal preservation, and total laryngectomy may be held in reserve as the ultimate option for salvage without compromising ultimate survival significantly.

In patients with early supraglottic cancer, laser microsurgery is comparable to open supraglottic laryngectomy in terms of local control and survival. With regard to organ preservation, laser microsurgery is equal to open supraglottic laryngectomy but superior to radiotherapy[38]. A recent study of T1 and T2 supraglottic

cancer showed that endoscopic resection coupled with neck dissection achieved good oncological results[39]. In another multi-institutional retrospective study it was shown that supracricoid partial laryngectomy as a treatment for selected recurrences after radiotherapy failure, resulted in a good local control and functional recovery despite a non negligible complication rate[40]. It goes without saying that no matter what treatment is chosen, a meticulous follow-up is necessary in order to recognize recurrences as soon as possible.

Functional outcomes and quality of life after endoscopic surgery and radiotherapy are comparable and excellent[31-33,41,42]. They are generally superior to open surgery. Voice quality worsens after laser cordectomy, but improves in a majority of patients with almost 50% of patients having a subjective normal or near normal voice, and depends on type of cordectomy[43]. This is especially true for subepithelial and subligamental cordectomies which have no significant difference in voice quality compared to controls[39]. However, phonatory outcome may be unsatisfactory and require additional phonosurgery in some patients[44].

Another important aspect is the cost of the treatment which varies between different countries and can vary for the different treatment options. Most studies conclude that endoscopic surgery is the cheapest option, followed by radiotherapy and the most expensive is open surgery[32,33,41,45].

The duration of treatment is six to seven weeks for radiotherapy, one to three weeks for open surgery and one to a few days for endoscopic surgery. One needs to consider these factors when choosing the optimal treatment for the patient. Finally the chosen treatment will also depend upon the acquired experience and availability of the different treatment options in the different centres.

## Conclusion

Globally the comparison of oncologic outcome of surgery, endoscopic or external, versus radiotherapy is equal. Functional outcomes and quality of life after endoscopic surgery and radiotherapy are comparable and are superior to open surgery. Another important aspect is the cost and the duration of the treatment. The choice of treatment should also depend on the age, general health, profession and, last but not least, the wish of the patient. If all this factors are kept in mind, Tis and T1a lesions, especially those of the midcord, could preferably be treated by the endoscopic approach whereas T1b and T2 lesions can be equally well treated by all different options and choice of treatment should depend upon multiple factors as discussed before. In the near future there is a need for randomised controlled trials comparing the different treatment options, preferably in a multicenter setting.

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# The Use of Prostheses in Head & Neck Oncological Surgery

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## Abstract

After ablative surgery for head and neck cancers there remains the challenge of reconstructing the defect in a cosmetically and functionally acceptable way for each patient. Prostheses have been used for a long time for these purposes. The use of prosthesis retained by osseo-integrated titanium screws has changed the application of prosthesis in head and neck surgery. In this review we discuss the application of these prostheses, a case study, salient issues in the surgery of inserting fixtures and quality issues.

## Key words

Osseo integration; Facial prosthesis; Head & Neck cancer

## Introduction

Prostheses are at the top of the reconstruction ladder to reconstruct defects after ablative surgery for cancer as well as reconstruction of congenital defects and following trauma. Reconstruction serves to achieve objectives such as cosmesis, restoration of speech, swallowing, sensation, oral continence, airway protection and facial expression as these may be sacrificed while trying to achieve total tumour clearance. Prostheses have traditionally been secured by various adhesives. The use of adhesives was difficult in hot and humid conditions, as well as in patients with oily skin, excessive hair and allergies. These drawbacks have largely been overcome with the advent of osseointegration. Osseo integration is a direct structural and functional connection between ordered, living bone and the surface of a load-carrying implant. In 1975 Branemark, using this concept considered that maintaing a permanent percutaneous implant may be possible1. In 1977 the first implants were installed in the temporal bone for connecting a percutaneous abutment to a bone anchored hearing aid and in 1979 the first implants were placed in the mastoid region to retain an auricular prosthesis.

The reconstruction ladder represents an algorithm of reconstruction possibilities. As a general rule the less complex and safest options are at the bottom of the ladder and the first to be employed. Osseointegration and autogenous reconstruction need not be seen as competing reconstructive options but as complimentary. There are indications and contraindications for each option which the reconstructive team carefully considers with each patient before concluding on either option.The use of prosthesis secured by osseointegrated screws have the advantage of being less expensive than several operative procedures and allows periodic evaluation of the surgical site. The anaplantologist also has complete control over the colour, shape and position of the prosthesis. The drawbacks of prosthesis secured by osseointegrated screws include irritationof the tissue site, the need for periodic remakes of the prosthesis and the reliance on osseointegration which

can fail. Implants may not necessarily be appropriate for every patients and factors such as age , personal hygiene, manual dexterity and compliance need to be considered.

Prostheses can be used in the reconstrution of the ear following ablative surgery for neoplastic disease or after a congenitally malformed ear has been excised. They may also be used in reconstruction after a rhinectomy, orbital exenteration of vaarious degrees of maxillofacial resections. They are also used extensively in dental rehabilitation, bone anchored hearing aids and in orthopaedic surgery. Osseointegrated implants have been used to retain a hairpiece where significant areas of hair loss have occured[2].

## Case study

A 79 year old retired miner developed a swelling around his left eye. This was followed by pain in the eye. On further questioning he admitted to a left sided nasal obstruction and streaking of blood for 12 months. A computerised tomography scan suggested the presence of an extensive tumour arising from the left ethmoid sinus air cells and extending into the orbit. There were no distant metastases. He subsequently underwent an exenteration of the left orbit via a left lateral rhinotomy with excision of the frontal/ethmoid tumour. The tumour was peeled off the frontal dura and there was concern about a cerebrospinal leak which was repaired. Four titanum screws were inserted at the time of the primary surgery at 2, 3, 4 & 5 O'clock. A split thickness skin graft from the thigh was laid and supported with a proflavin dressing (Fig 1).

Histology revealed a moderately differentiated transitional cell carcinoma with squamous differentiation. He then had 60Gy (in 30 fractions) which commenced 9 weeks after his ablative procedure. Five months after completing radiotherapy, the titanium screw caps were removed and replaced with abutments (Fig 2).

**Figure 1:** *Orbital defect with split thickness skin graft*

**Figure 2:** *Orbital defect with implanted titanium screws and prosthesis.*

The soft tissue around the titanium screw at 5 o'clock was also refashioned. His eye prostheses was eventually fitted (Fig 3).

He unfortunately died four years later of pulmonary disease unrelated to his primary tumour.

### Technique

The use of prostheses in head and neck oncological surgery requires an multidisciplinary approach involving the ablative surgeon (otolaryngologists or maxillofacial), plastic surgeons and prosthetists. Planning involves a stepwise multifactorial process and needs to tailored to each individual patient. Treatment specific charting, preoperative photographs, pretreatment moulages, psychological profiling, planning implant positions and available bone volume assessments where indicated are all prerequisites to surgery. Preoperative education, counselling and procedure specific consent is also essential. Skin assessment of the potential implant site is also required. Where there are concerns about the bone volume, CT scans and radiographic templates can be used to assess this. The overall general condition of the patient should be assessed to exclude systemic disease that can affect wound healing. Adequate tumour resection should not be compromised for reconstructive procedures.

**Figure 3:** *Orbital prosthesis in place*

Details of the surgical procedure is beyond the scope of this review but is well described in the literature[3]. The original technique is a two stage procedure is with three to four months between the stages. A one stage approach has been adopted for the mastoid bone for bone anchored hearing aids and ear prostheses but the two stage procedure continues to be the standard in paediatric patients, irradiated patients and in the midfacial and orbital regions. This is due to either a thin or poor quality bone cortex. The use of hyperbaric oxygen and delayed implant placement have been advocated to promote optimal osseointegration in irradiated patients[4].

Several principles are important with regards surgery for osseointegration. Periosteal reflection should be minimised as much as possible as the bone into which the inserts are fixed depend on the periosteum for their blood supply. Neither the surface of the titanum implants or the titanum instruments used for insertion should be compromised. The bone drills must be sharp and used with adequate irrgation to prevent heat necrosis of the bone. Implants should be placed at least 5mm apart to avoid problems with hygenic care. Electrocoagulation should as much as possible be avoided or when used should be sparingly used bipolar diathermy. The skin around the implant must be thinned to reduce relative motion between the skin and the percutaneous abutment.

Particularly in facial prosthesis, bone volume availability may be a limiting factor in the insertion of osseointegrated implants. The options in these circumstances include expansion of bone volume with the use of membranes and guided tissue regeneration[5]. The availabilty of bone itself after mandibular resections may also limit the use of osseointegrated prosthesis. The increasing use of the fibula osseocutaneous free flap provides implanted bone for osseointegration[6].

The number of titanium screws inserted depends on where they will be inserted (orbital rim, mastoid bone, temporal bone and zybomatic buttress). Usually this is between two and four screws. Sleeper implants may sometimes be inserted in complex situations where they act as reserves in the event of failure of osseointegration of the original implants. Implants used are either screw-shaped, cylindrical or plate like.

## Safety & Quality

As seen from above the insertion of each titanum screw is a meticulous process. Assessing the patients should ideally involve monitoring each screw. Westin et al[7] have described a meticulous process of collecting data on each titanum screw in patients with auricular prosthesis. This included allocating each screw to a specific position using a co-ordinate system. The co-ordinates are made in a clockwise fashion with the centre in the ear canal. The sector for each postion is given by the direction and distance from the ear canal. For each fixture a registration form was designed to record observations during surgery and post operative condition of healing and the surrounding skin. For each follow up visit there are also codes for findings and action taken to be filled in for each fixture. Abutment related complications can be monitored relative to the position of individual fixtures. These include cleaning difficulties, loss of tightening, loss due to trauma, red and moist tissue and grannulation tissue. Skin recations that the required nursing care were also found and carefully cared for.

In the same study a cohort of patients having recieved bone anchored auricular prostheses were asked about their experience of the system using a specially designed questionnaire. It was found that a mojority of patients wore their prosthesis in excess of fourteen hours a day. When asked specific questions about the system (i.e. osseointegration), their views reflected the high regard it has among clinicians and patients of the system (Figure 4).

Ninety nine patients were asked on various safety and quality aspects of their osseoingration system for the retention of their prosthetic ears[7]. Specifically they were asked about how they found it to handle the system?, was it comfortable?, did it affect their self-confidence?, what did they feel about the method?, what were the views of others?, what did they think about the aesthetics? and finally what were their experience on the stability of the system? The questions are given along the x-axis of the graph. The numbers of patients are on the y-axis and the answer alternatives along the y-axis. Except for one single patient marked in red the majority of patients show great satisfaction with the system. In fact a common comment was that “it feels as if the prosthetic ear is a part of myself”.

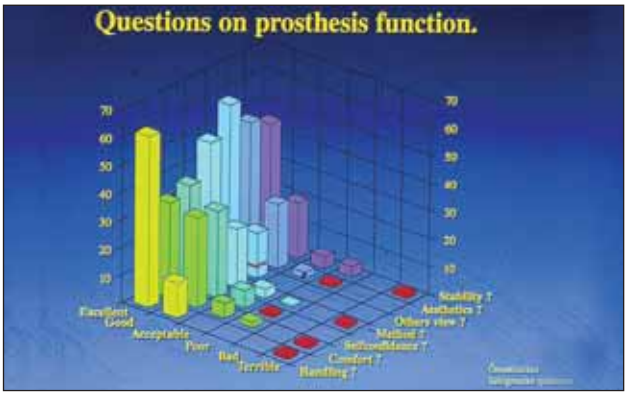


**Figure 4:** *Shows responses given by patients on prosthesis function*

## Conclusion

Osseointegration is a useful reconstructive tool not only in head and neck oncology but in hearing and dental rehabilitation. It has provided a secure method of retaining facial prostheses. The surgical procedure requires careful thought, planning and proper counselling. Safety and quality issues should always be considered to improve patient satisfaction.

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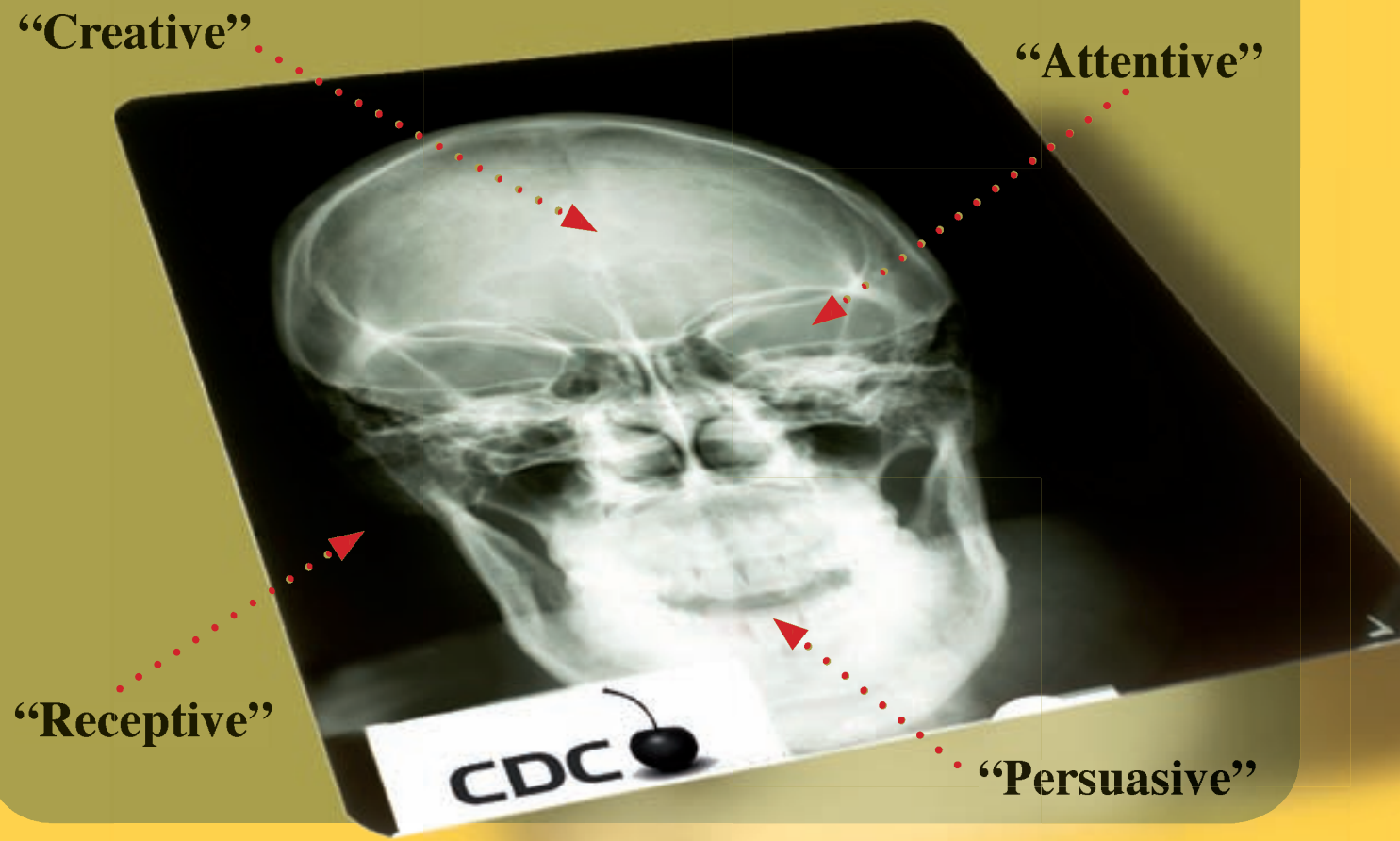


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